



Clinical trial results:

A Long-term, Open-Label Extension Study of Tofacitinib (CP-690,550) for the Treatment of Psoriatic Arthritis

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2011-002169-39 |
| Trial protocol | BE HU CZ BG SK PL ES DE |
| Global end of trial date | 20 May 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 22 May 2020 |
| First version publication date | 22 May 2020 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | A3921092 |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, 10017 |
| 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 | 20 May 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 20 May 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long term safety and tolerability of treatment with tofacitinib (5 mg twice daily [BID] and 10 mg BID) in adult subjects with active Psoriatic Arthritis (PsA) and to evaluate the long term efficacy of treatment with tofacitinib (5 mg BID and 10 mg BID) in adult subjects with active Psoriatic Arthritis (PsA)

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 | 17 February 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Belgium: 17 |
| Country: Number of subjects enrolled | Brazil: 7 |
| Country: Number of subjects enrolled | Bulgaria: 22 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Czech Republic: 18 |
| Country: Number of subjects enrolled | Germany: 36 |
| Country: Number of subjects enrolled | Hungary: 27 |
| Country: Number of subjects enrolled | Mexico: 56 |
| Country: Number of subjects enrolled | Poland: 196 |
| Country: Number of subjects enrolled | Russian Federation: 63 |
| Country: Number of subjects enrolled | Slovakia: 12 |
| Country: Number of subjects enrolled | Spain: 31 |
| Country: Number of subjects enrolled | Taiwan: 13 |
| Country: Number of subjects enrolled | United Kingdom: 31 |
| Country: Number of subjects enrolled | United States: 133 |
| Country: Number of subjects enrolled | Australia: 22 |
| Worldwide total number of subjects | 686 |
| EEA total number of subjects | 390 |

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) | 625 |
| From 65 to 84 years | 61 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Eligible subjects (who had previously participated in randomized PsA clinical studies with tofacitinib) from qualifying studies A3921091 (NCT01877668) and A3921125 (NCT01882439) were enrolled into this current study A3921092 (NCT01976364).

Pre-assignment

Screening details:

This main study was a long-term extension study, which also included a sub-study only for the purpose of efficacy, safety and tolerability of tofacitinib monotherapy as compared to tofacitinib combination therapy with methotrexate. Sub-study included eligible subjects from main study who consented to take part in sub-study.

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Main Study (36 Months) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|-----------|-------------|
| Arm title | Tofacitinib |
|-----------|-------------|

Arm description:

Subjects with active psoriatic arthritis (PsA) received tofacitinib 5 milligram (mg) oral tablet, twice daily (BID) with or without allowed concomitant disease-modifying anti-rheumatic drugs (DMARDs) examples as methotrexate, leflunomide or sulfasalazine, as background therapy, for up to 36 months. Tofacitinib dose was increased to 10 mg BID or decreased back to 5 mg BID per investigator's discretion.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tofacitinib 5 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tofacitinib 5 mg oral tablet, BID for 36 months.

| | |
|--|-------------------|
| Investigational medicinal product name | Tofacitinib 10 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two tablets of Tofacitinib 5 mg orally, BID for 36 months.

| Number of subjects in period 1 | Tofacitinib |
|--------------------------------|-------------|
| Started | 686 |
| Completed | 465 |
| Not completed | 221 |
| Adverse event, serious fatal | 5 |
| Consent withdrawn by subject | 69 |

| | |
|------------------------------------|----|
| Adverse event, non-fatal | 63 |
| Withdrawn due to pregnancy | 5 |
| No longer met eligibility criteria | 2 |
| Medication error | 1 |
| Unspecified | 13 |
| Lost to follow-up | 10 |
| Lack of efficacy | 40 |
| Protocol deviation | 13 |

Period 2

| | |
|------------------------------|---|
| Period 2 title | Sub-study (12 Months) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Tofacitinib 5 mg BID + Methotrexate (MTX) |

Arm description:

Subjects from main study received tofacitinib 5 mg oral tablet BID along with MTX capsules orally (dose range from 7.5 to 20 mg per week) for up to 12 months.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tofacitinib 5 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tofacitinib 5 mg oral tablet BID for up to 12 months.

| | |
|--|--------------------|
| Investigational medicinal product name | Methotrexate (MTX) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

MTX capsules orally (dose range from 7.5 mg to 20 mg per week), for up to 12 months.

| | |
|------------------|--------------------------------|
| Arm title | Tofacitinib 5 mg BID + Placebo |
|------------------|--------------------------------|

Arm description:

Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules for up to 12 months.

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

| | |
|---|------------------|
| Investigational medicinal product name | Tofacitinib 5 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Tofacitinib 5 mg oral tablet BID for up to 12 months. | |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| MTX matched placebo capsules orally weekly for up to 12 months. | |

| Number of subjects in period 2^[1] | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo |
|---|--|---------------------------------------|
| Started | 89 | 90 |
| Completed | 83 | 85 |
| Not completed | 6 | 5 |
| Consent withdrawn by subject | - | 1 |
| Adverse event, non-fatal | 4 | 3 |
| Lost to follow-up | 1 | - |
| Protocol deviation | 1 | 1 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects from main study who consented to take part in sub-study, continued into sub-study.

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------------|
| Reporting group title | Main Study (36 Months) |
|-----------------------|------------------------|

Reporting group description: -

| Reporting group values | Main Study (36 Months) | Total | |
|--|------------------------|-------|--|
| Number of subjects | 686 | 686 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 625 | 625 | |
| From 65-84 years | 61 | 61 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 48.8 | | |
| standard deviation | ± 11.8 | - | |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 370 | 370 | |
| Male | 316 | 316 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 21 | 21 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 2 | 2 | |
| White | 646 | 646 | |
| More than one race | 17 | 17 | |
| Unknown or Not Reported | 0 | 0 | |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Tofacitinib |
| Reporting group description: Subjects with active psoriatic arthritis (PsA) received tofacitinib 5 milligram (mg) oral tablet, twice daily (BID) with or without allowed concomitant disease-modifying anti-rheumatic drugs (DMARDs) examples as methotrexate, leflunomide or sulfasalazine, as background therapy, for up to 36 months. Tofacitinib dose was increased to 10 mg BID or decreased back to 5 mg BID per investigator's discretion. | |
| Reporting group title | Tofacitinib 5 mg BID + Methotrexate (MTX) |
| Reporting group description: Subjects from main study received tofacitinib 5 mg oral tablet BID along with MTX capsules orally (dose range from 7.5 to 20 mg per week) for up to 12 months. | |
| Reporting group title | Tofacitinib 5 mg BID + Placebo |
| Reporting group description: Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules for up to 12 months. | |
| Subject analysis set title | All Subjects |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Main Study: Subjects with active psoriatic arthritis (PsA) received tofacitinib 5 milligram (mg) oral tablet, twice daily (BID) with or without allowed concomitant disease-modifying anti-rheumatic drugs (DMARDs) examples as methotrexate, leflunomide or sulfasalazine, as background therapy, for up to 36 months. Tofacitinib dose was increased to 10 mg BID or decreased back to 5 mg BID per investigator's discretion. Sub-study: Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX capsules orally (dose range from 7.5 to 20 mg per week) or tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules, for up to 12 months. | |

Primary: Percentage of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

| | |
|---|--|
| End point title | Percentage of Subjects With Treatment-Emergent Adverse Events (AEs) 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 48 months that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and non-serious AEs. SAS included all subjects enrolled in this study who were part of a prior qualifying study, and who received at least one dose of open-label study medication in A3921092. Safety analysis included cumulative data for main and sub-study as pre-specified in protocol. | |
| End point type | Primary |
| End point timeframe: Date of first dose of study medication up to 48 months (36 months of main study and 12 months of sub-study) | |
| 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 | All Subjects | | | |
|-------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 686 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| AEs | 83.7 | | | |
| SAEs | 16.8 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Adverse Events (AEs) by Severity

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|-----------------|---|
| End point title | Number of Adverse Events (AEs) by Severity ^[2] |
|-----------------|---|

End point description:

An AE was any untoward medical occurrence attributed to study drug in a subject who received study drug. AEs were classified into 3 categories according to their severity as mild AEs (did not interfere with subject's usual function), moderate AEs (interfered to some extent with subject's usual function) and severe AEs (interfered significantly with subject's usual function). SAS included all subjects enrolled in this study who were part of a prior qualifying study, and who received at least one dose of open-label study medication in A3921092. Safety analysis included cumulative data for main and sub-study as pre-specified in protocol.

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

End point timeframe:

Date of first dose of study medication up to 48 months (36 months of main study and 12 months of sub-study)

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 | All Subjects | | | |
|------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 686 | | | |
| Units: adverse events | | | | |
| Number of adverse events: Mild | 1632 | | | |
| Number of adverse events: Moderate | 1045 | | | |
| Number of adverse events: Severe | 136 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Clinical Laboratory Values

| | |
|-----------------|--|
| End point title | Number of Subjects With Abnormal Clinical Laboratory Values ^[3] |
|-----------------|--|

End point description:

Laboratory tests: hematology (Hb, hematocrit, RBC count, platelets, reticulocytes, WBC count, count and absolute lymphocytes, neutrophils, basophils, eosinophils, monocytes. Liver function (bilirubin [total, direct, indirect], AST, ALT, alkaline phosphatase, gamma-glutamyl transferase, albumin, total protein),

renal function (blood urea nitrogen, creatinine), Lipids (cholesterol, HDL, LDL, triglyceride, apolipoprotein [A-1, B]), electrolytes (sodium, potassium, chloride, calcium, bicarbonate), chemistry (glucose, HbA1c, creatinine kinase), urinalysis dipstick(urine pH, glucose, ketones, protein, blood, leukocyte, esterase), urinalysis microscopy (urine- RBC, WBC, bacteria, epithelial cells), C-reactive protein. Laboratory abnormality: determined by investigator per pre-defined criteria. SAS was analyzed. Safety analysis included cumulative data for main and sub-study as pre-specified in protocol. Number of Subjects Analyzed= Subjects evaluable for this endpoint.

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

End point timeframe:

Date of first dose of study medication up to 48 months (36 months of main study and 12 months of sub-study)

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 | All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 683 | | | |
| Units: subjects | | | | |
| number (not applicable) | 646 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change from Baseline in Clinical Laboratory Values

| | |
|-----------------|--|
| End point title | Number of Subjects With Clinically Significant Change from Baseline in Clinical Laboratory Values ^[4] |
|-----------------|--|

End point description:

Laboratory tests: hematology (Hb, hematocrit, RBC count, platelets, reticulocytes, WBC count, count and absolute lymphocytes, neutrophils, basophils, eosinophils, monocytes. Liver function (bilirubin[total,direct,indirect], AST, ALT, alkaline phosphatase, gamma-glutamyl transferase, albumin, total protein), renal function (blood urea nitrogen, creatinine), Lipids(cholesterol, HDL, LDL, triglyceride, apolipoprotein [A-1, B]), electrolytes (sodium, potassium, chloride, calcium, bicarbonate), chemistry (glucose, HbA1c, creatinine kinase), urinalysis dipstick(urine-pH, glucose, ketones, protein, blood, leukocyte, esterase), urinalysis microscopy(urine- RBC, WBC, bacteria, epithelial cells), C-reactive protein. Clinically significant change: determined by investigator per pre-defined criteria. SAS was analyzed. Safety analysis included cumulative data for main and sub-study as pre-specified in protocol.

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

End point timeframe:

Date of first dose of study medication up to 48 months (36 months of main study and 12 months of sub-study)

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 | All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 686 | | | |
| Units: Subjects | | | | |
| number (not applicable) | 9 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Sub-study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Month 6

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Month 6 |
|-----------------|---|

End point description:

HAQ-DI assessed the degree of difficulty a subject had experienced during the past week in 8 domains of daily living activities: dressing/grooming, arising, eating, walking, reach, grip, hygiene, and other activities. There were total of 2-3 items distributed in each of these 8 domains. Each item was scored for level of difficulty on a 4-point scale from 0 to 3: 0= no difficulty; 1= some difficulty; 2= much difficulty; 3= unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible HAQ-DI score ranged from 0 (least difficulty) to 3 (extreme difficulty), where higher score indicated more difficulty while performing daily living activities. Full analysis set (FAS) of sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Month 6

| | | | | |
|-------------------------------------|---|--------------------------------|--|--|
| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | 0.0174 (\pm 0.02775) | 0.0428 (\pm 0.02714) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Analysis was based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
|-------------------|--|

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Least Square (LS) Mean difference |
| Point estimate | 0.0255 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0513 |
| upper limit | 0.1022 |

Primary: Sub-study: Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) at Month 6

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) at Month 6 |
|-----------------|---|

End point description:

PASDAS was composite PsA disease activity score that included following components: Physician and patient global assessment of disease activity (assessed on a 0-100 VAS) in millimeter (mm), swollen (66 joints) and tender joint counts (68 joints), Leeds enthesitis index (enthesitis assessed at 6 sites; total score of 0-6), tender dactylitic digit score (scored on a scale of 0-3, where 0= no tenderness and 3= extreme tenderness), short form-36 questionnaire (SF-36) physical component summary (norm-based domain scores were used in analyses; with a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity) and C-reactive protein (CRP) in milligram per liter (mg/L). PASDAS was composite score and was a weighted index with score range of 0 to 10, where higher score indicated more severe disease. FAS of main study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Month 6

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | 0.138 (± 0.0805) | 0.229 (± 0.0786) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|----------------------------|--|

Statistical analysis description:

Results are based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
|-------------------|--|

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.091 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.131 |
| upper limit | 0.313 |

Secondary: Main Study: Percentage of Subjects Achieving an American College of Rheumatology 20 Percent (%) (ACR20) Response

| | |
|-----------------|--|
| End point title | Main Study: Percentage of Subjects Achieving an American College of Rheumatology 20 Percent (%) (ACR20) Response |
|-----------------|--|

End point description:

Subjects with 20% improvement from baseline in tender and swollen joint counts and 20% improvement in at least 3 of the 5 measures: Patient's global assessment of arthritis (PtGA), Physician's global assessment of arthritis (PhyGA), subject's assessment of arthritis pain, HAQ-DI and C-reactive protein (CRP) in mg/L. PtGA: subject assessed health on VAS, 0 mm(very well) to 100 mm(worst health condition), higher score =worse condition. PhyGA: physician judged subjects' pain on VAS, 0(no pain) to 100 mm(extreme pain), higher score = more pain. Subject's assessment of arthritis pain: subject assessed pain on VAS, 0 mm(no pain) to 100 mm(most severe pain), higher score=more pain. HAQ-DI: functional disability evaluation, score: 0(no difficulty) to 3(extreme difficulty),higher score implied more disability. FAS population for long-term extension (LTE) main study. n=subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Month 1 (n = 673) | 66.12 (62.55 to 69.70) | | | |
| Month 3 (n =660) | 68.79 (65.25 to 72.32) | | | |
| Month 6 (n =634) | 70.66 (67.12 to 74.21) | | | |
| Month 9 (n =603) | 71.48 (67.87 to 75.08) | | | |
| Month 12 (n =581) | 74.18 (70.62 to 77.74) | | | |
| Month 15 (n =551) | 78.04 (74.58 to 81.50) | | | |
| Month 18 (n =537) | 77.65 (74.13 to 81.18) | | | |
| Month 21 (n =526) | 77.00 (73.40 to 80.59) | | | |

| | | | | |
|-------------------|------------------------|--|--|--|
| Month 24 (n =511) | 76.13 (72.43 to 79.82) | | | |
| Month 27 (n =495) | 78.18 (74.54 to 81.82) | | | |
| Month 30 (n =479) | 80.79 (77.27 to 84.32) | | | |
| Month 33 (n =452) | 77.88 (74.05 to 81.70) | | | |
| Month 36 (n =383) | 77.02 (72.81 to 81.24) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percentage of Subjects Achieving an American College of Rheumatology 50% (ACR50) Response

| | |
|-----------------|---|
| End point title | Main Study: Percentage of Subjects Achieving an American College of Rheumatology 50% (ACR50) Response |
|-----------------|---|

End point description:

Subjects with 50% improvement from baseline in tender and swollen joint counts and 50% improvement in at least 3 of the 5 measures: PtGA, PhyGA, subject's assessment of arthritis pain, HAQ-DI and CRP in mg/L. PtGA: subject assessed health on VAS, 0 mm(very well) to 100 mm(worst health condition), higher score =worse condition. PhyGA: physician judged subjects' pain on VAS, 0 (no pain) to 100 mm (extreme pain), higher score = more pain. Subject's assessment of arthritis pain: subject assessed pain on VAS, 0 mm (no pain) to 100 mm (most severe pain), higher score =more pain. HAQ-DI: functional disability evaluation, score: 0 (no difficulty) to 3 (extreme difficulty), higher score implied more disability. FAS population for LTE main study was analyzed. "n"=subjects evaluable for this endpoint at specified time points.

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| End point type | Secondary |
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End point timeframe:

Main Study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Month 1 (n =674) | 45.70 (41.94 to 49.46) | | | |
| Month 3 (n =661) | 43.27 (39.49 to 47.04) | | | |
| Month 6 (n =633) | 47.08 (43.19 to 50.97) | | | |
| Month 9 (n =605) | 50.41 (46.43 to 54.40) | | | |
| Month 12 (n =581) | 50.26 (46.19 to 54.32) | | | |
| Month 15 (n =554) | 55.42 (51.28 to 59.55) | | | |
| Month 18 (n =539) | 55.10 (50.90 to 59.30) | | | |

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|-------------------|------------------------|--|--|--|
| Month 21 (n =527) | 55.41 (51.16 to 59.65) | | | |
| Month 24 (n =511) | 57.34 (53.05 to 61.63) | | | |
| Month 27 (n =496) | 56.05 (51.68 to 60.42) | | | |
| Month 30 (n =478) | 60.46 (56.08 to 64.84) | | | |
| Month 33 (n =452) | 57.96 (53.41 to 62.52) | | | |
| Month 36 (n =384) | 58.85 (53.93 to 63.78) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percentage of Subjects Achieving an American College of Rheumatology 70% (ACR70) Response

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| End point title | Main Study: Percentage of Subjects Achieving an American College of Rheumatology 70% (ACR70) Response |
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End point description:

Subjects with 70% improvement from baseline in tender and swollen joint counts and 70% improvement in at least 3 of the 5 measures: PtGA, PhyGA, subject's assessment of arthritis pain, HAQ-DI and CRP in mg/L. PtGA: subject assessed health on VAS, 0 mm(very well) to 100 mm(worst health condition), higher score =worse condition. PhyGA: physician judged subjects' pain on VAS, 0 (no pain) to 100 mm (extreme pain), higher score = more pain. Subject's assessment of arthritis pain: subject assessed pain on VAS, 0 mm (no pain) to 100 mm (most severe pain), higher score =more pain. HAQ-DI: functional disability evaluation, score: 0 (no difficulty) to 3 (extreme difficulty), higher score implied more disability. FAS population for LTE main study was analyzed. "n"=subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|-----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Month 1 (n =676) | 24.85 (21.59 to 28.11) | | | |
| Month 3 (n =662) | 26.13 (22.79 to 29.48) | | | |
| Month 6 (n =636) | 30.50 (26.92 to 34.08) | | | |
| Month 9 (n =607) | 30.81 (27.13 to 34.48) | | | |
| Month 12 (n =582) | 32.13 (28.34 to 35.92) | | | |
| Month 15 (n =555) | 33.87 (29.94 to 37.81) | | | |

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|-------------------|------------------------|--|--|--|
| Month 18 (n =538) | 36.25 (32.18 to 40.31) | | | |
| Month 21 (n =527) | 34.35 (30.29 to 38.40) | | | |
| Month 24 (n =512) | 35.94 (31.78 to 40.09) | | | |
| Month 27 (n =496) | 38.10 (33.83 to 42.38) | | | |
| Month 30 (n =476) | 41.60 (37.17 to 46.02) | | | |
| Month 33 (n =453) | 38.19 (33.72 to 42.66) | | | |
| Month 36 (n =384) | 37.76 (32.91 to 42.61) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

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|-----------------|---|
| End point title | Main Study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
|-----------------|---|

End point description:

HAQ-DI assessed the degree of difficulty a participant had experienced during the past week in 8 domains of daily living activities: dressing/grooming, arising, eating, walking, reach, grip, hygiene, and other activities. There were total of 2-3 items distributed in these 8 domains. Each item was scored for level of difficulty on a 4-point scale from 0 to 3: 0= no difficulty; 1= some difficulty; 2= much difficulty; 3= unable to do. Overall score was computed as the sum of domain score and divided by the number of domains answered. Total possible score range 0 (least difficulty) and 3 (extreme difficulty), where higher score indicate more difficulty while performing daily living activities. FAS population for LTE main study was analyzed. "n"=subjects evaluable for this endpoint at specified time points.

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|----------------|-----------|
| End point type | Secondary |
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End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =675) | -0.4373 (± 0.55677) | | | |
| Change at Month 3 (n =661) | -0.4559 (± 0.55104) | | | |
| Change at Month 6 (n =636) | -0.4755 (± 0.57468) | | | |
| Change at Month 9 (n =605) | -0.4841 (± 0.58294) | | | |
| Change at Month 12 (n =582) | -0.4782 (± 0.60163) | | | |

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|-----------------------------|---------------------|--|--|--|
| Change at Month 15 (n =554) | -0.5108 (± 0.58277) | | | |
| Change at Month 18 (n =539) | -0.5116 (± 0.59401) | | | |
| Change at Month 21 (n =528) | -0.5211 (± 0.59568) | | | |
| Change at Month 24 (n =511) | -0.5068 (± 0.62016) | | | |
| Change at Month 27 (n =496) | -0.5219 (± 0.60833) | | | |
| Change at Month 30 (n =478) | -0.5356 (± 0.61316) | | | |
| Change at Month 33 (n =453) | -0.5276 (± 0.63803) | | | |
| Change at Month 36 (n =386) | -0.5476 (± 0.65226) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percentage of Subjects Achieving Psoriatic Arthritis Response Criteria (PsARC)

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|-----------------|--|
| End point title | Main Study: Percentage of Subjects Achieving Psoriatic Arthritis Response Criteria (PsARC) |
|-----------------|--|

End point description:

PsARC was comprised of 4 clinical improvement criteria: greater than or equal to (\geq) 20% improvement in PhyGA (VAS), \geq 20% improvement in patient's global assessment of arthritis (PtGA); and \geq 30% reduction in the number of tender joints; and \geq 30% reduction in the number of swollen joints. PtGA: subject assessed health on VAS, 0 mm (very well) to 100 mm (worst health condition), higher score = worse condition. PhyGA: physician judged subjects' pain on VAS, 0 (no pain) to 100 mm (extreme pain), higher score = more pain. To achieve a clinical response, the subject must improve in 2 of the 4 PsARC criteria, 1 of which has to be the number of tender or swollen joints and none of the 4 score could worsen. FAS population for LTE main study was analyzed. "n"= subjects evaluable for this outcome measure at specified time points.

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

End point timeframe:

Main Study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Month 1 (n =669) | 68.46 (64.94 to 71.98) | | | |
| Month 3 (n =657) | 69.56 (66.04 to 73.08) | | | |
| Month 6 (n =633) | 73.14 (69.69 to 76.60) | | | |
| Month 9 (n =599) | 74.46 (70.97 to 77.95) | | | |

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|-------------------|------------------------|--|--|--|
| Month 12 (n =577) | 76.08 (72.60 to 79.56) | | | |
| Month 15 (n =547) | 79.52 (76.14 to 82.91) | | | |
| Month 18 (n =534) | 80.15 (76.77 to 83.53) | | | |
| Month 21 (n =522) | 79.50 (76.04 to 82.96) | | | |
| Month 24 (n =507) | 77.51 (73.88 to 81.15) | | | |
| Month 27 (n =494) | 80.16 (76.65 to 83.68) | | | |
| Month 30 (n =475) | 82.11 (78.66 to 85.55) | | | |
| Month 33 (n =449) | 80.85 (77.21 to 84.49) | | | |
| Month 36 (n =381) | 77.17 (72.95 to 81.38) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Physician's Global Assessment of Psoriasis (PGA-PsO) Score (For Subjects with Baseline PGA-PsO Score Greater Than [$>$]0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

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|-----------------|---|
| End point title | Main Study: Change From Baseline in Physician's Global Assessment of Psoriasis (PGA-PsO) Score (For Subjects with Baseline PGA-PsO Score Greater Than [$>$]0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
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End point description:

The PGA-PsO was a 5-point scale, reflecting a global consideration of the erythema, induration, and scaling across all psoriatic lesions. Average erythema, induration, and scaling were scored separately over the whole body according to a 5-point severity scale (0-4). Higher score indicated higher disease severity. Severity score for each erythema, induration and scaling were summed and averaged after which the total average was rounded to the nearest whole number score to determine a PGA-PsO score on a scale of 0 to 4 (0= clear, except for any residual discoloration, 1= almost clear, 2= mild, 3= moderate, 4= severe). Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 and with baseline PGA-PsO score >0 . "n" =subjects evaluable for this endpoint at specified time points.

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|----------------|-----------|
| End point type | Secondary |
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End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 660 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =649) | -1.1 (\pm 1.04) | | | |
| Change at Month 3 (n =636) | -1.1 (\pm 1.04) | | | |
| Change at Month 6 (n =610) | -1.2 (\pm 1.03) | | | |

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|-----------------------------|---------------|--|--|--|
| Change at Month 9 (n =578) | -1.2 (± 1.06) | | | |
| Change at Month 12 (n =559) | -1.1 (± 1.06) | | | |
| Change at Month 15 (n =532) | -1.2 (± 1.07) | | | |
| Change at Month 18 (n =516) | -1.2 (± 1.05) | | | |
| Change at Month 21 (n =506) | -1.2 (± 1.06) | | | |
| Change at Month 24 (n =488) | -1.3 (± 1.02) | | | |
| Change at Month 27 (n =478) | -1.3 (± 1.02) | | | |
| Change at Month 30 (n =462) | -1.3 (± 1.05) | | | |
| Change at Month 33 (n =434) | -1.3 (± 1.02) | | | |
| Change at Month 36 (n =372) | -1.2 (± 1.02) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percentage of Subjects With a Psoriasis Area and Severity Index 75 (PASI75) Score (For Subjects With Baseline Body Surface Area [BSA] ≥ 3% and Baseline PASI Score > 0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

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|-----------------|---|
| End point title | Main Study: Percentage of Subjects With a Psoriasis Area and Severity Index 75 (PASI75) Score (For Subjects With Baseline Body Surface Area [BSA] ≥ 3% and Baseline PASI Score > 0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
|-----------------|---|

End point description:

PASI: combined assessment of lesion severity and body area affected into single score; range = 0 (no disease) - 72 (maximal disease). Higher score represented greater severity of psoriasis. PASI was composite scoring by investigator of degree of erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk including axillae and groin, and lower limbs including buttocks). For each section % area of skin involved was estimated: 0 (0%) - 6 (90-100%) and severity estimated by clinical signs of erythema, induration, scaling; ranged 0-4: 0 = none, 1 = slight, 2 = moderate, 3 = marked, 4 = very marked. Final PASI = sum of severity parameters for each section * area score * weighing factor (head = 0.1, upper limbs = 0.2, trunk = 0.3, lower limbs = 0.4). PASI75: ≥ 75% reduction in PASI relative to Baseline. FAS of main study with baseline: BSA ≥ 3%, PASI score > 0. n = subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main study: Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 474 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Month 1 (n =465) | 55.05 (50.53 to 59.58) | | | |
| Month 3 (n =452) | 57.96 (53.41 to 62.52) | | | |
| Month 6 (n =433) | 60.74 (56.14 to 65.34) | | | |
| Month 9 (n =411) | 61.07 (56.36 to 65.78) | | | |

| | | | | |
|-------------------|------------------------|--|--|--|
| Month 12 (n =399) | 63.16 (58.42 to 67.89) | | | |
| Month 15 (n =382) | 65.71 (60.95 to 70.47) | | | |
| Month 18 (n =368) | 65.22 (60.35 to 70.08) | | | |
| Month 21 (n =360) | 69.72 (64.98 to 74.47) | | | |
| Month 24 (n =347) | 71.47 (66.72 to 76.22) | | | |
| Month 27 (n =343) | 70.85 (66.04 to 75.66) | | | |
| Month 30 (n =331) | 68.58 (63.58 to 73.58) | | | |
| Month 33 (n =311) | 70.10 (65.01 to 75.18) | | | |
| Month 36 (n =260) | 68.08 (62.41 to 73.74) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percent Change From Baseline in PASI Composite Score (For Subjects With Baseline BSA \geq 3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| | |
|-----------------|---|
| End point title | Main Study: Percent Change From Baseline in PASI Composite Score (For Subjects With Baseline BSA \geq 3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
|-----------------|---|

End point description:

PASI: combined assessment of lesion severity & area affected into single score; range=0(no disease)-72(maximal disease). Higher score represented greater severity of psoriasis. PASI is a composite scoring by investigator of degree of erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk including axillae and groin, and lower limbs including buttocks). For each section % area of skin involved was estimated: 0(0%) - 6(90-100%) & severity estimated by clinical signs of erythema, induration, scaling; ranged 0-4: 0=none, 1=slight, 2=moderate, 3=marked, 4=very marked. Final PASI=sum of severity parameters for each section*area score*weighing factor (head=0.1, upper limbs=0.2, trunk=0.3, lower limbs=0.4). FAS of main study with baseline: BSA \geq 3%, PASI score >0 . n =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main study: Baseline, Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 474 | | | |
| Units: percent change | | | | |
| arithmetic mean (standard deviation) | | | | |
| At Month 1 (n =465) | -64.09 (\pm 57.473) | | | |

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|----------------------|-------------------|--|--|--|
| At Month 3 (n =452) | -66.98 (± 43.647) | | | |
| At Month 6 (n =433) | -68.58 (± 44.568) | | | |
| At Month 9 (n =411) | -70.42 (± 40.617) | | | |
| At Month 12 (n =399) | -71.58 (± 42.515) | | | |
| At Month 15 (n =382) | -73.13 (± 43.653) | | | |
| At Month 18 (n =368) | -73.51 (± 40.527) | | | |
| At Month 21 (n =360) | -75.15 (± 44.182) | | | |
| At Month 24 (n =347) | -78.36 (± 34.808) | | | |
| At Month 27 (n =343) | -78.37 (± 34.405) | | | |
| At Month 30 (n =331) | -78.28 (± 30.270) | | | |
| At Month 33 (n =311) | -77.47 (± 43.952) | | | |
| At Month 36 (n =260) | -76.85 (± 31.973) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percent Change From Baseline in PASI Clinical Signs Component Score (For Subjects With Baseline BSA≥3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

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|-----------------|--|
| End point title | Main Study: Percent Change From Baseline in PASI Clinical Signs Component Score (For Subjects With Baseline BSA≥3% and Baseline PASI Score >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
|-----------------|--|

End point description:

PASI: combined assessment of lesion severity & area affected into single score; range=0(no disease)-72(maximal disease). Higher score representing greater severity of psoriasis. PASI was a composite scoring by investigator of degree of clinical sign components for erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk including axillae and groin, and lower limbs including buttocks). For each section % area of skin involved was estimated: 0(0%) - 6(90-100%) and severity estimated by clinical signs components for erythema, induration, scaling; ranged 0-4: 0=none, 1=slight, 2=moderate, 3=marked, 4=very marked. Final PASI=sum of severity parameters for each section*area score*weighing factor (head=0.1, upper limbs=0.2, trunk=0.3, lower limbs=0.4). Analysis population included FAS of main study with baseline BSA≥3%, baseline PASI score >0. n=subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main study: Baseline(Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 474 | | | |
| Units: percent change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Induration: At Month 1 (n =456) | -62.60 (± 62.288) | | | |
| Induration: At Month 3 (n =442) | -66.92 (± 46.898) | | | |
| Induration: At Month 6 (n =423) | -68.63 (± 46.644) | | | |
| Induration: At Month 9 (n =402) | -70.33 (± 41.960) | | | |
| Induration: At Month 12 (n =390) | -70.81 (± 48.439) | | | |
| Induration: At Month 15 (n =373) | -72.49 (± 48.644) | | | |
| Induration: At Month 18 (n =359) | -73.16 (± 40.801) | | | |
| Induration: At Month 21 (n =352) | -74.34 (± 47.617) | | | |
| Induration: At Month 24 (n =338) | -78.45 (± 36.534) | | | |
| Induration: At Month 27 (n =335) | -77.85 (± 34.297) | | | |
| Induration: At Month 30 (n =322) | -78.55 (± 31.187) | | | |
| Induration: At Month 33 (n =303) | -77.09 (± 42.305) | | | |
| Induration: At Month 36 (n =256) | -76.11 (± 35.000) | | | |
| Erythema: At Month 1 (n =464) | -63.60 (± 67.818) | | | |
| Erythema: At Month 3 (n =451) | -66.69 (± 43.013) | | | |
| Erythema: At Month 6 (n =432) | -67.17 (± 46.756) | | | |
| Erythema: At Month 9 (n =410) | -69.75 (± 42.882) | | | |
| Erythema: At Month 12 (n =398) | -70.45 (± 46.575) | | | |
| Erythema: At Month 15 (n =381) | -71.55 (± 50.406) | | | |
| Erythema: At Month 18 (n =367) | -73.12 (± 45.194) | | | |
| Erythema: At Month 21 (n =359) | -75.06 (± 45.993) | | | |
| Erythema: At Month 24 (n =346) | -77.40 (± 38.093) | | | |
| Erythema: At Month 27 (n =342) | -77.83 (± 33.877) | | | |
| Erythema: At Month 30 (n =330) | -77.04 (± 33.478) | | | |
| Erythema: At Month 33 (n =310) | -75.17 (± 53.782) | | | |
| Erythema: At Month 36 (n =259) | -75.72 (± 34.823) | | | |
| Scaling: At Month 1 (n =453) | -64.26 (± 55.848) | | | |
| Scaling: At Month 3 (n =439) | -66.15 (± 52.568) | | | |

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|-------------------------------|-------------------|--|--|--|
| Scaling: At Month 6 (n =420) | -68.66 (± 49.145) | | | |
| Scaling: At Month 9 (n =399) | -69.09 (± 48.506) | | | |
| Scaling: At Month 12 (n =387) | -72.48 (± 45.755) | | | |
| Scaling: At Month 15 (n =370) | -73.83 (± 42.528) | | | |
| Scaling: At Month 18 (n =356) | -74.62 (± 39.708) | | | |
| Scaling: At Month 21 (n =348) | -75.11 (± 44.570) | | | |
| Scaling: At Month 24 (n =336) | -77.86 (± 38.041) | | | |
| Scaling: At Month 27 (n =332) | -79.34 (± 31.825) | | | |
| Scaling: At Month 30 (n =322) | -77.23 (± 37.819) | | | |
| Scaling: At Month 33 (n =302) | -77.94 (± 41.688) | | | |
| Scaling: At Month 36 (n =253) | -78.10 (± 30.391) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Dactylitis Severity Score (DSS) (For Subjects With Baseline DSS greater than [$>$] 0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in Dactylitis Severity Score (DSS) (For Subjects With Baseline DSS greater than [$>$] 0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
|-----------------|---|

End point description:

Dactylitis was characterized by swelling of the entire finger or toe. The DSS was a function of finger circumference and tenderness, assessed and summed across all dactylitic digits. The severity of dactylitis was scored on a scale of 0-3, where 0 =no tenderness and 3 =extreme tenderness in each digit of the hands and feet. The range of total dactylitis severity score for a participant was 0-60. Higher score indicated greater severity.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 366 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =360) | -6.7 (± 7.65) | | | |
| Change at Month 3 (n =352) | -6.8 (± 7.71) | | | |
| Change at Month 6 (n =335) | -7.2 (± 7.89) | | | |
| Change at Month 9 (n =313) | -7.4 (± 7.29) | | | |

| | | | | |
|-----------------------------|---------------|--|--|--|
| Change at Month 12 (n =305) | -7.6 (± 7.70) | | | |
| Change at Month 15 (n =290) | -7.7 (± 7.44) | | | |
| Change at Month 18 (n =282) | -7.7 (± 7.50) | | | |
| Change at Month 21 (n =275) | -7.8 (± 7.89) | | | |
| Change at Month 24 (n =269) | -7.9 (± 7.76) | | | |
| Change at Month 27 (n =265) | -8.1 (± 7.59) | | | |
| Change at Month 30 (n =257) | -8.0 (± 7.65) | | | |
| Change at Month 33 (n =250) | -8.1 (± 7.75) | | | |
| Change at Month 36 (n =212) | -7.7 (± 7.88) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Leeds Enthesitis Index (LEI) (For Subjects With Baseline LEI >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Leeds Enthesitis Index (LEI) (For Subjects With Baseline LEI >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
|-----------------|--|

End point description:

Enthesitis was inflammation in the tendon, ligament, and joint capsule fiber insertion into bone. The LEI assessed enthesitis in 6 sites including (right and left): lateral epicondyle humerus, medial femoral condyle and achilles tendon insertion. Tenderness is recorded as either present (score 1) or absent (score 0) for each of the 6 sites for a total score of 0-6. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 and with baseline LEI >0. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 458 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =449) | -1.5 (± 1.88) | | | |
| Change at Month 3 (n =437) | -1.6 (± 1.79) | | | |
| Change at Month 6 (n =418) | -1.7 (± 1.78) | | | |
| Change at Month 9 (n =398) | -1.8 (± 1.80) | | | |
| Change at Month 12 (n =380) | -1.7 (± 1.82) | | | |
| Change at Month 15 (n =364) | -2.0 (± 1.76) | | | |
| Change at Month 18 (n =347) | -1.9 (± 1.79) | | | |
| Change at Month 21 (n =340) | -1.9 (± 1.81) | | | |
| Change at Month 24 (n =327) | -2.0 (± 1.72) | | | |
| Change at Month 27 (n =317) | -2.0 (± 1.73) | | | |
| Change at Month 30 (n =306) | -2.0 (± 1.76) | | | |
| Change at Month 33 (n =288) | -2.0 (± 1.75) | | | |

| | | | | |
|-----------------------------|---------------|--|--|--|
| Change at Month 36 (n =253) | -2.1 (± 1.76) | | | |
|-----------------------------|---------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index (For Subjects with baseline SPARCC Enthesitis Index >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index (For Subjects with baseline SPARCC Enthesitis Index >0) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
|-----------------|---|

End point description:

The SPARCC enthesitis index identifies the presence or absence of tenderness at 16 enthesial sites, including (right and left): medial epicondyle humerus, lateral epicondyle humerus, supraspinatus insertion into greater tuberosity of humerus, greater trochanter, quadriceps insertion into superior border of patella, patellar ligament insertion into inferior pole of patella or tibial tubercle, Achilles tendon insertion into calcaneum and plantar fascia insertion into calcaneum. On examination, tenderness is recorded as present (1) or absent (0) for each of the 16 sites, with an overall total score ranging from 0 to 16. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 and with baseline SPARCC enthesitis index >0. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 525 | | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =517) | -2.8 (± 3.60) | | | |
| Change at Month 3 (n =504) | -3.0 (± 3.61) | | | |
| Change at Month 6 (n =481) | -3.2 (± 3.72) | | | |
| Change at Month 9 (n =457) | -3.4 (± 3.69) | | | |
| Change at Month 12 (n =438) | -3.5 (± 3.46) | | | |
| Change at Month 15 (n =415) | -3.7 (± 3.55) | | | |
| Change at Month 18 (n =400) | -3.5 (± 3.45) | | | |
| Change at Month 21 (n =394) | -3.6 (± 3.60) | | | |
| Change at Month 24 (n =379) | -3.7 (± 3.62) | | | |
| Change at Month 27 (n =369) | -3.7 (± 3.56) | | | |
| Change at Month 30 (n =359) | -3.8 (± 3.49) | | | |
| Change at Month 33 (n =340) | -3.9 (± 3.39) | | | |
| Change at Month 36 (n =290) | -3.9 (± 3.69) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Score (For Subjects with Presence of Spondylitis at Screening and Baseline BASDAI Score >0 cm) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Score (For Subjects with Presence of Spondylitis at Screening and Baseline BASDAI Score >0 cm) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
|-----------------|--|

End point description:

BASDAI was a validated self-assessment tool used to determine disease activity in subjects with ankylosing spondylitis. Utilizing a VAS of 0-10 cm (0= none and 10= very severe) subjects answered 6 questions pertaining to 5 symptoms including fatigue, spinal pain, joint pain/swelling, areas of localized tenderness and morning stiffness. The final BASDAI score was an average of answers to 6 questions, with an overall possible score range of 0 to 10 centimeter (cm) with higher score represented more severe ankylosing spondylitis disease activity. Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 with presence of spondylitis at screening and baseline BASDAI Score >0 cm. n =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 124 | | | |
| Units: centimeter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =124) | -2.26 (± 2.367) | | | |
| Change at Month 3 (n =121) | -2.10 (± 2.278) | | | |
| Change at Month 6 (n =116) | -2.40 (± 2.371) | | | |
| Change at Month 9 (n =106) | -2.35 (± 2.254) | | | |
| Change at Month 12 (n =105) | -2.41 (± 2.371) | | | |
| Change at Month 15 (n =99) | -2.35 (± 2.547) | | | |
| Change at Month 18 (n =95) | -2.41 (± 2.640) | | | |
| Change at Month 21 (n =89) | -2.28 (± 2.582) | | | |

| | | | | |
|----------------------------|-----------------|--|--|--|
| Change at Month 24 (n =85) | -2.47 (± 2.640) | | | |
| Change at Month 27 (n =83) | -2.65 (± 2.658) | | | |
| Change at Month 30 (n =82) | -2.95 (± 2.672) | | | |
| Change at Month 33 (n =80) | -2.85 (± 2.671) | | | |
| Change at Month 36 (n =71) | -2.88 (± 2.521) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Score (For Subjects With Presence of Spondylitis at Screening and Baseline BASDAI Score ≥ 4 cm) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Score (For Subjects With Presence of Spondylitis at Screening and Baseline BASDAI Score ≥ 4 cm) at Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36 |
|-----------------|--|

End point description:

BASDAI was a validated self-assessment tool used to determine disease activity in subjects with ankylosing spondylitis. Utilizing a VAS of 0-10 cm (0= none and 10= very severe) subjects answered 6 questions pertaining to 5 symptoms including fatigue, spinal pain, joint pain/swelling, areas of localized tenderness and morning stiffness. The final BASDAI score was an average of answers to 6 questions, with an overall possible score range of 0 to 10 cm with higher score represented more severe ankylosing spondylitis disease activity. Analysis population included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092 and with presence of spondylitis at screening and baseline BASDAI score ≥ 4 cm. n =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33 and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 106 | | | |
| Units: centimeter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =106) | -2.59 (± 2.324) | | | |
| Change at Month 3 (n =103) | -2.41 (± 2.227) | | | |
| Change at Month 6 (n =98) | -2.74 (± 2.350) | | | |
| Change at Month 9 (n =93) | -2.63 (± 2.175) | | | |
| Change at Month 12 (n =92) | -2.65 (± 2.364) | | | |

| | | | | |
|----------------------------|-----------------|--|--|--|
| Change at Month 15 (n =87) | -2.65 (± 2.487) | | | |
| Change at Month 18 (n =84) | -2.65 (± 2.652) | | | |
| Change at Month 21 (n =80) | -2.47 (± 2.602) | | | |
| Change at Month 24 (n =76) | -2.72 (± 2.616) | | | |
| Change at Month 27 (n =74) | -2.90 (± 2.640) | | | |
| Change at Month 30 (n =73) | -3.27 (± 2.596) | | | |
| Change at Month 33 (n =71) | -3.17 (± 2.589) | | | |
| Change at Month 36 (n =65) | -3.08 (± 2.459) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Component Summary Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Component Summary Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|---|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 8 health domains were aggregated into two summary scores known as the physical component summary (PCS) score and the mental component summary (MCS) score. Norm-based domain scores, PCS and MCS scores were used in the analyses; each of which has a population mean of 50 with a standard deviation (SD) of 10 points, and ranges from minus infinity to plus infinity. A higher PCS score represented better physical health status. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =668) | 6.44 (± 8.285) | | | |
| Change at Month 6 (n =630) | 6.71 (± 8.496) | | | |
| Change at Month 12 (n =578) | 7.23 (± 8.257) | | | |
| Change at Month 18 (n =534) | 7.44 (± 8.729) | | | |
| Change at Month 24 (n =502) | 7.79 (± 9.055) | | | |
| Change at Month 30 (n =471) | 8.06 (± 8.899) | | | |

| | | | | |
|-----------------------------|----------------|--|--|--|
| Change at Month 36 (n =384) | 7.77 (± 9.074) | | | |
|-----------------------------|----------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Component Summary Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Component Summary Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|---|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 8 health domains were aggregated into two summary scores known as the PCS score and the MCS score. Norm-based domain scores, PCS and MCS scores were used in the analyses; each of which has a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher MCS score represents better mental health status. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =668) | 4.72 (± 10.480) | | | |
| Change at Month 6 (n =630) | 4.98 (± 11.052) | | | |
| Change at Month 12 (n =578) | 5.25 (± 11.072) | | | |
| Change at Month 18 (n =534) | 5.53 (± 11.055) | | | |
| Change at Month 24 (n =502) | 5.79 (± 11.122) | | | |
| Change at Month 30 (n =471) | 5.82 (± 11.726) | | | |
| Change at Month 36 (n =384) | 6.18 (± 11.284) | | | |

Statistical analyses

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Functioning Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Functioning Domain Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|--|

End point description:

SF-36v2 was a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, & mental health. The 10 items of the physical functioning scale represented levels and kinds of limitations between extremes of physical activities, including lifting & carrying groceries; climbing stairs; bending, kneeling, or stooping; walking moderate distances; self-care limitations. The physical functioning items capture the presence & extent of physical limitations using a 3-level response continuum. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher physical functioning domain score represented better physical functioning. FAS of main study was analyzed. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | 6.06 (± 9.425) | | | |
| Change at Month 6 (n =635) | 6.44 (± 9.834) | | | |
| Change at Month 12 (n =582) | 7.00 (± 9.472) | | | |
| Change at Month 18 (n =536) | 7.31 (± 9.891) | | | |
| Change at Month 24 (n =505) | 7.69 (± 10.280) | | | |
| Change at Month 30 (n =472) | 7.96 (± 10.146) | | | |
| Change at Month 36 (n =386) | 7.80 (± 10.703) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Physical Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Physical Domain Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|---|

End point description:

SF-36v2 acute was a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, & mental health. The 4-item role-

physical scale covers an array of physical health-related role limitations, including: a) limitations in the kind of work or other usual activities; b) reductions in the amount of time spent on work or other usual activities; c) difficulty performing work or other usual activities; & d) accomplishing less. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher role-physical domain score represented better role-physical functioning. FAS of main study was analyzed. "n" =subjects evaluable for this endpoint at specified time points.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36 | |

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =669) | 6.19 (± 9.545) | | | |
| Change at Month 6 (n =631) | 6.56 (± 9.650) | | | |
| Change at Month 12 (n =579) | 6.61 (± 9.293) | | | |
| Change at Month 18 (n =534) | 7.07 (± 10.050) | | | |
| Change at Month 24 (n =503) | 7.46 (± 10.094) | | | |
| Change at Month 30 (n =473) | 7.64 (± 10.041) | | | |
| Change at Month 36 (n =384) | 7.40 (± 9.996) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Bodily Pain Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Bodily Pain Domain Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|---|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The bodily pain scale comprises of 2 items pertaining to the intensity of bodily pain and extent of interference with normal work activities. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher bodily pain domain score represented less bodily pain. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36 | |

| | | | | |
|--------------------------------------|------------------|--|--|--|
| End point values | Tofacitinib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =673) | 8.36 (± 9.797) | | | |
| Change at Month 6 (n =636) | 8.52 (± 10.033) | | | |
| Change at Month 12 (n =582) | 9.29 (± 9.777) | | | |
| Change at Month 18 (n =536) | 9.70 (± 10.271) | | | |
| Change at Month 24 (n =504) | 9.95 (± 10.980) | | | |
| Change at Month 30 (n =473) | 10.21 (± 10.645) | | | |
| Change at Month 36 (n =386) | 10.45 (± 10.627) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) General Health Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) General Health Domain Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|--|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The general health scale consisted of 5 items including a rating of health and 4 items addressing the respondent's view and expectations of his or her health. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher general health domain score represented better general health perceptions. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | 3.89 (± 8.033) | | | |
| Change at Month 6 (n =636) | 4.09 (± 8.640) | | | |
| Change at Month 12 (n =582) | 4.68 (± 8.652) | | | |
| Change at Month 18 (n =536) | 4.76 (± 8.386) | | | |
| Change at Month 24 (n =504) | 4.89 (± 8.608) | | | |
| Change at Month 30 (n =473) | 4.81 (± 8.590) | | | |
| Change at Month 36 (n =386) | 4.36 (± 8.847) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Vitality Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Vitality Domain Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|--|

End point description:

The SF-36v2 acute is a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 4-item measure of vitality captures a broad range of subjective evaluations of well-being from feelings of tiredness and being worn out to feeling full of energy all or most of the time. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher vitality domain score represents better vitality. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | 5.92 (± 10.160) | | | |
| Change at Month 6 (n =636) | 6.03 (± 10.546) | | | |
| Change at Month 12 (n =582) | 6.72 (± 10.367) | | | |
| Change at Month 18 (n =536) | 6.67 (± 10.147) | | | |

| | | | | |
|-----------------------------|-----------------|--|--|--|
| Change at Month 24 (n =504) | 7.10 (± 10.828) | | | |
| Change at Month 30 (n =474) | 7.62 (± 10.808) | | | |
| Change at Month 36 (n =386) | 7.65 (± 10.403) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Social Functioning Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Social Functioning Domain Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|--|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 2-item social functioning scale assessed health-related effects on quantity and quality of social activities. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher social functioning domain score represented better social functioning. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | 6.08 (± 11.028) | | | |
| Change at Month 6 (n =636) | 6.51 (± 10.923) | | | |
| Change at Month 12 (n =582) | 7.16 (± 10.932) | | | |
| Change at Month 18 (n =536) | 6.76 (± 11.272) | | | |
| Change at Month 24 (n =504) | 7.28 (± 11.487) | | | |
| Change at Month 30 (n =473) | 7.64 (± 11.597) | | | |
| Change at Month 36 (n =386) | 7.83 (± 11.977) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Emotional Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Emotional Domain Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|---|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 3-item role-emotional scale assessed mental health-related role limitations in terms of a) time spent in work or other usual activities; b) amount of work or activities accomplished; c) care with which work or other activities were performed. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher role-emotional domain score represented better role-emotional functioning. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =668) | 5.40 (± 11.962) | | | |
| Change at Month 6 (n =632) | 5.39 (± 12.445) | | | |
| Change at Month 12 (n =578) | 5.73 (± 12.235) | | | |
| Change at Month 18 (n =534) | 6.71 (± 12.647) | | | |
| Change at Month 24 (n =502) | 6.82 (± 12.154) | | | |
| Change at Month 30 (n =473) | 6.54 (± 12.843) | | | |
| Change at Month 36 (n =384) | 6.95 (± 12.859) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Health Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Short-Form-36 Health |
|-----------------|--|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 5-item mental health scale includes 1 or more items from each of 4 major mental health dimensions: anxiety, depression, loss of behavioral/emotional control, and psychological well-being. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher mental health domain score represented better mental health functioning. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | 4.85 (± 10.306) | | | |
| Change at Month 6 (n =636) | 5.39 (± 10.893) | | | |
| Change at Month 12 (n =582) | 5.56 (± 10.781) | | | |
| Change at Month 18 (n =536) | 5.82 (± 10.730) | | | |
| Change at Month 24 (n =504) | 6.09 (± 11.247) | | | |
| Change at Month 30 (n =474) | 6.18 (± 11.278) | | | |
| Change at Month 36 (n =386) | 6.37 (± 11.199) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol- 5D Health Questionnaire 3-Level (EQ-5D-3L) Mobility Domain at Months 1, 6, 12, 18, 24, 30 and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in EuroQol- 5D Health Questionnaire 3-Level (EQ-5D-3L) Mobility Domain at Months 1, 6, 12, 18, 24, 30 and 36 |
|-----------------|---|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L mobility domain score were reported in this outcome measure. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36 | |

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | -0.24 (± 0.529) | | | |
| Change at Month 6 (n =635) | -0.30 (± 0.540) | | | |
| Change at Month 12 (n =582) | -0.28 (± 0.511) | | | |
| Change at Month 18 (n =536) | -0.30 (± 0.538) | | | |
| Change at Month 24 (n =505) | -0.31 (± 0.545) | | | |
| Change at Month 30 (n =474) | -0.30 (± 0.526) | | | |
| Change at Month 36 (n =386) | -0.32 (± 0.555) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Self-Care Domain at Months 1, 6, 12, 18, 24, 30 and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Self-Care Domain at Months 1, 6, 12, 18, 24, 30 and 36 |
|-----------------|---|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L self-care domain score were reported in this outcome measure. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36 | |

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =673) | -0.19 (± 0.547) | | | |
| Change at Month 6 (n =633) | -0.20 (± 0.530) | | | |
| Change at Month 12 (n =581) | -0.19 (± 0.532) | | | |
| Change at Month 18 (n =535) | -0.21 (± 0.522) | | | |
| Change at Month 24 (n =503) | -0.21 (± 0.534) | | | |
| Change at Month 30 (n =473) | -0.23 (± 0.533) | | | |
| Change at Month 36 (n =385) | -0.24 (± 0.589) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Usual Activities Domain at Months 1, 6, 12, 18, 24, 30 and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Usual Activities Domain at Months 1, 6, 12, 18, 24, 30 and 36 |
|-----------------|--|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L usual activities domain score were reported in this measure. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | -0.27 (± 0.588) | | | |
| Change at Month 6 (n =635) | -0.30 (± 0.539) | | | |

| | | | | |
|-----------------------------|-----------------|--|--|--|
| Change at Month 12 (n =582) | -0.33 (± 0.547) | | | |
| Change at Month 18 (n =536) | -0.32 (± 0.579) | | | |
| Change at Month 24 (n =505) | -0.36 (± 0.547) | | | |
| Change at Month 30 (n =474) | -0.34 (± 0.571) | | | |
| Change at Month 36 (n =386) | -0.35 (± 0.594) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Pain/Discomfort Domain at Months 1, 6, 12, 18, 24, 30 and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Pain/Discomfort Domain at Months 1, 6, 12, 18, 24, 30 and 36 |
|-----------------|---|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L pain/discomfort domain score were reported in this endpoint. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | -0.31 (± 0.557) | | | |
| Change at Month 6 (n =635) | -0.32 (± 0.570) | | | |
| Change at Month 12 (n =582) | -0.36 (± 0.568) | | | |
| Change at Month 18 (n =536) | -0.40 (± 0.584) | | | |
| Change at Month 24 (n =505) | -0.41 (± 0.602) | | | |
| Change at Month 30 (n =474) | -0.41 (± 0.601) | | | |
| Change at Month 36 (n =386) | -0.40 (± 0.613) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Anxiety/Depression Domain at Months 1, 6, 12, 18, 24, 30 and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Anxiety/Depression Domain at Months 1, 6, 12, 18, 24, 30 and 36 |
|-----------------|--|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L anxiety/depression domain score were reported in this endpoint. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | -0.23 (± 0.600) | | | |
| Change at Month 6 (n =635) | -0.26 (± 0.623) | | | |
| Change at Month 12 (n =582) | -0.25 (± 0.594) | | | |
| Change at Month 18 (n =536) | -0.26 (± 0.604) | | | |
| Change at Month 24 (n =505) | -0.29 (± 0.605) | | | |
| Change at Month 30 (n =473) | -0.31 (± 0.608) | | | |
| Change at Month 36 (n =386) | -0.29 (± 0.651) | | | |

Statistical analyses

Secondary: Main Study: Change From Baseline in EuroQol - Visual Analog Scale (EQ-VAS) Your Own Health State Today Domain at Months 1, 6, 12, 18, 24, 30 and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in EuroQol - Visual Analog Scale (EQ-VAS) Your Own Health State Today Domain at Months 1, 6, 12, 18, 24, 30 and 36 |
|-----------------|---|

End point description:

The EQ VAS recorded the subject's self-rated health on a vertical VAS as standard vertical 0 (worst imaginable health state) to 100 mm (best imaginable health state) (similar to a thermometer) for recording an individual's rating for their current health-related quality of life state; higher score indicated a better health state. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: millimeter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | 14.12 (± 24.928) | | | |
| Change at Month 6 (n =636) | 15.71 (± 25.871) | | | |
| Change at Month 12 (n =582) | 16.00 (± 24.896) | | | |
| Change at Month 18 (n =535) | 16.68 (± 24.746) | | | |
| Change at Month 24 (n =505) | 17.43 (± 25.226) | | | |
| Change at Month 30 (n =473) | 17.87 (± 25.363) | | | |
| Change at Month 36 (n =386) | 18.07 (± 25.185) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Score at Months 1, 6, 12, 18, 24, 30 and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Score at Months 1, 6, 12, 18, 24, 30 and 36 |
|-----------------|--|

End point description:

FACIT-F:13-item questionnaire, each item scaled on 0(not at all) to 4(very much).3 endpoints derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less

daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing usual activities,frustrated by being too tired to do things wanted to do,had to limit social activity because tired);3)change in FACIT-F total score(0-52)= Summing 13 items,higher score indicated lower level of fatigue, better subject status.All responses added with equal weight to get total score.FAS.n=subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | 7.0 (± 9.78) | | | |
| Change at Month 6 (n =636) | 7.7 (± 10.13) | | | |
| Change at Month 12 (n =582) | 7.8 (± 9.70) | | | |
| Change at Month 18 (n =536) | 8.1 (± 10.06) | | | |
| Change at Month 24 (n =506) | 8.3 (± 10.61) | | | |
| Change at Month 30 (n =474) | 8.7 (± 10.93) | | | |
| Change at Month 36 (n =386) | 9.1 (± 11.05) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Experience Domain Score at Months 1, 6, 12, 18, 24, 30 and 36

| | |
|-----------------|--|
| End point title | Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Experience Domain Score at Months 1, 6, 12, 18, 24, 30 and 36 |
|-----------------|--|

End point description:

FACIT-F:13-item questionnaire, each item scaled on 0(not at all) to 4(very much).3 endpoints derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing usual activities,frustrated by being too tired to do things wanted to do,had to limit social activity because tired);3)change in FACIT-F total score(0-52)= Summing 13 items,higher score indicated lower level of fatigue, better subject status.All responses added with equal weight to get total score.FAS.n=subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =674) | 3.1 (± 4.47) | | | |
| Change at Month 6 (n =636) | 3.4 (± 4.61) | | | |
| Change at Month 12 (n =582) | 3.5 (± 4.48) | | | |
| Change at Month 18 (n =536) | 3.6 (± 4.63) | | | |
| Change at Month 24 (n =506) | 3.7 (± 4.93) | | | |
| Change at Month 30 (n =474) | 3.9 (± 5.02) | | | |
| Change at Month 36 (n =386) | 4.0 (± 4.90) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Impact Domain Score at Months 1, 6, 12, 18, 24, 30, and 36

| | |
|-----------------|---|
| End point title | Main Study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Impact Domain Score at Months 1, 6, 12, 18, 24, 30, and 36 |
|-----------------|---|

End point description:

FACIT-F:13-item questionnaire, each item scaled on 0(not at all) to 4(very much).3 endpoints derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing usual activities,frustrated by being too tired to do things wanted to do,had to limit social activity because tired); 3)change in FACIT-F total score(0-52,higher score indicated lower level of fatigue,better subject status)=summing 13 items,all responses added with equal weight to get total score.FAS. n=subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Main Study: Baseline (Day 1), Months 1, 6, 12, 18, 24, 30, and 36

| End point values | Tofacitinib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 686 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n= 674) | 3.9 (± 5.98) | | | |
| Change at Month 6 (n= 636) | 4.2 (± 6.19) | | | |
| Change at Month 12 (n= 582) | 4.4 (± 5.88) | | | |
| Change at Month 18 (n= 536) | 4.5 (± 6.05) | | | |
| Change at Month 24 (n= 506) | 4.6 (± 6.34) | | | |
| Change at Month 30 (n= 474) | 4.8 (± 6.46) | | | |

| | | | | |
|-----------------------------|--------------|--|--|--|
| Change at Month 36 (n= 386) | 5.0 (± 6.77) | | | |
|-----------------------------|--------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Sub-study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Months 1, 3, 9 and 12

| | |
|--|---|
| End point title | Sub-study: Change From Baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Months 1, 3, 9 and 12 |
| End point description: HAQ-DI assesses the degree of difficulty a subject has experienced during the past week in 8 domains of daily living activities: dressing/grooming, arising, eating, walking, reach, grip, hygiene, and other activities. There were total of 2-3 items distributed in these 8 domains. Each item was scored for level of difficulty on a 4-point scale from 0 to 3: 0= no difficulty; 1= some difficulty; 2= much difficulty; 3= unable to do. Overall score was computed as the sum of domain score and divided by the number of domains answered. Total possible score range 0 (least difficulty) and 3 (extreme difficulty), where higher score indicate more difficulty while performing daily living activities. FAS for sub-study included all subjects who were randomized to the sub-study and received at least 1 dose of (tofacitinib, MTX or placebo). | |
| End point type | Secondary |
| End point timeframe: Sub-study: Baseline (Day 1), Months 1, 3, 9 and 12 | |

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.0164 (± 0.02438) | 0.0322 (± 0.02411) | | |
| Change at Month 3 | 0.0057 (± 0.02512) | 0.0381 (± 0.02474) | | |
| Change at Month 9 | 0.0720 (± 0.03195) | 0.0663 (± 0.03125) | | |
| Change at Month 12 | 0.0467 (± 0.02998) | 0.0563 (± 0.02941) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 1: Results were based on a repeated measures model with the fixed effects of | |

treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.0486 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0192 |
| upper limit | 0.1163 |

Statistical analysis title

Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.0325 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0372 |
| upper limit | 0.1021 |

Statistical analysis title

Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.0058 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0941 |
| upper limit | 0.0825 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.0096 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0734 |
| upper limit | 0.0927 |

Secondary: Sub-study: Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) at Months 1, 3, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Psoriatic Arthritis Disease Activity Score (PASDAS) at Months 1, 3, 9 and 12 |
|-----------------|---|

End point description:

PASDAS was composite PsA disease activity score that included following components: Physician and patient global assessment of disease activity (assessed on a 0-100 VAS) in mm, swollen (66 joints) and tender joint counts (68 joints), Leeds enthesitis index (enthesitis assessed at 6 sites; total score of 0-6), tender dactylitic digit score (scored on a scale of 0-3, where 0= no tenderness and 3= extreme tenderness), SF-36 physical component summary (norm-based domain score were used in analyses; with a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity) and RP in mg/L. PASDAS was composite score and was a weighted index with score range of 0 to 10, where higher score indicated more severe disease. FAS of sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 0.000 (± 0.0701) | 0.032 (± 0.0696) | | |
| Change at Month 3 | 0.188 (± 0.0869) | 0.165 (± 0.0868) | | |
| Change at Month 9 | 0.158 (± 0.0934) | 0.371 (± 0.0912) | | |
| Change at Month 12 | 0.194 (± 0.0898) | 0.133 (± 0.0882) | | |

Statistical analyses

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.032 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.163 |
| upper limit | 0.227 |

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.024 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.266 |
| upper limit | 0.219 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.213 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.045 |
| upper limit | 0.47 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.061 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.309 |
| upper limit | 0.188 |

Secondary: Sub-study: Percentage of Subjects Achieving Psoriatic Arthritis Response Criteria (PsARC) at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Percentage of Subjects Achieving Psoriatic Arthritis Response Criteria (PsARC) at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

PsARC was comprised of 4 clinical improvement criteria: $\geq 20\%$ improvement in PhyGA, $\geq 20\%$ improvement in PtGA; and $\geq 30\%$ reduction in the number of tender joints; and $\geq 30\%$ reduction in the number of swollen joints. PtGA: subject assessed health on VAS, 0 mm (very well) to 100 mm (worst health condition), higher score = worse condition. PhyGA: physician judged subjects' pain on VAS, 0 (no pain) to 100 mm (extreme pain), higher score = more pain. To achieve a clinical response, the subject must improve in 2 of the 4 PsARC criteria, 1 of which has to be the number of tender or swollen joints and none of the 4 score could worsen. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Months 1, 3, 6, 9 and 12 | |

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Month 1 | 12.36 | 12.22 | | |
| Month 3 | 11.24 | 6.67 | | |
| Month 6 | 12.36 | 6.67 | | |
| Month 9 | 12.36 | 10.00 | | |
| Month 12 | 13.48 | 3.33 | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Month 1: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -0.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.76 |
| upper limit | 9.48 |

| | |
|--|--|
| | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|--|--|

| | |
|---|--|
| Statistical analysis title | |
| Statistical analysis description: | |
| Month 3: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -4.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.91 |
| upper limit | 3.77 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Month 6: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -5.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.26 |
| upper limit | 2.87 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Month 9: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -2.36 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.59 |
| upper limit | 6.87 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Month 12: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | -10.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.16 |
| upper limit | -2.14 |

Secondary: Sub-study: Change From Baseline in Physician's Global Assessment of Psoriasis (PGA-PsO) Score (For Subjects With Baseline PGA-PsO Score >0) at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Physician's Global Assessment of Psoriasis (PGA-PsO) Score (For Subjects With Baseline PGA-PsO Score >0) at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

The PGA-PsO was a 5-point scale, reflecting a global consideration of the erythema, induration, and scaling across all psoriatic lesions. Average erythema, induration, and scaling were scored separately over the whole body according to a 5-point severity scale (0-4). Higher score indicated higher disease severity. Severity score for each erythema, induration and scaling were summed and averaged after which the total average was rounded to the nearest whole number score to determine a PGA-PsO score on a scale of 0 to 4 (0= clear, except for any residual discoloration, 1= almost clear, 2= mild, 3= moderate, 4= severe). Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline PGA-PsO score >0.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 33 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.1 (± 0.10) | 0.2 (± 0.11) | | |
| Change at Month 3 | -0.1 (± 0.12) | 0.1 (± 0.14) | | |
| Change at Month 6 | -0.1 (± 0.11) | 0.2 (± 0.12) | | |
| Change at Month 9 | -0.3 (± 0.13) | 0.2 (± 0.13) | | |
| Change at Month 12 | 0.0 (± 0.15) | 0.3 (± 0.15) | | |

Statistical analyses

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 74 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.5 |

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 74 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.2 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.6 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 74 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.6 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 74 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.1 |
| upper limit | 0.8 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 74 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.7 |

Secondary: Sub-study: Percent Change from Baseline in Body Surface Area (BSA) (For Subjects With BSA >0%) With Psoriasis at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Percent Change from Baseline in Body Surface Area (BSA) (For Subjects With BSA >0%) With Psoriasis at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

Assessment of BSA with psoriasis was estimated by means of handprint method, where full palmar hand of subject (fully extended palm, fingers and thumb together) represented approximately 1% of total BSA. Body regions are assigned specific number of handprints with percentage (Head and neck = 10 handprints [1 handprint =10%], upper extremities = 20 handprints [1 handprint =5%], Trunk (including axillae and groin) = 30 handprints [1 handprint =3.33%], lower extremities (including buttocks) = 40 handprints [1 handprint =2.5%]. Number of handprints of psoriatic skin in a body region was used to determine extent (%) to which a body region was involved with psoriasis. Total BSA affected was summation of individual regions affected. Analysis population included all subjects who were randomized to sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline body surface Area >0. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 42 | | |
| Units: percent change | | | | |
| least squares mean (standard error) | | | | |
| At Month 1 (n =44, 42) | 28.47 (± 13.497) | 9.04 (± 13.972) | | |
| At Month 3 (n =44, 41) | 43.58 (± 18.679) | 13.47 (± 19.348) | | |
| At Month 6 (n =42, 41) | 41.51 (± 20.745) | 17.19 (± 21.157) | | |
| At Month 9 (n =40, 40) | 35.36 (± 17.309) | 23.72 (± 17.691) | | |
| At Month 12 (n =39, 38) | 34.74 (± 19.909) | 41.75 (± 20.333) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: At Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -19.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -58.06 |
| upper limit | 19.21 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: At Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -30.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -83.58 |
| upper limit | 23.37 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: At Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -24.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -83.35 |
| upper limit | 34.69 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

At Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -11.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -60.87 |
| upper limit | 37.58 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

At Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 7.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -49.73 |
| upper limit | 63.77 |

Secondary: Sub-study: Change From Baseline in Dactylitis Severity Score (DSS) (For Subjects with Baseline DSS >0) at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in Dactylitis Severity Score (DSS) (For Subjects with Baseline DSS >0) at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

Dactylitis was characterized by swelling of the entire finger or toe. The DSS was a function of finger circumference and tenderness, assessed and summed across all dactylitic digits. The severity of dactylitis was scored on a scale of 0-3, where 0 =no tenderness and 3 =extreme tenderness in each digit of the hands and feet. The range of total dactylitis score for a subject was 0-60. Higher score indicated greater degree of tenderness. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline DSS >0. 99999 =SD could not be estimated because only 1 subjects was analyzed. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|--------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 1 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Month 1 (n =7, 1) | -0.4 (± 0.79) | 0.0 (± 99999) | | |
| Change at Month 3 (n =6, 1) | -0.3 (± 0.52) | -1.0 (± 99999) | | |
| Change at Month 6 (n =6, 1) | -0.3 (± 0.52) | -1.0 (± 99999) | | |
| Change at Month 9 (n =6, 1) | -0.3 (± 0.52) | -1.0 (± 99999) | | |
| Change at Month 12(n =6, 1) | -0.3 (± 0.52) | -1.0 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Sub-study: Percentage of Subjects with Absence of Dactylitis (For Subjects With Baseline DSS >0) at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Percentage of Subjects with Absence of Dactylitis (For Subjects With Baseline DSS >0) at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

Dactylitis was characterized by swelling of the entire finger or toe. The DSS was a function of finger circumference and tenderness, assessed and summed across all dactylitic digits. The severity of dactylitis was scored on a scale of 0-3, where 0 =no tenderness and 3 =extreme tenderness in each digit of the hands and feet. The range of total dactylitis score for a subject was 0-60. Higher score indicated greater degree of tenderness. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline DSS >0.

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

End point timeframe:

Sub-study: Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 1 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Month 1 | 14.29 | 0.0 | | |
| Month 3 | 14.29 | 0.0 | | |
| Month 6 | 14.29 | 0.0 | | |
| Month 9 | 14.29 | 0.0 | | |
| Month 12 | 14.29 | 0.0 | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Month 1: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 8 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 6.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -59.58 |
| upper limit | 72.08 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Month 3: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 8 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 6.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -59.58 |
| upper limit | 72.08 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Month 6: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 8 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 6.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -59.58 |
| upper limit | 72.08 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Month 9: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 8 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 6.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -59.58 |
| upper limit | 72.08 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Month 12: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 8 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 6.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -59.58 |
| upper limit | 72.08 |

Secondary: Sub-study: Change From Baseline in Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI >0) at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI >0) at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

Enthesitis was inflammation in the tendon, ligament, and joint capsule fiber insertion into bone. The LEI assessed enthesitis in 6 sites including (right and left): lateral epicondyle humerus, medial femoral condyle and Achilles tendon insertion. Tenderness is recorded as either present (score 1) or absent (score 0) for each of the 6 sites for a total score of 0-6. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline Leeds enthesitis index >0. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 16 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 (n =15, 16) | -0.2 (± 0.25) | -0.4 (± 0.24) | | |
| Change at Month 3 (n =15, 15) | -0.3 (± 0.23) | -0.5 (± 0.23) | | |
| Change at Month 6 (n =15, 16) | -0.5 (± 0.29) | -0.7 (± 0.28) | | |
| Change at Month 9 (n =15, 16) | -0.3 (± 0.29) | 0.0 (± 0.28) | | |
| Change at Month 12 (n =15, 15) | -0.5 (± 0.28) | -0.3 (± 0.27) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 0.5 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 0.5 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance | |

matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 0.6 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 1.1 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 1 |

Secondary: Sub-study: Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI =0) at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI =0) at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

Enthesitis was inflammation in the tendon, ligament, and joint capsule fiber insertion into bone. The LEI assessed enthesitis in 6 sites including (right and left): lateral epicondyle humerus, medial femoral condyle and Achilles tendon insertion. Tenderness is recorded as either present (score 1) or absent (score 0) for each of the 6 sites for a total score of 0-6. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline LEI =0. "n" =subjects evaluable for this endpoint at specified time points.

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

End point timeframe:

Sub-study: Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|--------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 74 | 74 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Month 1 (n =72, 73) | 0.2 (± 0.64) | 0.1 (± 0.58) | | |
| Month 3 (n =71, 72) | 0.2 (± 0.56) | 0.0 (± 0.24) | | |
| Month 6 (n =69, 72) | 0.2 (± 0.76) | 0.2 (± 0.82) | | |
| Month 9 (n =68, 71) | 0.1 (± 0.24) | 0.1 (± 0.46) | | |
| Month 12 (n = 68, 70) | 0.2 (± 0.67) | 0.1 (± 0.49) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Sub-study: Percentage of Subjects With Absence of Enthesitis Assessed Using Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI >0) at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Percentage of Subjects With Absence of Enthesitis Assessed Using Leeds Enthesitis Index (LEI) (For Subjects with Baseline LEI >0) at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

Enthesitis was inflammation in the tendon, ligament, and joint capsule fiber insertion into bone. The LEI assessed enthesitis in 6 sites including (right and left): lateral epicondyle humerus, medial femoral condyle and achilles tendon insertion. Tenderness is recorded as either present (score 1) or absent (score 0) for each of the 6 sites for a total score of 0-6. Higher score indicated a greater number of sites that are affected by enthesitis. Analysis population included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo) with baseline LEI >0.

| | |
|-------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Sub-study: Months 1, 3, 6, 9 and 12 | |

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 16 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Month 1 | 13.33 | 25.00 | | |
| Month 3 | 13.33 | 43.75 | | |
| Month 6 | 26.67 | 56.25 | | |
| Month 9 | 13.33 | 37.50 | | |
| Month 12 | 26.67 | 43.75 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Month 1: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 11.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.65 |
| upper limit | 38.98 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Month 3: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------------------------|
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 30.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 60.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Month 6: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 29.58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.46 |
| upper limit | 62.62 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Month 9: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 24.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.14 |
| upper limit | 53.47 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Month 12: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 17.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.96 |
| upper limit | 50.12 |

Secondary: Sub-study: Percentage of Subjects With Minimal Disease Activity (MDA) at Months 1, 3, 6, 9 and 12

| | |
|--|---|
| End point title | Sub-study: Percentage of Subjects With Minimal Disease Activity (MDA) at Months 1, 3, 6, 9 and 12 |
| End point description: | |
| A psoriatic arthritis subject was considered with MDA if subject had ≥ 5 of 7 criteria: 1) tender/painful joint count ≤ 1 ; (2) swollen joint count ≤ 1 ; (3) BSA $\leq 3\%$; (4) Patient Assessment of Arthritis Pain (VAS) ≤ 15 mm; (5) PtGA (VAS) ≤ 20 mm; (6) HAQ-DI score ≤ 0.5 ; (7) tender enthesal points (using LEI) ≤ 1 . FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo). | |
| End point type | Secondary |
| End point timeframe: | |
| Sub-study: Months 1, 3, 6, 9 and 12 | |

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Month 1 | 50.56 | 55.56 | | |
| Month 3 | 50.56 | 54.44 | | |
| Month 6 | 46.07 | 48.89 | | |
| Month 9 | 42.70 | 46.67 | | |
| Month 12 | 41.57 | 44.44 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Month 1: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 4.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.61 |
| upper limit | 19.6 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Month 3: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 3.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.74 |
| upper limit | 18.5 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Month 6: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 2.82 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.8 |
| upper limit | 17.45 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Month 9: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 3.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.58 |
| upper limit | 18.52 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Month 12: Two-sided 95% CI was based on the normal approximation for the difference in binomial proportions.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Difference in percentage of subjects |
| Point estimate | 2.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.63 |
| upper limit | 17.37 |

Secondary: Sub-study: Change From Baseline in Tender/Painful Joint Count at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Tender/Painful Joint Count at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

68 joints were assessed to determine joints that are considered tender or painful. Response to pressure/motion on each joint was assessed using the following scale: Present/Absent/Not Done/Not Applicable (to be used for artificial or missing joints). The 68 joints assessed were: 1) Upper Body: temporomandibular, sternoclavicular, acromioclavicular. 2) Upper Extremity: shoulder, elbow, wrist (includes radiocarpal, carpal and carpometacarpal considered as one unit), metacarpophalangeals (MCP I, II, III, IV, V), thumb interphalangeal (IP), proximal interphalangeals (PIP II, III, IV, V), distal interphalangeals (DIP II, III, IV, V). 3) Lower Extremity: hip, knee, ankle, tarsus (includes subtalar, transverse tarsal and tarsometatarsal considered as one unit), metatarsophalangeals (MTP I, II, III, IV, V), great toe IP, proximal and distal interphalangeals combined (PIP II, III, IV, V). FAS for sub-study was analyzed.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: tender/painful joints | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 0.7 (± 0.37) | 0.3 (± 0.37) | | |
| Change at Month 3 | 1.3 (± 0.44) | 0.9 (± 0.44) | | |
| Change at Month 6 | 0.5 (± 0.37) | 0.5 (± 0.37) | | |
| Change at Month 9 | 0.4 (± 0.33) | 0.4 (± 0.32) | | |
| Change at Month 12 | 0.3 (± 0.32) | 0.5 (± 0.32) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5 |
| upper limit | 0.6 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | 0.8 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 1 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 0.9 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.7 |
| upper limit | 1.1 |

Secondary: Sub-study: Change From Baseline in Swollen Joint Count at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in Swollen Joint Count at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

Joints were assessed for swelling using the following scale: Present/Absent/Not Done/Not Applicable (to be used for artificial or missing joints). Sixty-six (66) joints were assessed for swelling. The 66 joints assessed were: 1) Upper Body: temporomandibular, sternoclavicular, acromioclavicular. 2) Upper Extremity: shoulder, elbow, wrist (includes radiocarpal, carpal and carpometacarpal considered as one unit), metacarpophalangeals (MCP I, II, III, IV, V), thumb interphalangeal (IP), proximal interphalangeals (PIP II, III, IV, V), distal interphalangeals (DIP II, III, IV, V). 3) Lower Extremity: knee, ankle, tarsus (includes subtalar, transverse tarsal and tarsometatarsal considered as one unit), metatarsophalangeals (MTP I, II, III, IV, V), great toe IP, proximal and distal interphalangeals combined (PIP II, III, IV, V). FAS for sub-study was analyzed.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: swollen joints | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.1 (± 0.14) | 99999 (± 0.14) | | |
| Change at Month 3 | 0.3 (± 0.21) | 0.3 (± 0.21) | | |
| Change at Month 6 | 0.1 (± 0.16) | 0.1 (± 0.15) | | |
| Change at Month 9 | 0.0 (± 0.17) | 0.2 (± 0.17) | | |
| Change at Month 12 | 0.1 (± 0.14) | 0.0 (± 0.14) | | |

Statistical analyses

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.3 |
| upper limit | 0.5 |

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 0.6 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.4 |
| upper limit | 0.5 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.3 |
| upper limit | 0.7 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.5 |
| upper limit | 0.3 |

Secondary: Sub-study: Change From Baseline in Physician's Global Assessment of Arthritis (PhyGA) at Months 1, 3, 6, 9 and 12

| | |
|------------------------|---|
| End point title | Sub-study: Change From Baseline in Physician's Global Assessment of Arthritis (PhyGA) at Months 1, 3, 6, 9 and 12 |
| End point description: | The investigator or qualified assessor assessed how the subject's overall arthritis appeared at the time of the visit. This was an evaluation based on the subject's disease signs, functional capacity and physical examination, and independent of the PtGA and Patient Assessment of Arthritis Pain. The investigator's response was recorded using a 100 mm VAS where 0 =PSA not active at all and 100 =PSA extremely active. Higher score indicated more PSA. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo). |
| End point type | Secondary |
| End point timeframe: | Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12 |

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: millimeter | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.42 (± 0.992) | -0.17 (± 0.981) | | |
| Change at Month 3 | 1.98 (± 1.225) | 2.76 (± 1.216) | | |
| Change at Month 6 | 1.18 (± 0.983) | 1.65 (± 0.966) | | |
| Change at Month 9 | 1.18 (± 1.316) | 3.35 (± 1.287) | | |
| Change at Month 12 | 0.86 (± 1.127) | 0.75 (± 1.111) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.51 |
| upper limit | 3.02 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.64 |
| upper limit | 4.18 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.26 |
| upper limit | 3.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 2.18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.46 |
| upper limit | 5.81 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.25 |
| upper limit | 3.01 |

Secondary: Sub-study: Change From Baseline in Patient's Global Assessment of Arthritis (PtGA) at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in Patient's Global Assessment of Arthritis (PtGA) at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

Subjects answered: "Considering all the ways your arthritis affects you, how are you feeling today?" Subject's response were recorded using a 0 - 100 mm VAS where 0 =not affected at all and 100 =extremely affected. Higher score indicated worse condition due to PSA.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: millimeter | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 1.35 (± 1.277) | -0.68 (± 1.264) | | |
| Change at Month 3 | 2.11 (± 1.537) | 1.68 (± 1.516) | | |
| Change at Month | 3.17 (± 1.725) | 4.45 (± 1.690) | | |
| Change at Month 9 | 2.63 (± 1.691) | 3.27 (± 1.655) | | |
| Change at Month 12 | 2.77 (± 1.629) | 2.65 (± 1.602) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|----------------------------|--|

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -2.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.58 |
| upper limit | 1.52 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.69 |
| upper limit | 3.84 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 1.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.48 |
| upper limit | 6.06 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.03 |
| upper limit | 5.32 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.64 |
| upper limit | 4.38 |

Secondary: Sub-study: Change From Baseline in Patient's Assessment of Arthritis Pain at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Patient's Assessment of Arthritis Pain at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

Subjects assessed the severity of their arthritis pain using a 100 millimeter (mm) VAS by placing a mark on the scale between 0 (no pain) and 100 (most severe pain), which corresponded to the magnitude of their pain. Higher scores indicated more severe pain. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo). Higher scores indicated more severe pain.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: millimeter | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.05 (± 1.383) | -1.16 (± 1.370) | | |
| Change at Month 3 | 1.59 (± 1.394) | 0.36 (± 1.380) | | |
| Change at Month 6 | 3.12 (± 1.709) | 4.07 (± 1.674) | | |
| Change at Month 9 | 2.44 (± 1.780) | 4.45 (± 1.741) | | |
| Change at Month 12 | 2.69 (± 1.692) | 3.35 (± 1.664) | | |

Statistical analyses

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.96 |
| upper limit | 2.74 |

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.23 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.11 |
| upper limit | 2.65 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.78 |
| upper limit | 5.69 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 2.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.92 |
| upper limit | 6.93 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.03 |
| upper limit | 5.35 |

Secondary: Sub-study: Change From Baseline in C-Reactive Protein (CRP) at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in C-Reactive Protein (CRP) at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

The test for CRP was a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: mg/L | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.1171 (± 0.71654) | -0.2706 (± 0.70892) | | |
| Change at Month 3 | -0.3625 (± 0.48088) | -0.9285 (± 0.47675) | | |
| Change at Month 6 | 0.5354 (± 0.79954) | -0.2637 (± 0.78002) | | |
| Change at Month 9 | -0.3217 (± 0.59271) | -0.2591 (± 0.57983) | | |
| Change at Month 12 | -0.1005 (± 0.78650) | 0.2667 (± 0.77230) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.1535 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.1444 |
| upper limit | 1.8374 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.566 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.9054 |
| upper limit | 0.7735 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.7991 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.0053 |
| upper limit | 1.4071 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.0626 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5767 |
| upper limit | 1.7018 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.3672 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.8107 |
| upper limit | 2.545 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Component Summary Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Component Summary Score at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

The SF-36v2 acute is a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 8 health domains are aggregated into two summary scores known as the physical component summary (PCS) score and the mental component summary (MCS) score. Norm-based domain scores, PCS and MCS scores are used in the analyses; each of which has a population mean of 50 with a standard deviation (SD) of 10 points, and ranges from minus infinity to plus infinity. A higher PCS score represented better physical health status. FAS of main study included all enrolled subjects who were part of a prior qualifying study, and who received at least one dose of tofacitinib in A3921092.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.55 (± 0.424) | -0.22 (± 0.419) | | |
| Change at Month 3 | -0.90 (± 0.492) | -0.57 (± 0.487) | | |
| Change at Month 6 | -0.65 (± 0.480) | -1.42 (± 0.466) | | |
| Change at Month 9 | -1.09 (± 0.607) | -1.85 (± 0.593) | | |
| Change at Month 12 | -1.52 (± 0.533) | -1.00 (± 0.523) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|----------------------------|--|

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
|-------------------|--|

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.85 |
| upper limit | 1.51 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.33 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.04 |
| upper limit | 1.69 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.09 |
| upper limit | 0.55 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.44 |
| upper limit | 0.91 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.96 |
| upper limit | 2 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Component Summary Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Component Summary Score at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

The SF-36v2 acute is a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. An additional item measures health transition. The 8 health domains are aggregated into two summary scores known as the PCS score and the MCS score. Norm-based domain scores, PCS and MCS scores are used in the

analyses; each of which has a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher MCS score represents better mental health status. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12 | |

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 0.35 (± 0.630) | -0.11 (± 0.622) | | |
| Change at Month 3 | 0.09 (± 0.642) | -0.77 (± 0.634) | | |
| Change at Month 6 | -0.23 (± 0.733) | -0.89 (± 0.713) | | |
| Change at Month 9 | -0.71 (± 0.749) | 0.06 (± 0.731) | | |
| Change at Month 12 | -0.38 (± 0.694) | -0.47 (± 0.681) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.22 |
| upper limit | 1.29 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.65 |
| upper limit | 0.92 |

Statistical analysis title

Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.68 |
| upper limit | 1.36 |

Statistical analysis title

Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.76 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.31 |
| upper limit | 2.83 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.01 |
| upper limit | 1.84 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Functioning Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Physical Functioning Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

SF-36v2 was a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, & mental health. The 10 items of the physical functioning scale represented levels and kinds of limitations between extremes of physical activities, including lifting & carrying groceries; climbing stairs; bending, kneeling, or stooping; walking moderate distances; self-care limitations. The physical functioning items capture the presence & extent of physical limitations using a 3-level response continuum. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher physical functioning domain score represented better physical functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.37 (± 0.472) | -0.15 (± 0.467) | | |
| Change at Month 3 | -0.50 (± 0.562) | -0.33 (± 0.556) | | |
| Change at Month 6 | -0.27 (± 0.586) | -0.80 (± 0.571) | | |
| Change at Month 9 | -1.43 (± 0.657) | -1.11 (± 0.643) | | |
| Change at Month 12 | -1.01 (± 0.676) | -1.02 (± 0.664) | | |

Statistical analyses

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.09 |
| upper limit | 1.53 |

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.39 |
| upper limit | 1.73 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.15 |
| upper limit | 1.08 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.49 |
| upper limit | 2.13 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.89 |
| upper limit | 1.86 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Physical Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role-Physical Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

SF-36v2 acute was a 36-item measure evaluating 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, & mental health. The 4-item role-physical scale covers an array of physical health-related role limitations, including: a) limitations in the kind of work or other usual activities; b) reductions in the amount of time spent on work or other usual activities; c) difficulty performing work or other usual activities; & d) accomplishing less. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher role-physical domain score represented better role-physical functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.27 (± 0.561) | 0.22 (± 0.555) | | |

| | | | | |
|--------------------|----------------------|----------------------|--|--|
| Change at Month 3 | -1.04 (\pm 0.626) | 0.21 (\pm 0.619) | | |
| Change at Month 6 | -1.57 (\pm 0.585) | -0.87 (\pm 0.569) | | |
| Change at Month 9 | -0.64 (\pm 0.638) | -0.44 (\pm 0.624) | | |
| Change at Month 12 | -1.85 (\pm 0.646) | -0.12 (\pm 0.635) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.08 |
| upper limit | 2.05 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 1.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.49 |
| upper limit | 2.99 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.91 |
| upper limit | 2.31 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.57 |
| upper limit | 1.96 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 1.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.06 |
| upper limit | 3.52 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Bodily Pain Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Bodily Pain Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The bodily pain scale comprises of 2 items pertaining to the intensity of bodily pain and extent of interference with normal work activities. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranges from minus infinity to plus infinity. A higher bodily pain domain score represented less bodily pain. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.77 (± 0.617) | -0.06 (± 0.609) | | |
| Change at Month 3 | -1.59 (± 0.661) | -1.24 (± 0.652) | | |
| Change at Month 6 | -0.61 (± 0.686) | -2.42 (± 0.669) | | |
| Change at Month 9 | -1.29 (± 0.808) | -3.05 (± 0.790) | | |
| Change at Month 12 | -1.69 (± 0.719) | -1.99 (± 0.706) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.01 |
| upper limit | 2.42 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.49 |
| upper limit | 2.18 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.7 |
| upper limit | 0.09 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.99 |
| upper limit | 0.48 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.3 |
| upper limit | 1.69 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) General Health Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) General Health Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The general health scale consisted of 5 items including a rating of health and 4 items addressing the respondent's view and expectations of his or her health. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher general health domain score represented better general health perceptions. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 0.20 (± 0.492) | -0.48 (± 0.487) | | |
| Change at Month 3 | 0.34 (± 0.516) | -0.79 (± 0.511) | | |
| Change at Month 6 | 0.24 (± 0.493) | -0.57 (± 0.481) | | |
| Change at Month 9 | -0.48 (± 0.562) | -0.46 (± 0.551) | | |
| Change at Month 12 | -0.32 (± 0.539) | -0.29 (± 0.530) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|----------------------------|--|

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
|-------------------|--|

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.05 |
| upper limit | 0.69 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.57 |
| upper limit | 0.31 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.17 |
| upper limit | 0.56 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.54 |
| upper limit | 1.57 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.46 |
| upper limit | 1.53 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Vitality Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Vitality Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 4-item measure of vitality captures a broad range of subjective evaluations of well-being from feelings of tiredness and being worn out to feeling full of energy all or most of the time. Norm-based domain

scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher vitality domain score represented better vitality. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12 | |

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.04 (± 0.614) | -0.39 (± 0.607) | | |
| Change at Month 3 | -0.26 (± 0.593) | -1.12 (± 0.586) | | |
| Change at Month 6 | 0.01 (± 0.705) | -1.70 (± 0.687) | | |
| Change at Month 9 | -0.80 (± 0.645) | -1.27 (± 0.632) | | |
| Change at Month 12 | -1.04 (± 0.640) | -0.09 (± 0.629) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.06 |
| upper limit | 1.35 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.51 |
| upper limit | 0.79 |

Statistical analysis title

Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.66 |
| upper limit | 0.23 |

Statistical analysis title

Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.47 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.25 |
| upper limit | 1.32 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.82 |
| upper limit | 2.73 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Social Functioning Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Social Functioning Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 2-item social functioning scale assessed health-related effects on quantity and quality of social activities. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher social functioning domain score represented better social functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.99 (± 0.734) | -0.22 (± 0.726) | | |
| Change at Month 3 | -0.80 (± 0.750) | -1.18 (± 0.740) | | |
| Change at Month 6 | -1.16 (± 0.776) | -1.74 (± 0.757) | | |
| Change at Month 9 | -1.50 (± 0.753) | -1.22 (± 0.737) | | |
| Change at Month 12 | -1.81 (± 0.758) | -1.28 (± 0.746) | | |

Statistical analyses

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.27 |
| upper limit | 2.82 |

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.46 |
| upper limit | 1.71 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.72 |
| upper limit | 1.57 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.81 |
| upper limit | 2.36 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.58 |
| upper limit | 2.63 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role Emotional Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Role Emotional Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 3-item role-emotional scale assessed mental health-related role limitations in terms of a) time spent in work or other usual activities; b) amount of work or activities accomplished; c) care with which work or other activities were performed. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher role-emotional domain score represented better role-emotional functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 1.14 (± 0.716) | -0.53 (± 0.707) | | |

| | | | | |
|--------------------|----------------------|----------------------|--|--|
| Change at Month 3 | 0.24 (\pm 0.807) | -0.38 (\pm 0.797) | | |
| Change at Month 6 | -0.72 (\pm 0.788) | -0.82 (\pm 0.769) | | |
| Change at Month 9 | -0.78 (\pm 0.803) | -0.06 (\pm 0.782) | | |
| Change at Month 12 | -0.33 (\pm 0.835) | -1.11 (\pm 0.820) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.67 |
| upper limit | 0.32 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.86 |
| upper limit | 1.63 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.27 |
| upper limit | 2.09 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.49 |
| upper limit | 2.95 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.1 |
| upper limit | 1.53 |

Secondary: Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Health Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Short-Form-36 Health Survey Version 2 (SF-36v2) Mental Health Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

The SF-36v2 acute was a 36-item measure that evaluates 8 domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The 5-item mental health scale includes 1 or more items from each of 4 major mental health dimensions: anxiety, depression, loss of behavioral/emotional control, and psychological well-being. Norm-based domain scores were used in the analyses; each of which had a population mean of 50 with a SD of 10 points, and ranged from minus infinity to plus infinity. A higher mental health domain score represented better mental health functioning. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.30 (± 0.676) | 0.63 (± 0.669) | | |
| Change at Month 3 | -0.42 (± 0.661) | -0.31 (± 0.653) | | |
| Change at Month 6 | -0.01 (± 0.780) | -0.26 (± 0.762) | | |
| Change at Month 9 | -0.72 (± 0.724) | 0.35 (± 0.710) | | |
| Change at Month 12 | -0.37 (± 0.723) | 0.01 (± 0.711) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.95 |
| upper limit | 2.81 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.72 |
| upper limit | 1.95 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.4 |
| upper limit | 1.9 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 1.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.93 |
| upper limit | 3.07 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.62 |
| upper limit | 2.38 |

Secondary: Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Total Score at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

FACIT-F:13-item questionnaire,with each item scaled from 0(not at all) to 4(very much). 3 endpoints were derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing my usual activities,frustrated by being too tired to do things wanted to do,had to limit my social activity because tired); 3)change in FACIT-F total score(0-52):calculated by summing 13 items,higher score indicated lower level of fatigue, better subject status. All responses were added with equal weight to get total score. FAS of sub-study.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -1.9 (± 0.61) | -1.1 (± 0.61) | | |
| Change at Month 3 | -1.8 (± 0.59) | -1.3 (± 0.58) | | |
| Change at Month 6 | -1.3 (± 0.61) | -2.0 (± 0.60) | | |
| Change at Month 9 | -2.1 (± 0.65) | -1.0 (± 0.64) | | |
| Change at Month 12 | -1.4 (± 0.66) | -0.7 (± 0.64) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|----------------------------|--|

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|-------------------|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
|-------------------|--|

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 2.5 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 2.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.4 |
| upper limit | 1 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 2.9 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 2.6 |

Secondary: Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Experience Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Experience Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

FACIT-F:13-item questionnaire, with each item scaled from 0(not at all) to 4(very much). 3 endpoints were derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],

felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing my usual activities,frustrated by being too tired to do things wanted to do,had to limit my social activity because tired); 3)change in FACIT-F total score(0-52,higher score indicated lower level of fatigue, better subject status):calculated by summing 13 items,all responses were added with equal weight to get total score.FAS of sub-study was analyzed.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12 | |

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -0.9 (± 0.29) | -0.5 (± 0.29) | | |
| Change at Month 3 | -0.8 (± 0.31) | -0.9 (± 0.30) | | |
| Change at Month 6 | -0.5 (± 0.29) | -1.3 (± 0.28) | | |
| Change at Month 9 | -0.7 (± 0.31) | -0.8 (± 0.30) | | |
| Change at Month 12 | -0.5 (± 0.31) | -0.5 (± 0.31) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.4 |
| upper limit | 1.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 0.7 |

Statistical analysis title

Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | 0.1 |

Statistical analysis title

Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 0.8 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 0.8 |

Secondary: Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Impact Domain Score at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Impact Domain Score at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

FACIT-F:13-item questionnaire, with each item scaled from 0(not at all) to 4(very much). 3 endpoints were derived:1)change in FACIT-F experience domain(score 0-20, higher score indicate less fatigue experience),calculated by summing 5 items(felt fatigued,felt weak all over,felt listless ["washed out"],felt tired,had energy; 2)change in FACIT-F impact domain(score 0-32,higher score indicate less fatigue impact on daily functioning),calculated by summing remaining 8 items(had trouble starting things as tired,had trouble finishing things as tired,was able to do usual activities,needed to sleep during day,too tired to eat,needed help doing my usual activities,frustrated by being too tired to do things wanted to do,had to limit my social activity because tired); 3)change in FACIT-F total score(0-52,higher score indicated lower level of fatigue, better subject status):calculated by summing 13 items,all responses were added with equal weight to get total score.FAS of sub-study was analyzed.

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | -1.1 (± 0.39) | -0.6 (± 0.39) | | |
| Change at Month 3 | -1.1 (± 0.35) | -0.4 (± 0.35) | | |
| Change at Month 6 | -0.8 (± 0.41) | -0.7 (± 0.40) | | |
| Change at Month 9 | -1.4 (± 0.42) | -0.2 (± 0.41) | | |
| Change at Month 12 | -0.9 (± 0.40) | -0.1 (± 0.40) | | |

Statistical analyses

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 1.6 |

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.7 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.3 |
| upper limit | 1.7 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 1.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 1.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 2.3 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.3 |
| upper limit | 1.9 |

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Mobility Domain at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Mobility Domain at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L mobility domain score were reported in this measure. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 0.0 (± 0.04) | 0.0 (± 0.04) | | |
| Change at Month 3 | 0.0 (± 0.04) | 0.0 (± 0.04) | | |
| Change at Month 6 | 0.0 (± 0.04) | 0.1 (± 0.04) | | |
| Change at Month 9 | 0.0 (± 0.04) | 0.1 (± 0.04) | | |
| Change at Month 12 | 0.0 (± 0.04) | 0.1 (± 0.04) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.2 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.2 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.2 |

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Self-Care Domain at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Self-Care Domain at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L self-care domain score were reported in this measure. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 0.0 (± 0.03) | 0.0 (± 0.03) | | |
| Change at Month 3 | 0.0 (± 0.03) | 0.0 (± 0.03) | | |
| Change at Month 6 | 0.0 (± 0.04) | 0.0 (± 0.03) | | |
| Change at Month 9 | 0.0 (± 0.04) | 0.0 (± 0.04) | | |
| Change at Month 12 | 0.0 (± 0.04) | 0.1 (± 0.04) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|----------------------------|--|

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.1 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.1 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.1 |

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Usual Activities Domain at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Usual Activities Domain at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L usual activities domain score were reported in this measure. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 0.0 (± 0.04) | 0.0 (± 0.04) | | |
| Change at Month 3 | 0.0 (± 0.04) | 0.0 (± 0.04) | | |
| Change at Month 6 | 0.0 (± 0.04) | 0.1 (± 0.04) | | |
| Change at Month 9 | 0.1 (± 0.04) | 0.1 (± 0.04) | | |
| Change at Month 12 | 0.0 (± 0.04) | 0.0 (± 0.04) | | |

Statistical analyses

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.1 |

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |

| | |
|---|--------------------|
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.1 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.2 |

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Pain/Discomfort Domain at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Pain/Discomfort Domain at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L pain/discomfort domain score were reported in this measure. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 0.1 (± 0.04) | 0.0 (± 0.04) | | |
| Change at Month 3 | 0.1 (± 0.04) | 0.1 (± 0.04) | | |
| Change at Month 6 | 0.1 (± 0.04) | 0.1 (± 0.04) | | |
| Change at Month 9 | 0.1 (± 0.05) | 0.1 (± 0.05) | | |

| | | | | |
|--------------------|-------------------|-------------------|--|--|
| Change at Month 12 | 0.1 (\pm 0.05) | 0.2 (\pm 0.05) | | |
|--------------------|-------------------|-------------------|--|--|

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.1 |

| | |
|---|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.2 |

| | |
|--|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
| Statistical analysis description: | |
| Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance | |

matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.1 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 0.2 |

Secondary: Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Anxiety/Depression Domain at Months 1, 3, 6, 9 and 12

| | |
|-----------------|---|
| End point title | Sub-study: Change From Baseline in EuroQol-5D Health Questionnaire 3-Level (EQ-5D-3L) Anxiety/Depression Domain at Months 1, 3, 6, 9 and 12 |
|-----------------|---|

End point description:

EQ-5D-3L, a health profile questionnaire was used to assess quality of life along 5 dimensions i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression) are assessed. The status of each dimension had 3 possible responses (1 =no problem, 2= some problem 3 =severe problems) in the relevant health dimension. Higher score indicated a worsening health condition. Data for change from baseline in EQ-5D-3L anxiety/depression domain score were reported in this endpoint. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 0.1 (± 0.04) | 0.0 (± 0.04) | | |
| Change at Month 3 | 0.0 (± 0.05) | 0.0 (± 0.04) | | |
| Change at Month 6 | 0.1 (± 0.05) | 0.0 (± 0.05) | | |
| Change at Month 9 | 0.1 (± 0.05) | 0.0 (± 0.05) | | |
| Change at Month 12 | 0.1 (± 0.05) | 0.0 (± 0.05) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.2 |
| upper limit | 0.1 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.2 |
| upper limit | 0.1 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.2 |
| upper limit | 0.1 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.3 |
| upper limit | 0 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.2 |
| upper limit | 0 |

Secondary: Sub-study: Change From Baseline in EuroQol - Visual Analog Scale (EQ-VAS) Your Own Health State Today Domain at Months 1, 3, 6, 9 and 12

| | |
|-----------------|--|
| End point title | Sub-study: Change From Baseline in EuroQol - Visual Analog Scale (EQ-VAS) Your Own Health State Today Domain at Months 1, 3, 6, 9 and 12 |
|-----------------|--|

End point description:

The EQ VAS recorded the subject's self-rated health on a vertical VAS as standard verticle 0 (worst imaginable health state) to 100 mm (best imaginable health state) (similar to a thermometer) for recording an individual's rating for their current health-related quality of life state; higher score indicated a better health state. FAS for sub-study included all subjects who were randomized to the sub-study and received at least one dose of the sub-study drug (tofacitinib, MTX or placebo).

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

End point timeframe:

Sub-study: Baseline (Day 1), Months 1, 3, 6, 9 and 12

| End point values | Tofacitinib 5 mg BID + Methotrexate (MTX) | Tofacitinib 5 mg BID + Placebo | | |
|-------------------------------------|---|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: millimeter | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 1 | 2.0 (± 1.19) | -0.9 (± 1.16) | | |
| Change at Month 3 | 0.5 (± 1.54) | -1.1 (± 1.52) | | |
| Change at Month 6 | 4.4 (± 1.41) | -1.9 (± 1.38) | | |
| Change at Month 9 | 2.5 (± 1.59) | -0.4 (± 1.56) | | |
| Change at Month 12 | 3.0 (± 1.82) | -1.9 (± 1.78) | | |

Statistical analyses

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 1: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -2.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.2 |
| upper limit | 0.4 |

| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|---|--|
| Statistical analysis description: | |
| Change at Month 3: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used. | |
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.5 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.8 |
| upper limit | 2.7 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 6: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -6.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.2 |
| upper limit | -2.4 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 9: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -2.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | 1.6 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Tofa 5 mg BID + Placebo vs Tofa 5 mg BID + MTX |
|-----------------------------------|--|

Statistical analysis description:

Change at Month 12: Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction and baseline value; a common unstructured covariance

matrix was used.

| | |
|---|--|
| Comparison groups | Tofacitinib 5 mg BID + Methotrexate (MTX) v Tofacitinib 5 mg BID + Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -4.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.9 |
| upper limit | 0.2 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (Day 1) up to last dose of main study (maximum up to 36 months) if not enrolled into sub-study or from baseline up to last dose of sub-study (maximum up to 48 months) if enrolled into sub-study

Adverse event reporting additional description:

As pre-specified in protocol/SAP, safety data were planned to be assessed as a single group in main study. For main study, analysis of safety data included cumulative data from main and sub-study as single group. Safety data collected in sub-study was analyzed for tofacitinib 5 mg BID + MTX and tofacitinib 5 mg BID + placebo, separately.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 22.0 |

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | All Tofacitinib |
|-----------------------|-----------------|

Reporting group description:

Main Study: Subjects with active PsA received tofacitinib 5 mg oral tablet, BID with or without allowed concomitant DMARDs examples as methotrexate, leflunomide or sulfasalazine, as background therapy, for up to 36 months. Tofacitinib dose was increased to 10 mg BID or decreased back to 5 mg BID per investigator's discretion. Sub-study: Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX capsules orally (dose range from 7.5 to 20 mg per week) or tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules, for up to 12 months.

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

Reporting group description:

Subjects from main study received tofacitinib 5 mg oral tablet BID with MTX matched placebo capsules for up to 12 months.

| | |
|-----------------------|---|
| Reporting group title | Tofacitinib 5 mg BID + Methotrexate (MTX) |
|-----------------------|---|

Reporting group description:

Subjects from main study received tofacitinib 5 mg oral tablet BID along with MTX capsules orally (dose range from 7.5 to 20 mg per week) for up to 12 months.

| Serious adverse events | All Tofacitinib | Tofacitinib 5 mg BID + Placebo | Tofacitinib 5 mg BID + Methotrexate (MTX) |
|---|--------------------|--------------------------------|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 115 / 686 (16.76%) | 4 / 90 (4.44%) | 3 / 89 (3.37%) |
| number of deaths (all causes) | 6 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal cell carcinoma | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder cancer | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 1 / 90 (1.11%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder neoplasm | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic myelomonocytic leukaemia | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal cancer | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medullary thyroid cancer | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic carcinoma metastatic | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer metastatic | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal cancer | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal cell carcinoma | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid neoplasm | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine leiomyoma | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| B-cell lymphoma | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleomorphic adenoma | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post thrombotic syndrome | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion missed | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nodule | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Social circumstances | | | |
| Miscarriage of partner | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast disorder female | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometriosis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|----------------|
| Ovarian cyst | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Apnoea | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiectasis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meconium aspiration syndrome | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|----------------|
| Psychiatric disorders | | | |
| Bipolar I disorder | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bipolar disorder | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Device loosening | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Heart rate decreased | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cartilage injury | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chemical poisoning | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial bones fracture | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fractured sacrum | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hand fracture | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint injury | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ligament injury | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meniscus injury | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin laceration | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal compression fracture | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon rupture | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Forearm fracture | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 1 / 90 (1.11%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina unstable | | | |
| subjects affected / exposed | 3 / 686 (0.44%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prinzmetal angina | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stress cardiomyopathy | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 1 / 90 (1.11%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Presyncope | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient global amnesia | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Lymphadenitis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |

| | | | |
|---|-----------------|----------------|----------------|
| Deafness neurosensory | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Chorioretinopathy | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal adhesions | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Crohn's disease | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematemesis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|----------------|----------------|
| Incarcerated umbilical hernia subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Melaena subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal prolapse subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorder subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders Erythrodermic psoriasis subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders Renal colic subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|----------------|
| Urinary retention | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot deformity | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 4 / 686 (0.58%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|----------------|
| Joint swelling | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 7 / 686 (1.02%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteochondrosis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psoriatic arthropathy | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 1 / 90 (1.11%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal stenosis | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spondylolisthesis | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Synovial cyst | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vertebral foraminal stenosis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vertebral lateral recess stenosis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epiglottitis | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HIV infection | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neurosyphilis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media acute | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 686 (0.29%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyoderma | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serratia sepsis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia herpes viral | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related sepsis | | | |
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Cardiometabolic syndrome | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 686 (0.15%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | All Tofacitinib | Tofacitinib 5 mg BID + Placebo | Tofacitinib 5 mg BID + Methotrexate (MTX) |
|---|--------------------|-----------------------------------|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 457 / 686 (66.62%) | 24 / 90 (26.67%) | 25 / 89 (28.09%) |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 34 / 686 (4.96%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 45 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 21 / 686 (3.06%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 23 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 36 / 686 (5.25%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 44 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 22 / 686 (3.21%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 28 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 15 / 686 (2.19%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 19 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 24 / 686 (3.50%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 24 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 50 / 686 (7.29%) | 2 / 90 (2.22%) | 2 / 89 (2.25%) |
| occurrences (all) | 52 | 2 | 2 |
| Nervous system disorders | | | |

| | | | |
|--|------------------------|---------------------|---------------------|
| Dizziness subjects affected / exposed occurrences (all) | 20 / 686 (2.92%) 22 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 32 / 686 (4.66%) 45 | 0 / 90 (0.00%) 0 | 2 / 89 (2.25%) 2 |
| Sciatica subjects affected / exposed occurrences (all) | 19 / 686 (2.77%) 24 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 15 / 686 (2.19%) 15 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all) | 14 / 686 (2.04%) 14 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 25 / 686 (3.64%) 35 | 3 / 90 (3.33%) 4 | 0 / 89 (0.00%) 0 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 17 / 686 (2.48%) 19 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Dyspepsia subjects affected / exposed occurrences (all) | 15 / 686 (2.19%) 17 | 0 / 90 (0.00%) 0 | 2 / 89 (2.25%) 2 |
| Nausea subjects affected / exposed occurrences (all) | 27 / 686 (3.94%) 32 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 17 / 686 (2.48%) 22 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Oropharyngeal pain | | | |

| | | | |
|---|---------------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 14 / 686 (2.04%) 16 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Psoriasis subjects affected / exposed occurrences (all) | 32 / 686 (4.66%) 40 | 1 / 90 (1.11%) 1 | 2 / 89 (2.25%) 2 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 32 / 686 (4.66%) 44 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 31 / 686 (4.52%) 39 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Psoriatic arthropathy subjects affected / exposed occurrences (all) | 44 / 686 (6.41%) 51 | 0 / 90 (0.00%) 0 | 3 / 89 (3.37%) 3 |
| Intervertebral disc disorder subjects affected / exposed occurrences (all) | 0 / 686 (0.00%) 0 | 2 / 90 (2.22%) 2 | 0 / 89 (0.00%) 0 |
| Osteoporosis subjects affected / exposed occurrences (all) | 0 / 686 (0.00%) 0 | 2 / 90 (2.22%) 2 | 0 / 89 (0.00%) 0 |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) | 67 / 686 (9.77%) 84 | 3 / 90 (3.33%) 3 | 2 / 89 (2.25%) 3 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 19 / 686 (2.77%) 25 | 0 / 90 (0.00%) 0 | 0 / 89 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 104 / 686 (15.16%) 172 | 3 / 90 (3.33%) 4 | 1 / 89 (1.12%) 2 |
| Pharyngitis subjects affected / exposed occurrences (all) | 38 / 686 (5.54%) 48 | 3 / 90 (3.33%) 3 | 3 / 89 (3.37%) 3 |
| Respiratory tract infection | | | |

| | | | |
|------------------------------------|--------------------|----------------|----------------|
| subjects affected / exposed | 17 / 686 (2.48%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 32 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 33 / 686 (4.81%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 44 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 124 / 686 (18.08%) | 4 / 90 (4.44%) | 6 / 89 (6.74%) |
| occurrences (all) | 190 | 4 | 6 |
| Urinary tract infection | | | |
| subjects affected / exposed | 66 / 686 (9.62%) | 4 / 90 (4.44%) | 3 / 89 (3.37%) |
| occurrences (all) | 92 | 5 | 5 |
| Herpes zoster | | | |
| subjects affected / exposed | 26 / 686 (3.79%) | 1 / 90 (1.11%) | 2 / 89 (2.25%) |
| occurrences (all) | 27 | 1 | 2 |
| Influenza | | | |
| subjects affected / exposed | 19 / 686 (2.77%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 23 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 19 / 686 (2.77%) | 1 / 90 (1.11%) | 2 / 89 (2.25%) |
| occurrences (all) | 37 | 2 | 4 |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 14 / 686 (2.04%) | 0 / 90 (0.00%) | 0 / 89 (0.00%) |
| occurrences (all) | 14 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 12 April 2017 | Protocol Summary updated to reflect new sub-study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported