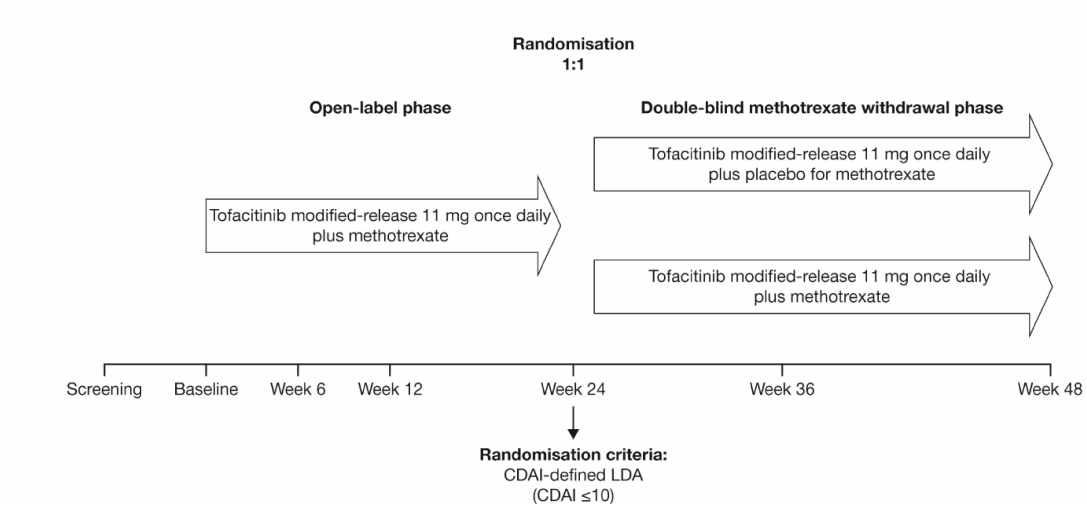
**SUPPLEMENTARY MATERIAL**

The following patient demographics and baseline characteristics were assessed as covariates for the post hoc analyses of baseline predictors of low disease activity and remission:

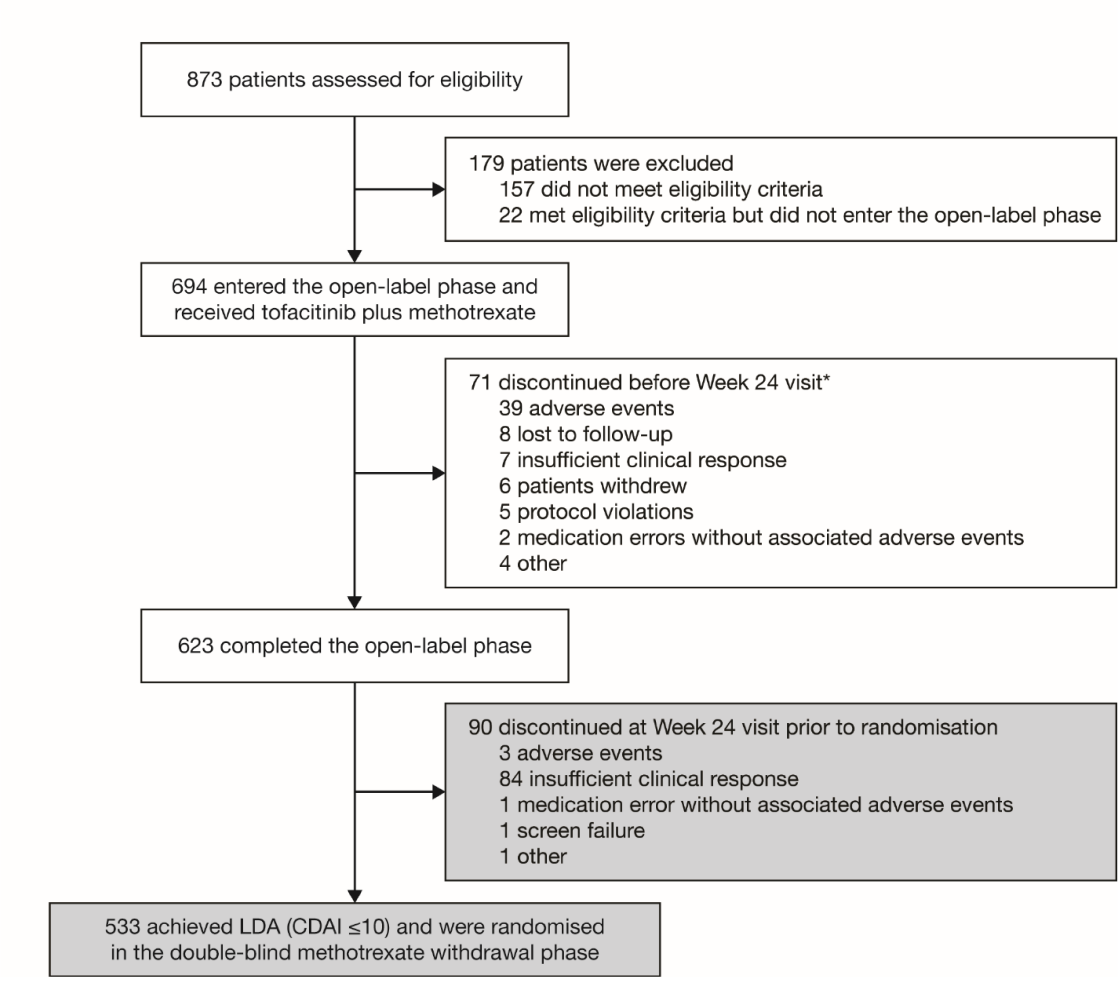
- Age (per 10-year increase)
- Anti-cyclic citrullinated peptide antibody presence (yes/no)
- Body mass index (kg/m$^2$)
- C-reactive protein (per 10-unit increase)
- Clinical disease activity index (per 10-unit increase)
- Disease duration (years)
- Disease severity:
    - Moderate (Disease Activity Score in 28 joints, erythrocyte sedimentation rate DAS28-4[ESR] ≥3.2 and ≤5.1)
    - Severe (DAS28-4[ESR] >5.1)
- ESR (per 10-unit increase)
- Geographic region:
    - United States
    - Europe
    - Latin America
    - Rest of the World
- Health Assessment Questionnaire-Disability Index score (per 1-unit increase)
- Patient Global Assessment of Disease Activity (per 1-unit increase)
- Physician Global Assessment (per 1-unit increase)
- Prior biologic disease-modifying antirheumatic drug use (yes/no)
- Rheumatoid factor (positive/negative)
- Smoking status:
    - Smoker
    - Ex-smoker
    - Non-smoker
- Steroid use (yes/no)
- Swollen joint count (28 joints) (per 1-unit increase)
- Tender joint count (28 joints) (per 1-unit increase)
- Weekly methotrexate dose ranges:
    - <15 mg
    - 15–17.5 mg
    - >17.5 mg

**Online supplementary figure 1** ORAL Shift study design




Randomisation was stratified based on whether the patient had received a prior biologic disease-modifying antirheumatic drug.
CDAI, Clinical Disease Activity Index; LDA, low disease activity.

**Online supplementary figure 2** Patient disposition in the open-label run-in phase



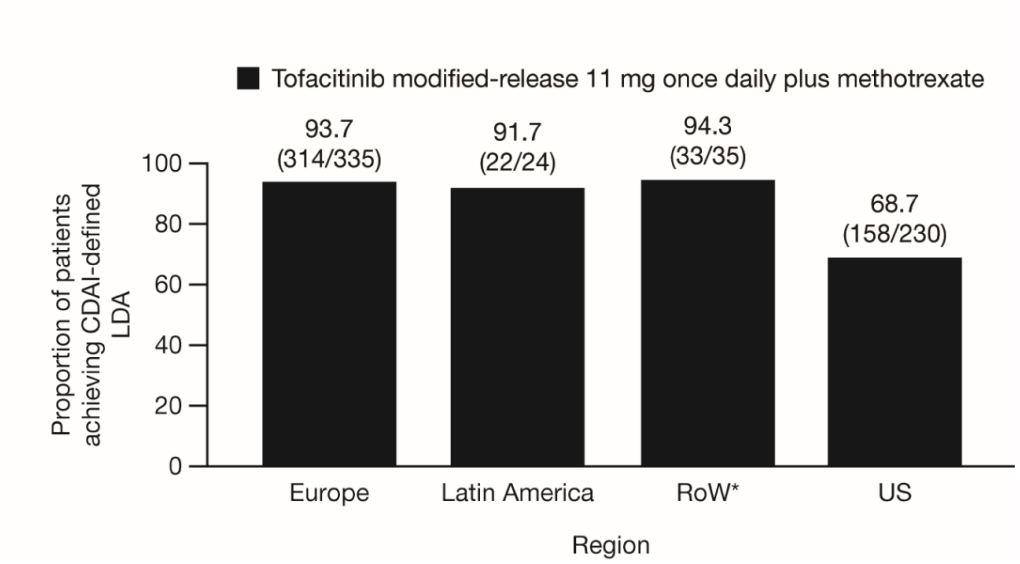

Grey boxes indicate patient discontinuations after completion of the open-label phase through to the double-blind phase, and the number of patients who achieved LDA (CDAI ≤10) and were randomised in the double-blind phase.
*Week 24 data were available for some outcomes for 1 patient who discontinued during the open-label phase.
CDAI, Clinical Disease Activity Index; LDA, low disease activity.

**Online supplementary table 1** Mean (SD) change from baseline* in the SF-36v2 eight domain scores with tofacitinib modified-release 11 mg once daily plus methotrexate at Weeks 12 and 24 of the open-label phase

| | **Tofacitinib modified-release 11 mg once daily plus methotrexate** | |
|---|---|---|
| | Week 12 | Week 24 |
| Physical functioning | 657 | 624 |
| Change from baseline | 5.7 (9.1) | 8.2 (9.9) |
| Role-physical | 657 | 624 |
| Change from baseline | 6.4 (9.0) | 8.7 (9.8) |
| Social functioning | 657 | 624 |
| Change from baseline | 5.9 (10.5) | 7.9 (11.2) |
| Bodily pain | 657 | 624 |
| Change from baseline | 8.6 (9.2) | 11.4 (9.8) |
| Mental health | 657 | 623 |
| Change from baseline | 4.5 (9.4) | 5.8 (10.2) |
| Role-emotional | 657 | 624 |
| Change from baseline | 5.4 (12.1) | 7.5 (12.3) |
| Vitality | 657 | 623 |
| Change from baseline | 6.2 (9.3) | 7.9 (10.4) |
| General health | 657 | 624 |
| Change from baseline | 4.5 (7.2) | 6.2 (8.6) |

Data are n or mean (SD).
*The value at baseline is defined as the last non-missing measurement on or before the first dosing date in the open-label phase.
n, number of patients evaluable for each outcome measure; SD, standard deviation; SF-36v2, Short Form-36 Health Survey (version 2; acute).

**Online supplementary figure 3** Rates of LDA (CDAI ≤10) with tofacitinib modified-release 11 mg once daily plus methotrexate at Week 24 of the open-label phase, stratified by region




Data are % (n/N). Based on observed case data only.
*Australia, Philippines, South Korea and South Africa.
CDAI, Clinical Disease Activity Index; LDA, low disease activity; n, number of patients achieving a response; N, number of patients evaluable; RoW, Rest of the World; US, United States.

**Online supplementary table 2** LDA, remission and ACR20/50/70* and HAQ-DI† response with tofacitinib 11 mg modified-release once daily plus methotrexate at Week 24 of the open-label phase, stratified by prior bDMARD/tsDMARD use

| | **Prior bDMARD/tsDMARD use‡,§** | | |
|---|---|---|---|
| | **Yes** | **Yes** | **No** |
| | **Discontinued due to inadequate pain relief** | **Discontinued due to adverse event or other reason** | |
| **LDA** | | | |
| DAS28-4(ESR) ≤3.2 | 33/70 (47.1%) | 73/172 (42.4%) | 169/376 (45.0%) |
| CDAI ≤10 | 56/71 (78.9%) | 149/172 (86.6%) | 322/381 (84.5%) |
| **Remission** | | | |
| DAS28-4(ESR) <2.6 | 18/70 (25.7%) | 42/172 (24.4%) | 97/376 (25.8%) |
| CDAI ≤2.8 | 18/71 (25.4%) | 41/172 (23.8%) | 87/381 (22.8%) |
| **ACR response*** | | | |
| ACR20 | 58/71 (81.7%) | 149/171 (87.1%) | 329/377 (87.3%) |
| ACR50 | 48/70 (68.6%) | 118/170 (69.4%) | 262/369 (69.1%) |
| ACR70 | 38/70 (54.3%) | 66/172 (38.4%) | 140/377 (37.1%) |
| **HAQ-DI response†** | | | |
| HAQ-DI | 54/71 (76.1%) | 121/172 (70.4%) | 291/381 (76.4%) |

Data are n/N (%). Based on observed case data only.
*20% (ACR20), 50% (ACR50) and 70% (ACR70) improvement from baseline in tender and swollen joint counts and 20%, 50% and 70% improvement in at least three of the five other criteria (PtGA VAS, PGA VAS, HAQ-DI, Pain VAS and CRP).
†HAQ-DI decrease of at least 0.22 from baseline.
‡All bDMARDs were included. Two patients were enrolled before a protocol amendment excluding previous Janus kinase inhibitors; other patients received fostamatinib, apremilast and a Bruton's tyrosine kinase inhibitor.
§Prior bDMARD/tsDMARD use was compared with prior use and discontinuation due to inadequate pain relief, and with prior use and discontinuation due to adverse events or other reasons.
ACR, American College of Rheumatology; bDMARD, biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDA, low disease activity; n, number of patients achieving a response; N, number of patients evaluable for each outcome measure; PGA, Physician Global Assessment; PtGA, Patient Global Assessment of Disease Activity; tsDMARD, targeted synthetic disease-modifying antirheumatic drug; VAS, Visual Analogue Scale.

**Online supplementary table 3** Liver function tests and laboratory test abnormalities of interest with tofacitinib modified-release 11 mg once daily plus methotrexate during the open-label phase

| | **Tofacitinib modified-release 11 mg once daily plus methotrexate (N=688)** |
|---|---|
| Alanine aminotransferase* | |
| ≥1× ULN | 201 (29.2%) |
| ≥2× ULN | 51 (7.4%) |
| ≥3× ULN | 19 (2.8%) |
| Aspartate aminotransferase* | |
| ≥1× ULN | 182 (26.5%) |
| ≥2× ULN | 26 (3.8%) |
| ≥3× ULN | 10 (1.5%) |
| Total bilirubin | |
| ≥1× ULN | 23 (3.3%) |
| ≥2× ULN | 2 (0.3%) |
| ≥3× ULN | 0 |
| Lymphocytes† | |
| <0.8× LLN | 44 (6.4%) |
| Creatine kinase | |
| >2× ULN | 20 (2.9%) |

Data are n (%).
*Two patients discontinued from the study during the open-label phase due to elevated alanine aminotransferase and aspartate aminotransferase levels.
†One patient discontinued from the study during the open-label phase due to low lymphocyte count.
LLN, lower limit of normal; n, number of patients meeting the ULN for each laboratory test; N, number of patients evaluable for each laboratory test; ULN, upper limit of normal.