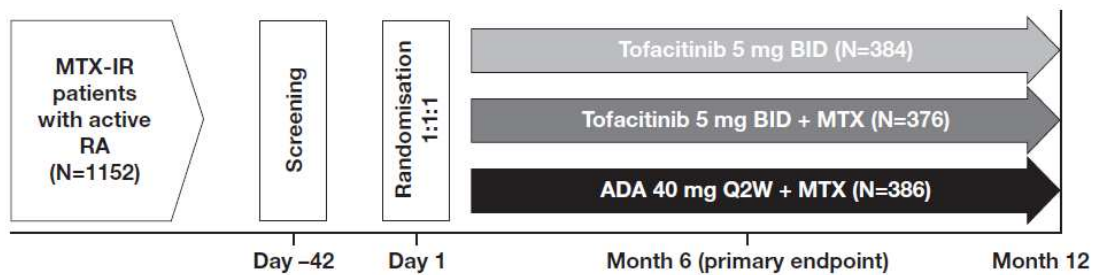


Online supplementary figure S1 ORAL Strategy (A) study design and (B) secondary PRO

measures

A**B**

| Secondary PRO measures | |
|------------------------|---|
| PtGA | Patients answered the question “Considering all the ways your arthritis affects you, how are you feeling today?”. Their response was recorded using a VAS of 0–100 mm, with higher scores representing a higher level of disease activity. |
| Pain | Patients placed a mark on a VAS of 0–100 mm (0=no pain; 100=most severe pain). |
| HAQ-DI | Patients selected a level of difficulty score (0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do) on 8 domains of daily living (dressing and grooming, arising, eating, walking, hygiene, reach, grip and other activities) over the past week. |
| FACIT-F | Patients completed a 13-item questionnaire; instrument scoring yields a range from 0 to 52, with higher scores representing less fatigue. |
| SF-36 | Patients selected responses to convey general health status on 36 items across 8 domains (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health). |

ADA, adalimumab; BID, twice daily; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, inadequate response; MTX, methotrexate; PtGA, Patient Global Assessment of disease activity; Q2W, every other week; RA, rheumatoid arthritis; SF-36, 36-Item Short-Form Health Survey;

VAS, visual analogue scale.

Online supplementary table S1 Proportion of patients reporting PRO scores within normative values (FAS)

| PRO (normative score) | Tofacitinib monotherapy | | | | Tofacitinib + MTX | | | | ADA + MTX | | | |
|----------------------------|-------------------------|-------------------|---------|----------|-------------------|-------------------|---------|-------------------|--------------------|-------------------|-------------------|-------------------|
| | Month 3 | Month 6 | Month 9 | Month 12 | Month 3 | Month 6 | Month 9 | Month 12 | Month 3 | Month 6 | Month 9 | Month 12 |
| | (N=367) | (N=358) | (N=337) | (N=321) | (N=366) | (N=348) | (N=322) | (N=311) | (N=374) | (N=354) | (N=335) | (N=317) |
| HAQ-DI (≤ 0.25), % | 17.2 | 20.7 ^a | 22.0 | 25.2 | 18.6 | 16.7 | 21.1 | 22.2 | 16.6 | 20.3 | 21.6 ^b | 25.3 ^c |
| HAQ-DI (< 0.5), % | 20.7 | 26.1 | 27.0 | 31.2 | 23.5 | 23.0 | 25.5 | 28.3 | 19.3 | 25.1 | 26.9 | 32.3 |
| FACIT-F (≥ 40.1), % | 32.2 ^d | 30.7 | 34.4 | 34.9 | 28.4 | 31.0 | 31.7 | 34.7 | 24.9 ^{e†} | 27.7 | 32.5 | 35.3 |
| FACIT-F (≥ 43.5), % | 17.5 ^d | 20.9 | 24.3 | 24.6 | 16.1 | 19.5 | 20.5 | 26.0 | 14.7 ^e | 20.1 | 22.7 | 27.4 |
| SF-36 domains, % | | | | | | | | | | | | |
| PF (78.79) | 15.8 | 17.9 | 19.3 | 23.1 | 15.6 | 18.4 | 20.2 | 24.1 | 13.6 | 21.5 ^f | 22.8 ^b | 25.6 |
| RP (79.78) | 18.3 | 20.7 | 15.1 | 20.2 | 14.2 ^g | 18.7 ^h | 19.6 | 23.9 ⁱ | 14.2 | 17.2 | 21.5 [†] | 21.8 |
| BP (70.60) | 24.5 | 24.0 | 25.5 | 31.8 | 30.6 | 27.9 | 27.0 | 32.8 | 24.6 | 28.2 | 32.8 [†] | 31.9 |
| GH (68.95) | 17.7 | 19.6 | 16.6 | 18.4 | 15.3 | 14.9 | 18.0 | 16.4 | 15.0 | 18.6 | 20.3 | 20.3 ^c |
| VT (57.21) | 35.7 | 36.3 | 37.4 | 41.1 | 33.3 | 36.8 | 35.7 | 43.7 | 32.1 | 36.4 | 40.0 | 43.2 |

| | | | | | | | | | | | | |
|------------|------|------|------|------|-------------------|-------------------|------|-------------------|------|------|------|------|
| SF (83.30) | 26.7 | 28.8 | 26.1 | 33.0 | 24.6 | 28.7 | 27.6 | 32.2 | 25.9 | 27.1 | 32.5 | 33.4 |
| RE (86.30) | 21.0 | 22.3 | 22.6 | 22.1 | 21.9 ^g | 23.1 ^h | 25.8 | 22.6 ⁱ | 17.9 | 19.8 | 23.9 | 25.9 |
| MH (74.83) | 36.2 | 36.6 | 38.0 | 38.6 | 33.1 | 37.4 | 37.3 | 40.8 | 36.4 | 38.7 | 41.5 | 44.8 |

Normative values for SF-36 domain scores were based on acute-form age-sex norms found in the SF-36 v2 Scoring Manual,[36] combined with frequencies observed in ORAL Strategy.

Normative values for HAQ-DI and FACIT-F have previously been defined.[32-34] Functional remission for HAQ-DI has previously been defined.[32]

^aN=357; ^bN=334; ^cN=316; ^dN=366; ^eN=373; ^fN=353; ^gN=365; ^hN=347; ⁱN=310; [†]p<0.05 ADA + MTX vs tofacitinib monotherapy.

ADA, adalimumab; BP, Bodily Pain; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FAS, full analysis set; GH, General Health; HAQ-DI, Health Assessment Questionnaire-Disability Index; MH, Mental Health; MTX, methotrexate; PRO, patient-reported outcome; PF, Physical Functioning; RE, Role Emotional; RP, Role Physical; SF, Social Functioning; SF-36, 36-Item Short-Form Health Survey; VT, Vitality.

Online supplementary table S2 Baseline SF-36 domain scores and changes from baseline at month 6 (FAS)

| | Baseline, mean (SE) score | | | LSM changes from baseline (\pm SE) at month 6 | | |
|----------------------------|---------------------------|---------------------------|------------------------|--|---------------------------|-------------------------|
| | Tofacitinib | Tofacitinib | ADA + MTX | Tofacitinib | Tofacitinib | ADA + MTX |
| | 5 mg BID (N=384) | 5 mg BID + MTX (N=376) | (N=386) | 5 mg BID (N=384) | 5 mg BID + MTX (N=376) | (N=386) |
| SF-36 domains (norm-based) | | | | | | |
| PF | (N=382) 30.6 (0.48) | (N=376) 30.2 (0.46) | (N=382) 30.0 (0.49) | (N=356) 6.4 (0.52) | (N=348) 7.3 (0.52) | (N=349) 7.3 (0.52) |
| RP | (N=382) 33.4 (0.44) | (N=376) 32.9 (0.45) | (N=382) 33.0 (0.45) | (N=356) 6.7 (0.47) | (N=347) 7.0 (0.47) | (N=350) 6.3 (0.47) |
| BP | (N=382) 32.4 (0.39) | (N=376) 32.1 (0.36) | (N=382) 32.2 (0.38) | (N=356) 8.2 (0.48) | (N=348) 10.3 (0.48)** | (N=350) 9.9 (0.48)†† |
| GH | (N=383) 34.8 (0.42) | (N=375) 34.0 (0.39) | (N=382) 34.8 (0.45) | (N=357) 5.1 (0.44) | (N=347) 6.3 (0.44)* | (N=350) 5.4 (0.44) |
| VT | (N=383) 41.3 (0.50) | (N=376) 39.7 (0.48) | (N=382) 41.0 (0.45) | (N=357) 5.6 (0.48) | (N=348) 6.1 (0.47) | (N=350) 5.7 (0.47) |
| SF | (N=383) 35.3 (0.55) | (N=376) 34.8 (0.52) | (N=382) 35.4 (0.55) | (N=357) 6.3 (0.52) | (N=348) 7.2 (0.52) | (N=350) 6.2 (0.52) |
| RE | (N=382) 32.6 (0.62) | (N=376) 32.5 (0.64) | (N=382) 32.7 (0.64) | (N=356) 6.7 (0.58) | (N=347) 7.7 (0.58) | (N=350) 6.0 (0.58)‡ |
| MH | (N=382) 38.3 (0.59) | (N=376) 38.2 (0.58) | (N=382) 39.0 (0.56) | (N=356) 5.3 (0.52) | (N=348) 5.5 (0.52) | (N=350) 5.0 (0.52) |

* $p < 0.05$, ** $p < 0.01$, tofacitinib + MTX vs tofacitinib monotherapy; †† $p < 0.01$, ADA + MTX vs tofacitinib monotherapy; ‡ $p < 0.05$, tofacitinib + MTX vs ADA + MTX. ADA, adalimumab; BID, twice daily; BP, Bodily Pain; FAS, full analysis set; GH, General Health; LSM, least squares mean; MH, Mental Health; MTX, methotrexate; PF, Physical Functioning; RE, Role Emotional; RP, Role Physical; SE, standard error; SF, Social Functioning; SF-36, 36-Item Short-Form Health Survey; VT, Vitality.

Online supplementary table S3 Proportion of patients reporting improvements \geq MCID in SF-36 domains (FAS)

| % (n/N) | Month 3 | | | Month 6 | | | Month 9 | | | Month 12 | | |
|------------|----------------------------|----------------------|-------------------|----------------------------|----------------------|-------------------|----------------------------|----------------------|--------------------|----------------------------|----------------------|-------------------|
| | Tofacitinib monotherapy | Tofacitinib + MTX | ADA + MTX | Tofacitinib monotherapy | Tofacitinib + MTX | ADA + MTX | Tofacitinib monotherapy | Tofacitinib + MTX | ADA + MTX | Tofacitinib monotherapy | Tofacitinib + MTX | ADA + MTX |
| PF | 47.9 (175/365) | 51.4 (188/366) | 49.5 (183/370) | 52.8 (188/356) | 55.2 (192/348) | 55.6 (194/349) | 56.7 (190/335) | 60.2 (194/322) | 58.5 (193/330) | 58.3 (186/319) | 64.6 (201/311) | 61.1 (192/314) |
| RP | 46.6 (170/365) | 47.1 (172/365) | 45.4 (168/370) | 50.3 (179/356) | 51.9 (180/347) | 48.0 (168/350) | 49.0 (164/335) | 55.6 (179/322) | 52.6 (174/331) | 50.2 (160/319) | 59.7 (185/310)* | 55.4 (174/314) |
| BP | 58.6 (214/365) | 64.5 (236/366) | 59.5 (220/370) | 56.2 (200/356) | 66.4 (231/348)** | 62.9 (220/350) | 58.8 (197/335) | 68.0 (219/322)* | 67.4 (223/331)† | 61.4 (196/319) | 70.4 (219/311)* | 66.2 (208/314) |
| GH | 45.4 (166/366) | 52.6 (192/365)** | 42.2 (156/370) | 46.2 (165/357) | 50.7 (176/347) | 45.1 (158/350) | 44.3 (149/336) | 52.6 (169/321)* | 51.1 (169/331) | 42.2 (135/320) | 54.8 (170/310)** | 46.6 (146/313) |
| VT | 53.3 (195/366) | 56.8 (208/366) | 52.7 (195/370) | 51.0 (182/357) | 58.3 (203/348)* | 55.4 (194/350) | 53.9 (181/336) | 63.7 (205/322)* | 58.3 (193/331) | 53.8 (172/320) | 62.7 (195/311)* | 60.5 (190/314) |
| SF | 62.8 (230/366) | 64.8 (237/366) | 58.9 (218/370) | 57.7 (206/357) | 63.5 (221/348) | 63.1 (221/350) | 59.5 (200/336) | 64.6 (208/322) | 64.0 (212/331) | 60.9 (195/320) | 68.5 (213/311)* | 64.0 (201/314) |
| RE | 46.6 (170/365) | 47.7 (174/365) | 42.2 (156/370) | 46.6 (166/356) | 51.9 (180/347) | 46.3 (162/350) | 49.3 (165/335) | 53.7 (173/322) | 49.2 (163/331) | 47.0 (150/319) | 52.3 (162/310) | 52.2 (164/314) |
| MH | 51.0 (186/365) | 47.0 (172/366) | 48.1 (178/370) | 51.7 (184/356) | 53.4 (186/348) | 48.3 (169/350) | 48.8 (164/336) | 51.2 (165/322) | 51.7 (171/331) | 55.3 (177/320) | 56.9 (177/311) | 52.9 (166/314) |

SF-36 domain MCID: \geq 5-point improvement.* $p < 0.05$; ** $p < 0.01$ tofacitinib + MTX vs tofacitinib monotherapy; † $p < 0.05$ ADA + MTX vs tofacitinib monotherapy; ‡ $p < 0.05$, §§ $p < 0.01$ tofacitinib + MTX vs ADA + MTX.

ADA, adalimumab; BP, Bodily Pain; FAS, full analysis set; GH, General Health; MCID, minimum clinically important difference; MH, Mental Health; MTX, methotrexate; PF, Physical Functioning; RE, Role Emotional; RP, Role Physical; SF, Social Functioning; SF-36, 36-Item Short-Form Health Survey; VT, Vitality.