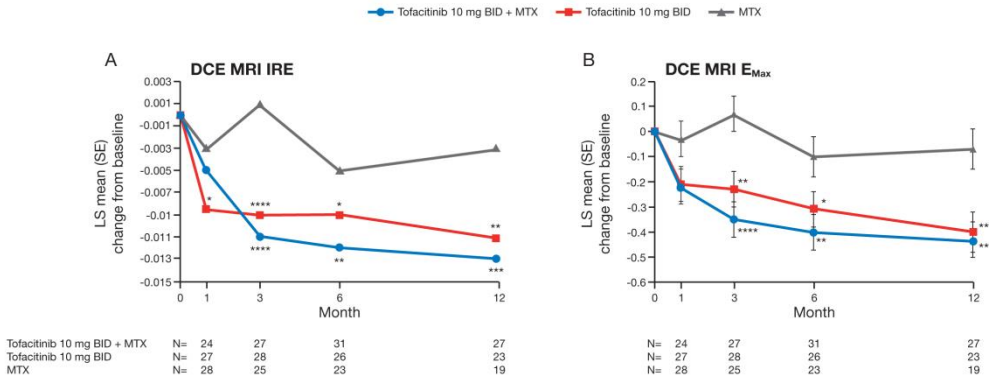
SUPPLEMENTARY MATERIALS

Supplementary Figure 1. LS mean change from baseline in wrist DCE MRI A) IRE, and B) E_{Max} (evaluable set)

Supplementary Figure 1



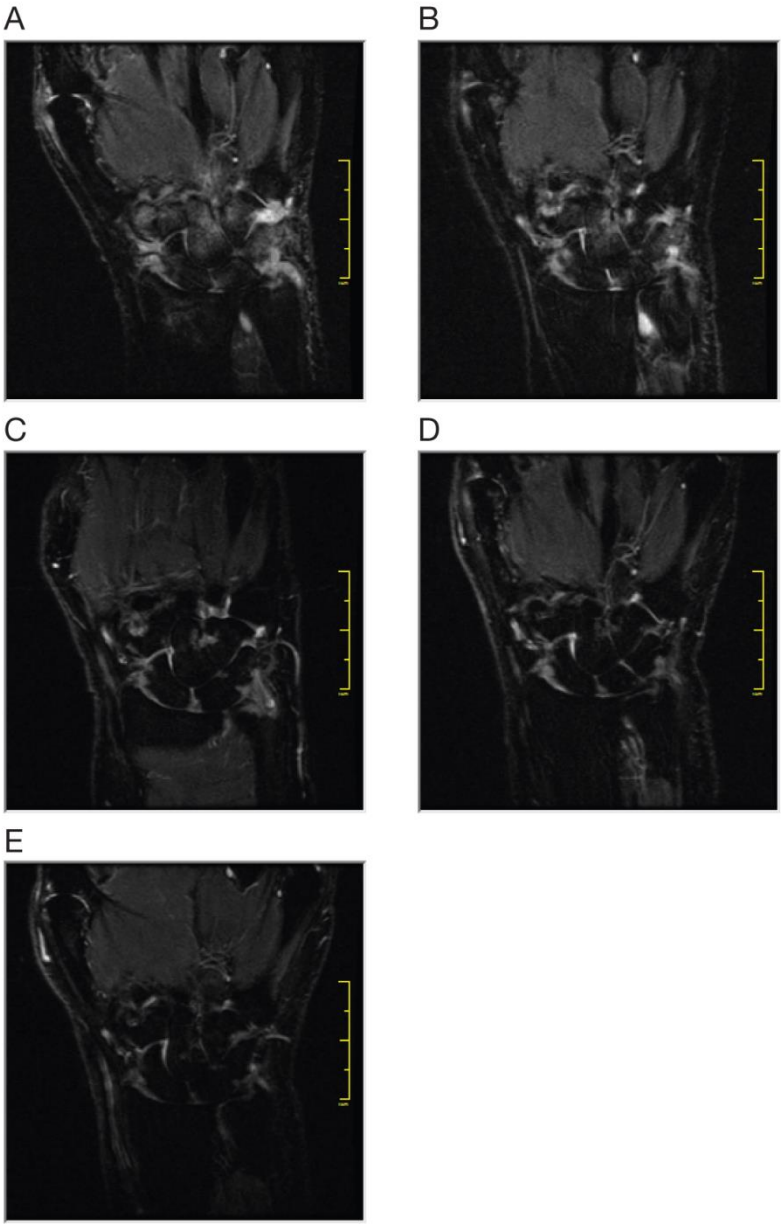
*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 vs MTX monotherapy, using a mixed-effect model for repeated measures.

DCE MRI measurements relate to MRIs of the index wrist using ROIs defined within the area encompassing the distal radioulnar joint, the radiocarpal joint and the intercarpal-carpometacarpophalangeal joints.

BID, twice daily; BME, bone marrow edema; DCE MRI, dynamic contrast-enhanced magnetic resonance imaging; E_{Max}, maximum enhancement; IRE, initial rate of enhancement; LS, least squares; MCP, metacarpophalangeal; MTX, methotrexate; N_{Vox}, number of enhancing voxels; RAMRIQ, quantitative rheumatoid arthritis magnetic resonance imaging score; RAMRIS, rheumatoid arthritis magnetic resonance imaging score; ROI, region of interest; SE, standard error.

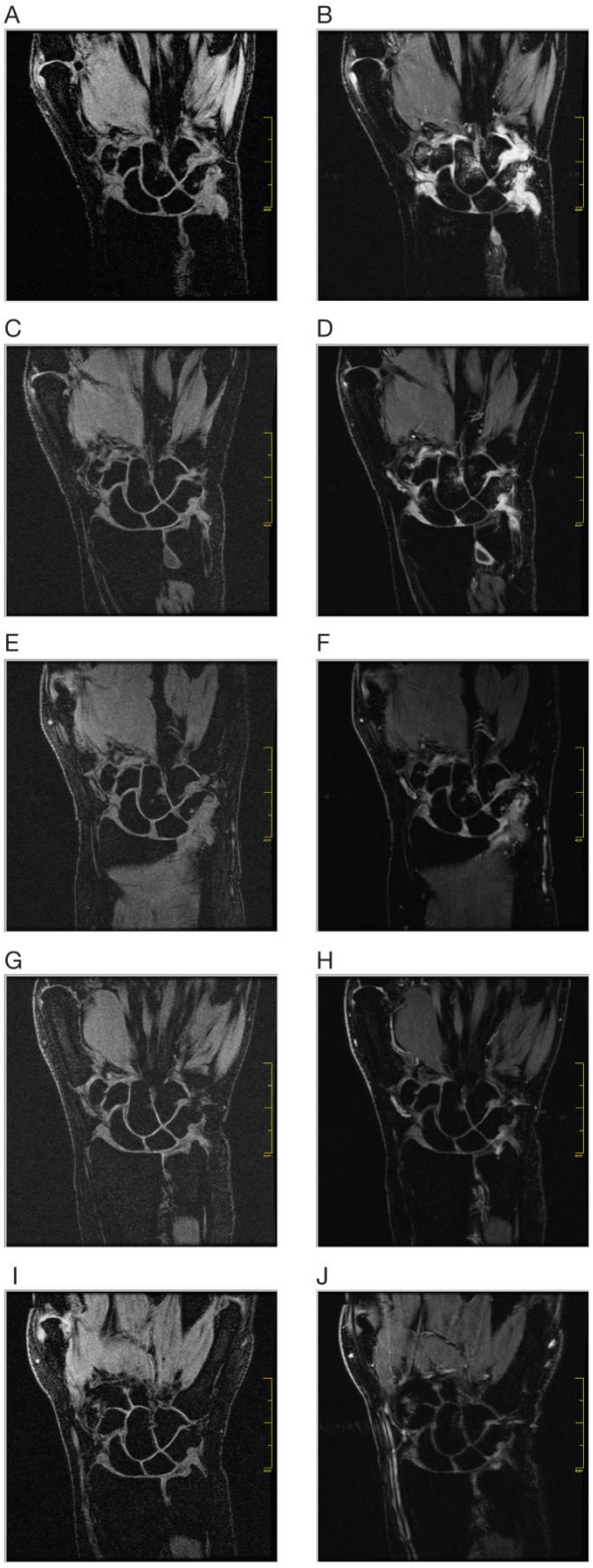
Supplementary Figure 2. Representative images for BME in a patient randomised to tofacitinib monotherapy at A) Baseline, B) Month 1, C) Month 3, D) Month 6, and E) Month 12.

Supplementary Figure 2



Supplementary Figure 3. Representative images for synovitis in a patient randomised to tofacitinib monotherapy at A) baseline pre-contrast, B) baseline post-contrast, C) Month 1 pre-contrast, D) Month 1 post-contrast, E) Month 3 pre-contrast, F) Month 3 post-contrast, G) Month 6 pre-contrast, H) Month 6 post-contrast, I) Month 12 pre-contrast and J) Month 12 post-contrast.

Supplementary Figure 3



Supplementary Table 1. Semi-quantitative and quantitative MRI measures over time (evaluable set)

Mean (SD) [N]	Tofacitinib 10 mg BID + MTX	Tofacitinib 10 mg BID monotherapy	MTX monotherapy
RAMRIS BME			
Baseline/Month 0	1.9 (3.7) [36]	2.6 (3.7) [36]	2.2 (5.1) [37]
Month 1	1.4 (2.3) [28]	2.6 (3.6) [31]	2.3 (5.1) [35]
Month 3	1.1 (1.8) [30]	1.7 (2.5) [32]	2.2 (4.2) [31]
Month 6	0.6 (1.0) [33]	1.2 (2.5) [29]	2.1 (4.2) [28]
Month 12	0.4 (0.9) [29]	0.9 (1.3) [26]	2.7 (4.2) [21]
RAMRIQ BME			
Baseline/Month 0	1.4 (2.8) [36]	1.1 (2.7) [36]	1.4 (2.7) [37]
Month 1	0.8 (1.0) [28]	0.6 (1.0) [30]	2.6 (5.3) [34]
Month 3	0.6 (1.2) [30]	0.4 (0.5) [32]	2.0 (4.1) [28]
Month 6	0.3 (0.7) [33]	0.4 (0.8) [28]	2.2 (5.9) [28]
Month 12	0.3 (0.7) [29]	0.2 (0.2) [25]	2.2 (4.7) [20]
RAMRIS synovitis[a]			
Baseline/Month 0	5.8 (3.8) [36]	5.7 (3.5) [36]	5.3 (3.9) [37]
Month 1	5.3 (3.3) [28]	5.1 (3.1) [31]	5.1 (3.5) [35]
Month 3	5.1 (3.2) [30]	5.0 (3.0) [32]	5.3 (3.8) [31]
Month 6	4.4 (3.4) [33]	4.4 (2.8) [29]	5.0 (3.3) [28]
Month 12	3.5 (2.6) [29]	4.6 (2.7) [26]	5.1 (3.6) [21]
RAMRIQ synovitis			
Baseline/Month 0	7750.4 (5432.8) [36]	7971.8 (5510.1) [36]	6980.7 (6304.8) [37]
Month 1	6584.2 (4530.1) [28]	6173.2 (4436.4) [30]	8140.3 (5989.8) [34]

Month 3	5112.0 (3960.7) [30]	5654.3 (3943.6) [32]	7737.1 (5537.8) [28]
Month 6	3611.2 (2782.0) [33]	4374.3 (3042.0) [28]	7372.7 (5505.2) [28]
Month 12	3564.6 (2609.7) [29]	3841.2 (2357.6) [25]	7369.8 (5278.2) [21]
DCE MRI N_{Vox}			
Baseline/Month 0	3013.6 (3605.6) [34]	2767.6 (2140.2) [32]	3079.8 (3704.9) [32]
Month 1	2899.0 (3675.8) [25]	2476.2 (2370.4) [29]	3301.6 (3731.5) [28]
Month 3	2184.4 (2332.2) [29]	2137.6 (1871.5) [29]	3662.3 (4434.2) [25]
Month 6	1632.8 (1754.0) [33]	1603.9 (1449.9) [27]	3404.4 (4095.2) [23]
Month 12	1584.0 (1632.6) [29]	1535.4 (1475.7) [25]	4060.1 (4566.6) [19]
RAMRIS bone erosions			
Baseline/Month 0	9.4 (10.8) [36]	7.5 (7.6) [36]	12.2 (14.9) [37]
Month 1	9.1 (11.6) [28]	6.0 (5.1) [31]	12.7 (15.2) [35]
Month 3	10.0 (11.4) [30]	7.9 (8.1) [32]	12.7 (15.0) [31]
Month 6	9.5 (11.1) [33]	7.8 (8.2) [29]	9.3 (10.9) [28]
Month 12	10.3 (11.5) [29]	6.6 (6.2) [26]	11.2 (12.0) [21]
RAMRIQ bone erosions			
Baseline/Month 0	1.6 (0.9) [36]	1.6 (0.8) [36]	1.9 (1.3) [37]
Month 1	1.5 (0.9) [28]	1.5 (0.6) [31]	1.9 (1.2) [35]
Month 3	1.5 (0.8) [30]	1.5 (0.7) [32]	1.9 (1.1) [30]
Month 6	1.4 (0.7) [33]	1.5 (0.8) [28]	1.8 (1.1) [28]
Month 12	1.3 (0.6) [29]	1.3 (0.6) [26]	1.8 (1.5) [20]
DCE MRI IRE			
Baseline/Month 0	0.017 (0.021) [34]	0.022 (0.029) [32]	0.013 (0.010) [32]
Month 1	0.012 (0.016) [25]	0.011 (0.009) [29]	0.013 (0.011) [28]
Month 3	0.008 (0.007) [29]	0.009 (0.006) [29]	0.019 (0.017) [25]
Month 6	0.006 (0.005) [33]	0.008 (0.009) [27]	0.014 (0.012) [23]
Month 12	0.006 (0.005) [29]	0.007 (0.004) [25]	0.016 (0.016) [19]

DCE MRI E_{Max}			
Baseline/Month 0	1.885 (0.493) [34]	1.994 (0.453) [32]	1.757 (0.560) [32]
Month 1	1.685 (0.573) [25]	1.756 (0.474) [29]	1.803 (0.576) [28]
Month 3	1.587 (0.453) [29]	1.739 (0.434) [29]	1.935 (0.429) [25]
Month 6	1.502 (0.423) [33]	1.611 (0.406) [27]	1.808 (0.545) [23]
Month 12	1.507 (0.297) [29]	1.553 (0.417) [25]	1.800 (0.409) [19]

[a]LOCF imputation was applied to a total of six assessments with missing MRI component scores across all visits and treatment groups

BID, twice daily; BME, bone marrow edema; DCE MRI, dynamic contrast-enhanced magnetic resonance imaging; E_{Max}, maximum enhancement; IRE, initial rate of enhancement; MTX, methotrexate; N_{Vox}, number of enhancing voxels; RAMRIQ, quantitative rheumatoid arthritis magnetic resonance imaging score; RAMRIS, rheumatoid arthritis magnetic resonance imaging score; SD, standard deviation.

Eligibility criteria

For participants with both hands showing confirmed synovitis, the index hand was chosen according to radiographic evidence of erosions. If erosions were present on both hands, then the hand with the greater burden of synovitis, or the dominant hand if both were equally affected, was designated as the index hand.

The protocol inclusion criteria required evidence of at least one erosion, and this was not confirmed centrally prior to randomization. Based on the central reading of hand and foot radiographs by the van der Heijde modified Sharp score, the following discrepancies with the local assessment were observed: 6 out of 34 patients receiving tofacitinib 10 mg BID + MTX, 4 out of 36 patients receiving tofacitinib 10 mg BID monotherapy, and 7 out of 37 patients receiving MTX monotherapy. These were found to be non-erosive on van der Heijde modified Sharp scoring. However, this may be partly explained by the fact that not all anatomical locations are assessed by this method.

Background arthritis therapy

Patients were permitted to continue any stable background arthritis therapy, which may have included non-steroidal anti-inflammatory drugs (NSAIDs), cyclo-oxygenase (COX)-2 inhibitors, opioids, acetaminophen, and/or low dose oral corticosteroids (≤10 mg prednisone or equivalent per day) throughout the study. Daily dosages of NSAIDs/COX-2 inhibitors and corticosteroids were required to be stable for at least 4 weeks prior to first study dose and to remain stable during the study treatment period through Month 6, except if adjustment was needed to protect a

patient's safety. Intravenous or intramuscular corticosteroids were not permitted during this study.

Handling of missing MRI values

The RAMRIS wrist and MCP synovitis score (range 0 to 21), was obtained by the summation of seven scores, each ranging from 0 to 3. If any of these components was missing, then the missing component was substituted with the last observed component score from the previous visit, so that the full RAMRIS score at a given time point could be a combination of observed measures and the measures from the last recorded measures for missing components (ie, LOCF imputation). This rule was also applicable to the calculation of RAMRIS wrist and MCP BME and erosions scores.