

Supplementary Table S1. Characteristics of patients enrolled in ARM-2 or ARM-3 at baseline.

Patient background at baseline	Whole patients (n=134)	ARM-2 (n=68)	ARM-3 (n=66)	p-value (ARM-2 vs. ARM3)
Age (years)	56.4 ± 15.1, 57.0 [46.0, 68.0]	56.5 ± 14.8, 56.5 [46.5, 67.5]	56.2 ± 15.5, 57.5 [46.0, 68.0]	0.97
Height (cm)	158.1 ± 7.3, 158.0 [153.0, 163.6]	158.6 ± 7.6, 158.5 [153.4, 163.7]	157.7 ± 7.0, 157.6 [152.0, 163.0]	0.56
Weight (kg)	57.9 ± 11.9, 55.7 [49.1, 64.8]	58.5 ± 12.2, 57.9 [49.4, 66.2]	57.3 ± 11.8, 53.7 [49.0, 63.2]	0.40
RA disease duration (days)	23.7 ± 46.7, 13.5 [0.0, 23.8]	26.1 ± 60.0, 12.0 [2.0, 21.5]	21.3 ± 27.4, 14.0 [0.0, 28.0]	0.88
Sex (Female)	107 (80.0)	50 (73.5)	57 (86.4)	0.06
Race (Asian)	134 (100)	68 (100)	66 (100)	–
Smoking status: Never	94 (70.0)	44 (64.7)	50 (75.8)	0.28
Current smoker	22 (16.4)	12 (17.6)	10 (15.2)	
Past smoker	18 (13.4)	12 (17.6)	6 (9.0)	
RF positive (qualitative)	101 (75.4)	45 (66.2)	56 (84.9)	0.01
RF (IU/mL) (quantitative)	169.1.8 ± 293.1, 66.1 [19.5, 167.8]	126.6 ± 196.7, 33.4 [14.0, 141.5]	212.8 ± 363.4, 98.5 [38.5, 202.4]	0.01
Anti-CCP antibody positive (qualitative)	99 (73.9)	43 (63.2)	56 (86.2)	0.003
Anti-CCP antibody (U/mL) (quantitative)	311.7 ± 549.8, 130.4 [5.3, 340.0]	274.3 ± 484.0, 56.8 [0.9, 340.0]	350.8 ± 612.5, 196.5 [31.0, 417.1]	0.04

Values are described as mean ± standard deviation, median (interquartile range) or number (%). Nominal variables were compared using Chi-square test and continuous variables using Wilcoxon signed-rank test. RA; rheumatoid arthritis; RF: rheumatoid factor; CCP: cyclic citrullinated peptide.

Supplementary Table S2. Rheumatoid arthritis disease activity and serum markers of patients at week 0 and week 24.

	ARM-2 (n=68)	ARM-3 (n=66)	p-value (ARM-2 vs. ARM3)
Sequential changes in RA disease activity and serum markers			
SDAI (week 0)	29.5 ± 12.9, 27.7 [19.4, 36.8]	28.7 ± 14.2, 25.5 [18.9, 35.1]	0.53
SDAI (week 24)	13.7 ± 7.9, 11.5 [8.8, 17.5]	14.0 ± 9.4, 11.7 [8.0, 17.7]	0.75
MMP-3 (ng/mL) (week 0)	242.1 ± 328.4, 125.7 [70.3, 279.2]	269.9 ± 367.5, 158.9 [67.7, 259.0]	0.50
MMP-3 (ng/mL) (week 24)	162.5 ± 223.6, 79.0 [53.1, 195.4]	121.9 ± 114.1, 82.2 [49.6, 159.6]	0.72
Interleukin-6 (pg/mL) (week 0)	29.0 ± 42.2, 13.3 [3.3, 38.4]	31.4 ± 54.4, 13.3 [6.4, 34.2]	0.50
Interleukin-6 (pg/mL) (week 24)	16.4 ± 31.3, 3.6 [1.2, 17.3]	11.7 ± 17.0, 5.3 [1.5, 11.8]	0.46
VEGF (pg/mL) (week 0)	110.0 ± 102.0, 79.2 [36.2, 141.0]	108.0 ± 96.7, 67.0 [41.8, 154.0]	0.88
VEGF (pg/mL) (week 24)	76.3 ± 74.7, 51.5 [28.0, 94.0]	72.2 ± 60.6, 53.0 [30.7, 98.2]	0.89
Plasma microRNA levels at week 24			
miR-143-3p	0.07 ± 0.08, 0.05 [0.03, 0.07]	0.07 ± 0.08, 0.04 [0.03, 0.09]	0.56
miR-146a-5p	0.17 ± 0.17, 0.11 [0.04, 0.23]	0.24 ± 0.35, 0.15 [0.04, 0.33]	0.42
miR-155-5p	0.01 ± 0.01, 0.001 [0, 0.01]	0.004 ± 0.01, 0 [0, 0.01]	0.23
miR-182-5p	0.001 ± 0.002, 0 [0, 0.001]	0.001 ± 0.001, 0 [0, 0.001]	0.92
miR-21-5p	0.46 ± 0.36, 0.37 [0.22, 0.58]	0.51 ± 0.46, 0.39 [0.26, 0.58]	0.60
miR-221-3p	0.06 ± 0.05, 0.05 [0.02, 0.10]	0.08 ± 0.08, 0.06 [0.03, 0.11]	0.66

Values are described as mean ± standard deviation, median (interquartile range) or number (%). Nominal variables were compared using Chi-square test and continuous variables using Wilcoxon signed-rank test. SDAI; Simplified Disease Activity Index; MMP: matrix metalloproteinase; VEGF: vascular endothelial growth factor; RNA: ribonucleic acid; miR; microRNA.

Supplementary Table S3. Univariable and multivariable analyses for predicting structural non-remission (Δ mTSS >0.5) under 24-week treatment.

	Univariable analysis			Multivariable analysis *		
	OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value
Arm (Arm-3)	1.17	0.42–3.28	0.76	–	–	–
RF positivity ^y	0.94	0.37–2.71	0.90	–	–	–
Anti-CCP antibody positivity ^y	3.95	1.11–25.20	0.03	–	–	–
SDAI	1.05	1.01–1.10	0.01	–	–	–
MMP-3	1.00	1.00–1.01	0.01	1.00	1.00–1.01	0.09
Interleukin-6	1.01	0.99–1.02	0.33	1.00	0.97–1.02	0.66
VEGF	1.01	1.00–1.01	0.07	1.00	0.99–1.01	0.71
miR-143-3p (per 0.01 units)	1.08	1.03–1.15	0.002	1.08	1.03–1.16	0.003
miR-146a-5p (per 0.01 units)	1.02	1.00–1.04	0.03	1.02	1.00–1.05	0.02
miR-155-5p (per 0.01 units)	1.20	0.75–1.83	0.39	1.10	0.69–1.71	0.65
miR-182-5p (per 0.001 units)	1.13	0.86–1.43	0.33	1.15	0.89–1.48	0.29
miR-21-5p (per 0.01 units)	1.01	1.00–1.03	0.01	1.01	1.00–1.03	0.01
miR-221-3p (per 0.01 units)	1.08	1.01–1.16	0.02	1.09	1.02–1.20	0.01

*adjusted by ARM, baseline RF positivity and anti-CCP antibody positivity, and SDAI at week 24

^ymeasured at week 0 .

^{||}scored or measured at week 24.

mTSS: modified total Sharp score; OR: odds ratio; CI: confidential interval; RF: rheumatoid factor; CCP: cyclic citrullinated peptide; SDAI: Simplified Disease Activity Index; MMP: matrix metalloprotease; VEGF: vascular endothelial growth factor; miR; microRNA.

Supplementary Table S4. Levels of miRNA predicting structural non-remission (Δ mTSS >0.5).

miRNA	Cut-off	Sensitivity	Specificity	AUC
miR-143-3p	0.075	80.0%	58.8%	0.652
miR-146a-5p	0.14	56.0%	64.7%	0.591
miR-21-5p	0.69	84.0%	47.1%	0.672
miR-221-3p	0.036	38.0%	88.2%	0.618

mTSS: modified total Sharp score; RNA: ribonucleic acid; miR; microRNA; AUC: area under curve.