

Supplementary File

Radiographic progression in clinical trials in rheumatoid arthritis: A systemic literature review of trials performed by industry

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Tables

Supplementary Table 1. Radiographic outcomes of each trial

Genant score																		
Patients Population	MTX naïve					MTX IR										TNFi IR		
Trial Name	IMAGE			AGREE		IL1-Ra				AIM		LITHE			ACT-RAY		REFLEX	
Intervention ^a	MTX	RTX (2x500mg) + MTX	RTX (2x1000mg) + MTX	MTX	ABA + MTX	PBO	IL-1RA (30mg)	IL-1RA (75mg)	IL-1RA (150mg)	MTX	ABA + MTX	MTX	TCZ (4mg/kg) + MTX	TCZ (8mg/kg) + MTX	TCZ → TCZ	TCZ → TCZ + MTX	MTX	RTX + MTX
Estimated yearly progression	(n=249)	(n=249)	(n=250)	(n=253)	(n=256)	(n=121)	(n=119)	(n=116)	(n=116)	(n=219)	(n=433)	(n=393)	(n=399)	(n=398)	(n=277)	(n=279)	(n=209)	(n=308)
Estimated yearly progression	8.2	7.8	8.6	-	-	7.4	6.9	6.9	6.3	5.0	5.2	3.2	3.1	3.1	4.5	4.5	4.1	4.0
Baseline Genant scores																		
TGS																		
mean (SD)	7.4 (10.9)	7.7 (11.7)	6.9 (10.6)	6.7 (8.8)	7.5 (9.7)	27.4 (28.6)	29.6 (29.2)	29.1 (25.4)	24.7 (25.5)	44.9 (37.7)	44.5 (37.3)	28.5	28.7	28.8	37.1 (40.5)	30.4 (31.8)	47.9 (36.0)	48.3 (34.9)
median (IQR)	-	-	-	3.8	3.4	-	-	-	-	33.4	31.9	-	-	-	-	-	-	-
range	-	-	-	0.0-54.6	0.0-57.3	-	-	-	-	2.3-190.1	0.5-221.0	0.0-190.5	0.0-171.4	0.0-178.7	-	-	-	-
ES																		
mean (SD)	-	-	-	4.8 (5.4)	5.4 (6.1)	15.1 (14.5)	15.4 (14.7)	14.7 (12.0)	13.7 (13.7)	21.8 (18.6)	21.7 (18.1)	-	-	-	-	-	-	-
median (IQR)	-	-	-	3.1	2.9	-	-	-	-	16.7	16.6	-	-	-	-	-	-	-
range	-	-	-	0.0-36.9	0.0-29.1	-	-	-	-	0.3-95.8	0.0-112.2	-	-	-	-	-	-	-
JSN score																		
mean (SD)	-	-	-	1.9 (4.0)	2.1 (4.2)	12.3 (14.9)	14.2 (15.3)	14.3 (14.6)	11.0 (12.7)	23.0 (20.4)	22.8 (20.2)	-	-	-	-	-	-	-
median (IQR)	-	-	-	0.5	0.2	-	-	-	-	16.6	16.2	-	-	-	-	-	-	-
range	-	-	-	0.0-28.0	0.0-28.2	-	-	-	-	0.0-94.3	0.0-108.8	-	-	-	-	-	-	-
Change in Genant scores at 6 months																		

ΔTGS																		
mean (SD)	0.7	0.6	0.3	0.7	0.5	3.5 (5.0)	1.8 (3.2)	1.8 (2.4)	1.9 (3.4)	-	-	-	-	-	0.2 (1.1)	0.1 (1.9)	1.2 (3.3)	0.6 (1.9)
median (IQR)	-	-	-	-	-	2.0	0.5	1.0	0.5	-	-	-	-	-	-	-	-	-
ΔES																		
mean (SD)	0.5	0.4	0.2	0.6	0.4	1.9 (2.6)	1.0 (1.9)	1.3 (1.7)	1.2 (2.5)	-	-	-	-	-	0.1 (0.6)	-0.0 (0.8)	0.8 (2.0)	0.4 (1.3)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔJSN score																		
mean (SD)	0.2	0.2	0.1	0.1	0.1	1.7 (3.1)	0.8 (1.7)	0.6 (1.2)	0.7 (1.4)	-	-	-	-	-	0.1 (0.7)	0.1 (1.5)	0.5 (1.5)	0.2 (0.8)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Change in Genant scores at 1 year																		
ΔTGS																		
mean (SD)	1.1	0.7	0.4	1.1	0.6	4.8		3.0 ^b		2.3	1.2	1.1	0.3	0.3	0.6 (0.4) ^c	0.4 (0.4) ^c	2.3	1.0
median (IQR)	-	-	-	0.0	0.0	-	-	-	-	0.5 (0.0-2.5)	0.3 (0.0-1.8)	-	-	-	-	-	-	-
ΔES																		
mean (SD)	0.7	0.5	0.2	0.9	0.5	2.6		1.8 ^b		1.1	0.6	0.7	0.2	0.2	0.3 (0.1) ^c	-0.1 (0.1) ^c	1.3	0.6
median (IQR)	-	-	-	0.0	0.0	-	-	-	-	0.3 (0.0-1.3)	0.0 (0.0-1.0)	-	-	-	-	-	-	-
ΔJSN score																		
mean (SD)	0.1	0.0	0.0	0.2	0.1	2.1		1.2 ^b		1.2	0.6	0.4	0.1	0.1	0.4 (0.3) ^c	0.5 (0.3) ^c	1.0	0.4
median (IQR)	-	-	-	0.0	0.0	-	-	-	-	0.0 (0.0-1.0)	0.0 (0.0-0.5)	-	-	-	-	-	-	-
Non-progressors at 1 year, %																		
≤ 0 TGS	53.0	58.0	64.0	52.9	61.2	33 ^d		48 ^d		-	46.0	67.0	81.0	84.0	59.1	65.7	53.0	46.0
≤ SDC	-	-	-	-	-	-	-	-	-	-	-	-	-	-	87.3	90.6	-	-

(Supplementary Table 1 Cont'd)

Sharp-van der Heijde score

MTX naïve

Trial Name	ASPIRE			COMET		GO-BEFORE				OPTIMA		FUNCTION			
Intervention ^a	MTX	IFX (3mg/kg) + MTX	IFX (6mg/kg) + MTX	MTX	ETN (50mg) + MTX	MTX	GOL (100mg)	GOL (50mg) + MTX	GOL (100mg) + MTX	MTX	ADA + MTX	MTX	TCZ (8mg/kg)	TCZ (4mg/kg) + MTX	TCZ (8mg/kg) + MTX
	(n=282)	(n=359)	(n=363)	(n=230) ^e	(n=246) ^e	(n=160)	(n=159)	(n=159)	(n=159)	(n=517)	(n=515)	(n=287)	(n=292)	(n=288)	(n=290)
Estimated yearly progression	12.5	14.5	12.4	-	-	12.7	12.1	13.7	10.3	-	-	-	-	-	-
Baseline SvdH scores															
TSS															
mean (SD)	11.3 (15.9)	11.6 (15.2)	11.2 (15.2)	-	-	19.7 (35.4)	20.4 (30.9)	18.7 (32.4)	18.2 (35.5)	11.2 (17.4)	11.8 (18.1)	5.7 (14.6)	6.9 (16.1)	7.7 (17.2)	6.2 (11.1)
median (IQR)	5.1 (1.4-14.6)	5.2 (1.8-15.1)	5.3 (1.7-14.6)	-	-	5.3 (2.0-18.1)	6.0 (2.5-26.5)	5.5 (2.0-19.5)	6.0 (2.5-18.0)	-	-	1.5	1.5	2.0	2.0
range	0.0-102.7	0.0-81.3	0.0-102.7	-	-	-	-	-	-	-	-	-	-	-	-
ES															
mean (SD)	8.25 (12.3)	8.75 (12.1)	8.27 (11.8)	-	-	11.3 (18.6)	11.7 (16.3)	10.8 (17.4)	10.5 (19.4)	5.1 (8.4)	5.4 (9.1)	3.3 (7.6)	3.9 (8.3)	4.1 (8.5)	3.5 (5.7)
median (IQR)	3.0 (0.5-10.5)	3.8 (1.0-11.0)	3.8 (1.0-10.8)	-	-	4.0 (1.5-12.1)	4.5 (2.0-16.5)	4.5 (1.5-11.5)	4.5 (1.5-12.0)	-	-	1.0	1.0	1.5	1.5
range	0.0-72.3	0.0-57.3	0.0-76.8	-	-	-	-	-	-	-	-	-	-	-	-
JSN score															
mean (SD)	3.0 (4.8)	2.9 (4.4)	2.9 (5.2)	-	-	8.4 (17.8)	8.7 (15.7)	7.9 (16.1)	7.8 (17.2)	6.1 (10.2)	6.4 (10.4)	2.3 (7.5)	3.0 (8.6)	3.6 (9.6)	2.7 (6.5)
median (IQR)	1.0 (0.0-3.9)	1.0 (0.0-3.8)	1.0 (0.0-3.6)	-	-	1.0 (0.0-6.8)	1.0 (0.0-10.5)	1.5 (0.0-6.5)	1.0 (0.0-6.5)	-	-	0.0	0.0	0.0	0.0
range	0.0-30.4	0.0-24.6	0.0-43.8	-	-	-	-	-	-	-	-	-	-	-	-
Change in SvdH at 6 months															
ΔTSS															
mean (SD)	2.5 (7.0)	0.3 (4.9)	0.2 (4.2)	-	-	1.1 (3.9)	0.6 (3.6)	0.7 (3.8)	0.0 (1.5)	1.0	0.2	-	-	-	-

median (IQR)	0.5 (0.0-3.2)	0.0 (-0.9-1.3)	0.0 (-1.0-1.0)	-	-	0.0 (0.0-1.0)	0.0 (0.0-0.5)	0.0 (0.0-0.5)	0.0 (0.0-0.5)	-	-	-	-	-	-
ΔES															
mean (SD)	2.3 (6.2)	0.3 (4.2)	0.1 (3.8)	-	-	0.8 (2.6)	0.6 (3.1)	0.5 (2.1)	-0.0 (1.2)	0.5	0.1	-	-	-	-
median (IQR)	0.5 (0-3)	0.0 (-0.5-1.3)	0.0 (-1.0-0.5)	-	-	0.0 (0.0-1.0)	0.0 (0.0-0.5)	0.0 (0.0-0.5)	0.0 (0.5-0.5)	-	-	-	-	-	-
ΔJSN score															
mean (SD)	0.3 (1.5)	-0.0 (1.4)	0.1 (1.1)	-	-	0.4 (2.2)	0.1 (1.3)	0.3 (2.1)	0.0 (0.7)	0.5	0.1	-	-	-	-
median (IQR)	0.0 (0-0.4)	0.0 (0-0)	0.0 (0-0)	-	-	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	-	-	-	-	-	-
Change in SvdH at 1 year															
ΔTSS															
mean (SD)	3.7 (9.6)	0.4 (5.8)	0.5 (5.6)	2.4	0.3	1.3 (4.6)	1.3 (6.2)	0.7 (5.2)	0.1 (1.8)	-	-	1.1 (4.3)	0.3 (1.9)	0.4 (2.9)	0.1 (2.1)
median (IQR)	0.4 (0.0-4.5)	0.0 (-0.8-1.3)	0.0 (-1.0-1.3)	-	-	0.0 (0.0-1.5)	0.0 (0.0-1.0)	0.0 (-0.5-0.5)	0.0 (0.0-0.5)	-	-	-	-	-	-
ΔES															
mean (SD)	3.0 (7.8) ^e	0.3 (4.9) ^e	0.1 (4.2) ^e	-	-	0.7 (2.8)	0.8 (3.9)	0.5 (2.1)	0.1 (1.4)	-	-	0.6	0.2	0.3	0.1
median (IQR)	0.3 ^e (0.0-3.8)	0.0 ^e (-0.8-1.3)	0.0 ^e (-1.0-1.0)	-	-	0.0 (0.0-0.5)	0.0 (-0.0-0.5)	0.0 (0.0-0.5)	0.0 (-0.5-0.5)	-	-	-	-	-	-
ΔJSN score															
mean (SD)	0.6 (2.1) ^e	0.1 (1.6) ^e	0.2 (1.4) ^e	-	-	0.6 (2.3)	0.4 (1.7)	0.2 (2.0)	0.0 (0.9)	-	-	0.5	0.1	0.2	0.0
median (IQR)	0.0 ^e (0.0-0.4)	0.0 ^e (0.0-0.0)	0.0 ^e (0.0-0.2)	-	-	0.0 (0.0-0.0)	0.0 (0.0-0.5)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	-	-	-	-	-	-
Non-progressors at 1 year, %															
≤ 0 TSS	-	-	-	54.0	75.0	53.9	59.9	71.4	61.2	-	-	73.0	82.0	79.0	83.0
≤ SDC	-	-	-	-	-	87.9	91.2	93.6	97.8	-	-	-	-	-	-
≤ SDD	89.0	96.1	98.1	-	-	-	-	-	-	-	-	-	-	-	-
≤ 0.5 TSS	-	-	-	59.0	80.0	-	-	-	-	72.0 ^d	87.0 ^d	-	-	-	-

(Supplementary Table 1 Cont'd)

Sharp-van der Heijde score										
	MTX naïve									
Trial Name	ORAL Start			C-OPERA		C-EARLY		RA-BEGIN		
Intervention ^a	MTX	TOF (5mg bid)	TOF (10mg bid)	MTX	CZP + MTX	MTX	CZP + MTX	MTX	BAR (4mg)	BAR (4mg) + MTX
	(n=186)	(n=373)	(n=397)	(n=157)	(n=159)	(n=163)	(n=528)	(n=210)	(n=159)	(n=215)
Estimated yearly progression	-	-	-	-	-	-	-	-	-	-
Baseline SvdH scores										
TSS										
mean (SD)	16.1	19.1	17.9	6.0 (15.3)	5.2 (8.8)	8.5 (17.5)	7.2 (13.8)	11.8 (22.2)	13.3 (27.0)	11.4 (20.1)
median (IQR)	3.5	3.5	3.0	-	-	8.7	6.6	-	-	-
range	-	-	-	-	-	0.0-161.0	0.0-130.0	-	-	-
ES										
mean (SD)	8.4	9.1	9.1	2.8 (7.9)	2.2 (4.4)	-	-	7.9 (12.5)	8.7 (15.8)	7.5 (11.7)
median (IQR)	-	-	-	-	-	1.5	1.5	-	-	-
range	-	-	-	-	-	0.0-68.0	0.0-65.0	-	-	-
JSN score										
mean (SD)	7.7	10.0	8.8	3.2 (8.6)	2.9 (5.8)	-	-	3.9 (10.4)	4.6 (11.9)	4.0 (9.6)
median (IQR)	-	-	-	-	-	0.0	0.0	-	-	-
range	-	-	-	-	-	0.0-94.0	0.0-65.0	-	-	-
Change in SvdH at 6 months										
ΔTSS										
mean (SD)	0.8 (0.2) ^c	0.2 (0.1) ^c	0.0 (0.1) ^c	0.9 (2.4)	0.3 (1.6)	-	-	0.6 (1.8) ^f	0.4 (1.2) ^f	0.3 (1.1) ^f

median (IQR)	-	-	-	-	-	-	-	-	-	-
ΔES										
mean (SD)	0.4 (0.1) ^c	0.1 (0.0) ^c	0.1 (0.0) ^c	-	-	-	-	0.5 (1.1) ^f	0.3 (0.9) ^f	0.3 (1.0) ^f
median (IQR)	-	-	-	-	-	-	-	-	-	-
ΔJSN score										
mean (SD)	0.3 (0.1) ^c	0.1 (0.1) ^c	0.1 (0.1) ^c	-	-	-	-	0.1 (0.9) ^f	0.1 (0.4) ^f	0.0 (0.4) ^f
median (IQR)	-	-	-	-	-	-	-	-	-	-
Change in SvdH at 1 year										
ΔTSS										
mean (SD)	1.2 (0.2) ^c	0.4 (0.1) ^c	0.2 (0.1) ^c	1.6 (4.9)	0.4 (2.7)	1.8 ^f	0.2 ^f	1.0 (2.4) ^f	0.8 (2.2) ^f	0.4 (1.7) ^f
median (IQR)	-	-	-	-	-	-	-	-	-	-
ΔES										
mean (SD)	0.6 (0.1) ^c	0.1 (0.1) ^c	0.1 (0.1) ^c	-	-	1.1 ^f	0.1 ^f	0.8 (1.8) ^f	0.6 (1.5) ^f	0.3 (1.2) ^f
median (IQR)	-	-	-	-	-	-	-	-	-	-
ΔJSN score										
mean (SD)	0.6 (0.1) ^c	0.2 (0.1) ^c	0.1 (0.1) ^c	-	-	0.7 ^f	0.1 ^f	0.2 (1.0) ^f	0.3 (1.1) ^f	0.1 (0.9) ^f
median (IQR)	-	-	-	-	-	-	-	-	-	-
Non-progressors at 1 year, %										
≤ 0 TSS	-	-	-	-	-	-	-	66.1	68.8	79.9
≤ SDC	-	-	-	-	-	-	-	78.1	85.1	89.9
≤ SDD	-	-	-	-	-	-	-	-	-	-
≤ 0.5 TSS	69.0	82.4	87.7	70.7	82.9	49.7	70.3	71.9	78.6	85.9

(Supplementary Table 1 Cont'd)

Sharp-van der Heijde score

MTX IR

Trial Name	ATTRACT					RAPID 1			RAPID 2			GO-FORWARD			
Intervention ^a	MTX	IFX (3mg/kg, q8w) + MTX	IFX (3mg/kg, q4w)+ MTX	IFX (10mg/kg, q8w) + MTX	IFX (10mg/kg, q 4w) + MTX	MTX	CZP (200mg) + MTX	CZP 400mg + MTX	MTX	CZP (200mg) + MTX	CZP (400mg) + MTX	MTX	GOL (100mg)	GOL (50mg) + MTX	GOL (100mg) + MTX
	(n=88)	(n=86)	(n=86)	(n=87)	(n=81)	(n=199)	(n=393)	(n=390)	(n=127)	(n=246)	(n=246)	(n=133)	(n=133)	(n=89)	(n=89)
Estimated yearly progression	7.4	7.9	7.9	6.1	6.3	4.3	4.4	4.4	8.7	6.6	7.4	5.0	5.2	5.3	6.0
Baseline SvdH scores															
TSS															
mean (SD)	82.0 (77.0)	79.0 (73.0)	71.0 (73.0)	67.0 (61.0)	76.0 (72.0)	27.0	27.0	27.5	46.5 (58.6)	39.6 (50.1)	46.7 (56.0)	36.7 (52.1)	37.4 (52.5)	29.7 (39.3)	39.6 (56.1)
median (IQR)	61.8	55.5	45.5	49.5	48.8	-	-	-	-	-	-	17.5 (1.5-49.5)	15.3 (2.5-49.0)	9.5 (2.0-49.6)	17.0 (3.0-47.0)
range	0.0-335.0	2.0-346.0	0.5-382.0	0.0-300.0	2.0-322.0	0.5-254.0	0.0-313.5	0.0-267.0	-	-	-	-	-	-	-
ES															
mean (SD)	-	-	-	-	-	-	-	-	23.1 (32.1)	19.0 (26.8)	21.6 (29.7)	18.7 (27.1)	19.1 (27.2)	16.2 (22.2)	19.7 (29.7)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	5.5 (1.0-25.0)	8.0 (1.5-25.0)	5.8 (1.5-22.3)	7.0 (2.2-23.5)
JSN score															
mean (SD)	-	-	-	-	-	-	-	-	23.4 (27.7)	20.6 (24.4)	25.1 (28.1)	18.0 (25.9)	18.4 (27.1)	13.5 (18.5)	19.9 (27.8)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	4.5 (0.0-26.0)	6.5 (0.0-25.0)	4.0 (0.0-23.8)	9.0 (0.0-26.0)
Change in SvdH at 6 months															
ΔTSS															
mean (SD)	4.8 (8.6) ^g	1.0 (4.6) ^g	0.6 (5.9) ^g	-0.5 (5.9) ^g	-0.4 (2.5) ^g	2.7	0.4	0.3	1.2	0.2	-0.4	0.6 (2.6)	0.3 (1.6)	0.6 (2.7)	0.2 (1.3)
median (IQR)	2.5 (0.0-6.5) ^g	0.1 (-1.5-2.5) ^g	0.0 (-2.0-2.0) ^g	-0.3 (-2.4-1.3) ^g	-0.5 (-1.7-1.0) ^g	-	-	-	-	-	-	0.0 (0.0-0.5)	0.0 (0.0-0.5)	0.0 (0.0-0.5)	0.0 (0.0-0.5)

Δ ES																			
mean (SD)	-	-	-	-	-	-	-	-	0.7	0.1	-0.3	0.2 (0.8)	0.0 (0.9)	0.3 (1.6)	0.1 (1.0)				
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	0.0 (0.0-0.5)	0.0 (0.0-0.2)	0.0 (0.0-0.5)	0.0 (0.0-0.0)				
Δ JSN score																			
mean (SD)	-	-	-	-	-	-	-	-	0.5	0.1	-0.1	0.3 (1.8)	0.2 (1.2)	0.2 (0.9)	0.2 (0.9)				
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)				
Change in SvdH at 1 year																			
Δ TSS																			
mean (SD)	7.0 (10.3)	1.3 (6.0)	1.6 (8.5)	0.2 (3.6)	-0.7 (3.8)	2.8	0.4	0.2	0.7 (1.7)	0.6 (5.7)		1.1	0.9	0.9	0.2				
median (IQR)	4.0 (0.5-9.7)	0.5 (-1.5-3.0)	0.1 (-2.5-3.0)	0.5 (-1.5-2.0)	-0.5 (-3.0-1.5)	-	-	-	-	-	-	0.0 (0.0-1.1)	0.0 (0.0-1.0)	0.0 (0.0-0.5)	0.0 (0.0-0.9)				
Δ ES																			
mean (SD)	4.0 (7.9)	0.2 (2.9)	0.3 (4.7)	0.2 (2.9)	-0.7 (3.0)	-	-	-	-	-	-	0.2 (0.8)	0.2 (1.4)	0.3 (1.6)	0.1 (1.4)				
median (IQR)	2.0 (0.5-5.8)	0.0 (-1.4-1.5)	0.0 (-1.5-1.5)	0.5 (-1.0-1.5)	-0.5 (-1.8-0.8)	-	-	-	-	-	-	0.0 (0.0-0.5)	0.0 (-0.2-0.5)	0.0 (0.0-0.5)	0.0 (0.0-0.5)				
Δ JSN score																			
mean (SD)	2.9 (4.2)	1.1 (4.4)	0.7 (4.3)	0.0 (3.1)	0.0 (2.5)	-	-	-	-	-	-	0.4 (2.3)	0.6 (2.5)	0.2 (0.9)	0.2 (0.9)				
median (IQR)	1.5 (0.0-5.8)	0.0 (-1.0-2.0)	0.0 (-1.0-2.0)	0.0 (-0.9-1.0)	0.0 (-1.5-1.0)	-	-	-	-	-	-	0.0 (0.0-0.0)	0.0 (0.0-0.5)	0.0 (0.0-0.2)	0.0 (0.0-0.0)				
Non-progressors at 1 year, %																			
≤ 0 TSS	-	-	-	-	-	51.9	69.0	71.6	-	-	-	66.4 ^h	68.5 ^h	66.3 ^h	69.0 ^h				
\leq SDC	-	-	-	-	-	-	-	-	-	-	-	95.9 ^h	96.0 ^h	94.2 ^h	96.4 ^h				
\leq SDD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
≤ 0.5 TSS	20.0	48.0	49.0	48.0	67.0	-	-	-	-	81.3	-	-	-	-	-				

(Supplementary Table 1 Cont'd)

				Sharp-van der Heijde score									
				MTX IR									
Trial Name	GO-FORTH			J-RAPID				ORAL-SCAN				GO-FURTHER	
Intervention ^a	MTX	GOL (50mg) + MTX	GOL (100mg) + MTX	MTX	CZP (100mg) + MTX	CZP (200mg) + MTX	CZP (400mg) + MTX	MTX→TOF (5mg, bid)	MTX →TOF (10mg, bid)	MTX + TOF (5mg, bid)	MTX + TOF (10mg, bid)	MTX	GOL (2mg/kg) + MTX
	(n=88)	(n=86)	(n=87)	(n=77)	(n=72)	(n=82)	(n=85)	(n=81)	(n=79)	(n=321)	(n=316)	(n=197)	(n=395)
Estimated yearly progression	-	-	-	-	-	-	-	-	-	5.0	5.5	-	-
Baseline SvdH scores													
TSS													
mean (SD)	54.2 (62.9)	58 (62.4)	53.2 (48.4)	52.7 (57.3)	54.8 (62.5)	50.4 (53.4)	49.9 (47.2)	35.0 (43.2)	30.1 (40.5)	31.1 (47.7)	37.3 (54.1)	50.3 (59.9)	47.6 (54.6)
median (IQR)	32.3	35.0	43.0	37.5 (10.5-75.5)	27.5 (8.5-84.5)	31.3 (9.5-86.0)	40.0 (7.5-77.3)	16.0 (46.5)	14.0 (44.3)	13.0 (37.0)	13.0 (45.0)	29.0 (8.5-77.2)	28.0 (9.0-67.5)
range	0.0-289.2	0.0-300.5	0.0-215.0	-	-	-	-	0.0-170.5	0.0-208.5	0.0-337.0	0.0-311.5	-	-
ES													
mean (SD)	30.8 (37.1)	32.1 (34.7)	29.3 (26.3)	28.2 (33.3)	29.4 (35.9)	25.6 (30.0)	26.0 (25.9)	14.5 (18.7)	14.3 (20.3)	13.8 (24.3)	17.7 (27.8)	25.6 (32.4)	23.9 (29.0)
median (IQR)	17.8	20.8	21.0	15.0 (5.0-40.0)	14.8 (5.5-43.0)	13.5 (4.0-39.5)	18.5 (4.3-42.3)	6 (21.5)	5.5 (17.8)	4.5 (13.5)	6.0 (21.0)	13.0 (4.0-36.0)	13.5 (4.0-32.0)
range	0.0-190.0	0.0-185.0	0.0-116.0	-	-	-	-	0.0-86.0	0.0-106.5	0.0-197.0	0.0-188.0	-	-
JSN score													
mean (SD)	23.4 (27.4)	25.9 (29.4)	23.9 (24.5)	24.5 (25.6)	25.4 (28.1)	24.7 (24.5)	24.0 (22.9)	20.5 (26.7)	15.8 (21.4)	17.3 (25.1)	19.6 (27.8)	24.6 (29.5)	23.7 (28.3)
median (IQR)	13.5	14.5	16.5	16.0 (5.0-37.0)	15.0 (2.5-39.5)	18.0 (5.0-42.0)	22.3 (1.3-38.8)	9.5 (26.0)	6.75 (26.0)	6.5 (22.5)	6.0 (29.0)	12.5 (4.0-37.5)	13.0 (3.0-35.5)
range	0.0-128.0	0.0-127.0	0.0-99.0	-	-	-	-	0.0-97.0	0.0-102.0	0.0-140.0	0.0-137.5	-	-
Change in SvdH at 6 months													
ΔTSS													
mean (SD)	2.5 (5.5)	1.1 (3.7)	0.3 (2.7)	2.8 ^f	1.0 ^f	0.2 ^f	0.7 ^f	0.5 (2.0) ^f		0.1 (1.7) ^f	0.1 (2.0) ^f	1.1 (3.2)	0.0 (1.9)

median (IQR)	0.3	0.0	0.0	-	-	-	-	0.0 (0.5) ^f	0.0 (0.0) ^f	0.0 (0.0) ^f	0.0 (0.0-1.5)	0.0 (-0.5-0.5)
ΔES												
mean (SD)	1.7 (3.7)	0.5 (1.6)	0.0 (1.4)	2.0 ^f	0.7 ^f	0.0 ^f	0.3 ^f	0.1 (1.0) ^f	0.1 (1.0) ^f	0 (0.7) ^f	0.5 (2.1)	-0.1 (1.2)
median (IQR)	0.0	0.0	0.0	-	-	-	-	0.0 (0.0) ^f	0.0 (0.0) ^f	0.0 (0.0) ^f	0.0 (0.0-0.5)	0.0 (-0.5-0.0)
ΔJSN score												
mean (SD)	0.8 (2.3)	0.7 (2.9)	0.3 (1.5)	0.8 ^f	0.4 ^f	0.2 ^f	0.4 ^f	0.3 (1.5) ^f	0.1 (1.1) ^f	0.1 (1.8) ^f	0.6 (1.7)	0.1 (1.3)
median (IQR)	0.0	0.0	0.0	-	-	-	-	0.0 (0.0) ^f	0.0 (0.0) ^f	0.0 (0.0) ^f	0.0 (0.0-0.5)	0.0 (0.0-0.0)
Change in SvdH at 1 year												
ΔTSS												
mean (SD)	2.0 (8.7)	1.6 (7.4)	0.6 (6.0)	-	-	-	-	1.0 (3.9) ^f	0.3 (3.0) ^f	0.1 (2.9) ^f	1.2	0.1
median (IQR)	0.0	0.0	0.0	-	-	-	-	0.0 (0.9) ^f	0.0 (0.0) ^f	0.0 (0.0) ^f	0.0	0.0
ΔES												
mean (SD)	-	-	-	-	-	-	-	0.3 (2.0) ^f	0.2 (1.7) ^f	0.0 (1.1) ^f	-	-
median (IQR)	-	-	-	-	-	-	-	0.0 (0.0) ^f	0.0 (0.0) ^f	0.0 (0.0) ^f	-	-
ΔJSN score												
mean (SD)	-	-	-	-	-	-	-	0.7 (2.9) ^f	0.1 (1.9) ^f	0.1 (2.6) ^f	-	-
median (IQR)	-	-	-	-	-	-	-	0.0 (0.0) ^f	0.0 (0.0) ^f	0.0 (0.0) ^f	-	-
Non-progressors at 1 year, %												
≤ 0 TSS	50.0 ^h	59.3 ^h	70.1 ^h	-	-	-	-	-	-	-	-	-
≤ SDC	78.4 ^h	83.7 ^h	94.3 ^h	-	-	-	-	-	-	-	80.7 ^h	91.4 ^h
≤ SDD	-	-	-	-	-	-	-	-	-	-	-	-
≤ 0.5 TSS	-	-	-	47.4 ^h	-	74.1 ^h	70.2 ^h	74.1	86.0	86.4	-	-

(Supplementary Table 1 Cont'd)

Δ ES												
mean (SD)	-	-	-	-	-	-	-	-	-	-	-	-
Δ JSN score												
mean (SD)	-	-	-	-	-	-	-	-	-	-	-	-
Change in SvdH at 1 year												
Δ TSS												
mean (SD)	0.4 (5.0)	0.6 (3.2)	1.0	0.3	0.1	0.1	0.6 (5.6)	1.0 (6.3)	2.8 (7.7)	0.9 (4.7)	0.3 (4.6)	
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	
Δ ES												
mean (SD)	0.0 (2.8)	0.3 (1.8)	-	-	-	-	0.0 (3.4)	0.7 (3.9)	-	-	-	
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	
Δ JSN score												
mean (SD)	0.4 (2.5)	0.3 (1.9)	-	-	-	-	0.7 (4.0)	0.4 (4.2)	-	-	-	
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	
Non-progressors at 1 year, %												
≤ 0 TSS	-	-	62.5 ⁱ	78.8 ⁱ	80.5 ⁱ	83.5 ⁱ	51.4	51.7	38.7	47.8	55.6	
\leq SDC	88.6	84.8	-	-	-	-	-	-	-	-	-	
\leq SDD	-	-	-	-	-	-	-	-	-	-	-	
≤ 0.5 TSS	-	-	-	-	-	-	57.8	58.1	-	-	-	

(Supplementary Table 1 Cont'd)

Sharp-van der Heijde score

MTX IR

Trial Name	RA-BEAM			SB4		SB2		RAJ4			SELECT-COMPARE		
Intervention ^a	DMARDs	BAR + DMARDs	ADA + DMARDs	ETN + MTX	SB4 + MTX	IFX + MTX	SB2 + MTX	MTX	PEF (100mg) + MTX	PEF (150 mg) + MTX	MTX	UPA + MTX	ADA + MTX
	(n=488)	(n=487)	(n=330)	(n=297)	(n=299)	(n=293)	(n=291)	(n=170)	(n=174)	(n=174)	(n=651)	(n=651)	(n=327)
Estimated yearly progression	-	-	-	-	-	-	-	-	-	-	-	-	-
Baseline SvdH scores													
TSS													
mean (SD)	45.0 (50.0)	43.0 (50.0)	44.0 (51.0)	38.9 (53.3)	43.3 (67.1)	38.9 (56.3)	37.1 (57.5)	28.4 (36.3)	25.2 (35.5)	25.0 (32.4)	35.0 (52.0)	34.0 (50.0)	35.0 (47.0)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-
range	-	-	-	-	-	-	-	-	-	-	-	-	-
ES													
mean (SD)	27.0 (29.0)	25.0 (28.0)	26.0 (29.0)	20.5 (28.3)	24.0 (39.6)	20.5 (31.1)	19.2 (31.7)	11.0 (18.0)	10.3 (17.5)	9.8 (15.9)	17.0 (27.0)	17.0 (26.0)	15.0 (23.0)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-
range	-	-	-	-	-	-	-	-	-	-	-	-	-
JSN score													
mean (SD)	18.0 (23.0)	17.0 (23.0)	18.0 (24.0)	18.4 (26.5)	19.2 (28.8)	18.4 (26.8)	17.8 (27.7)	17.4 (20.1)	14.9 (19.5)	15.2 (18.3)	19.0 (26.0)	18.0 (25.0)	19.0 (26.0)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-
range	-	-	-	-	-	-	-	-	-	-	-	-	-
Change in SvdH at 6 months													
ΔTSS													

mean (SD)	0.9 ^f	0.4 ^f	0.3 ^f	-	-	-	-	3.4	1.6	1.0	0.9 ^f	0.2 ^f	0.1 ^f
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔES													
mean (SD)	0.6 ^f	0.3 ^f	0.2 ^f	-	-	-	-	1.9	1.0	0.8	0.4 ^f	0.0 ^f	0.0 ^f
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔJSN score													
mean (SD)	0.3 ^f	0.1 ^f	0.1 ^f	-	-	-	-	1.4	0.6	0.2	0.6 ^f	0.2 ^f	0.1 ^f
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-
Change in SvdH at 1 year													
ΔTSS													
mean (SD)	1.8 ^f	0.7 ^f	0.6 ^f	0.7 (3.4)	0.5 (2.5)	0.4	0.4	-	-	-	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔES													
mean (SD)	1.2 ^f	0.5 ^f	0.4 ^f	0.3 (1.7)	0.3 (1.6)	0.0	0.1	-	-	-	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔJSN score													
mean (SD)	0.6 ^f	0.2 ^f	0.2 ^f	0.4 (2.1)	0.2 (1.1)	0.4	0.2	-	-	-	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-
Non-progressors at 1 year, %													
≤ 0 TSS	70.4	79.1	81.1	65.8	70.0	-	-	42.5	55.5	61.6	-	-	-
≤ SDC	76.8	89.4	90.1	86.0	91.6	-	-	-	-	-	-	-	-
≤ SDD	-	-	-	-	-	-	-	-	-	-	-	-	-
≤ 0.5 TSS	70.4	85.2	86.5	-	-	-	-	42.5	64.0	68.9	-	-	-

(Supplementary Table 1 Cont'd)

Sharp-van der Heijde score

DMARD IR

Trial Name	TEMPO			SAMURAI		GO-MONO			HIKARI	
Intervention ^a	MTX	ETN	ETN + MTX	DMARDs	TCZ + DMARDs	PBO	GOL (50mg)	GOL (100mg)	DMARDs	CZP + DMARDs
	(n=228)	(n=223)	(n=231)	(n=145)	(n=157)	(n=105)	(n=101)	(n=102)	(n=114)	(n=116)
Estimated yearly progression	10.3	11.0	8.4	12.3	14.1	-	-	-	-	-
Baseline SvdH scores										
TSS										
mean (SD)	26.8	28.8	34.7	30.6 (42.0)	28.3 (43.9)	56.1 (62.2)	43.8 (50.6)	56.9 (57.0)	46.1 (54.4)	36.5 (51.3)
median (IQR)	26.8 (5.5-70.5)	21.8 (7.5-58.6)	21.8 (5.5-61.6)	-	-	-	-	-	23.8 (7.5-62.0)	15.8 (2.0-54.5)
range	-	-	-	-	-	-	-	-	-	-
ES										
mean (SD)	-	-	-	13.9 (21.7)	13.8 (24.6)	30.2 (33.8)	23.9 (28.3)	31.7 (33.0)	-	-
median (IQR)	11.5 (2.5-35.5)	8.0 (2.8-26.0)	9.5 (2.5-30.0)	-	-	-	-	-	-	-
range	-	-	-	-	-	-	-	-	-	-
JSN score										
mean (SD)	-	-	-	16.7 (21.8)	14.5 (20.8)	25.9 (30.2)	19.9 (24.0)	25.3 (26.2)	-	-
median (IQR)	13.3 (2.0-37.0)	11.5 (2.0-30.2)	10.3 (2.0-35.5)	-	-	-	-	-	-	-
range	-	-	-	-	-	-	-	-	-	-
Change in SvdH at 6 months										
ΔTSS										
mean (SD)	1.7	0.3	-0.4	4.5 (3.1-6.0)	1.9 (1.2-2.6)	2.6 (4.7)	1.9 (4.1)	2.1 (10.4)	2.5	0.5

median (IQR)	-	-	-	1.0 (0.0-5.0)	0.5 (0.0-2.0)	1.0	0.5	0.0	-	-
Δ ES										
mean (SD)	-	-	-	2.4 (1.6-3.2)	0.8 (0.4-1.2)	1.3 (2.5)	1.0 (2.1)	1.1 (5.7)	1.3	0.1
median (IQR)	-	-	-	0.5 (0.0-2.5)	0.0 (0.0-1.0)	0.5	0.5	0.0	-	-
Δ JSN score										
mean (SD)	-	-	-	2.2 (1.4-2.9)	1.1 (0.7-1.6)	0.9 (1.9)	1.0 (2.8)	1.0 (5.1)	1.1	0.4
median (IQR)	-	-	-	0.0 (0.0-2.0)	0.0 (0.0-1.0)	0.0	0.0	0.0	-	-
Change in SvdH at 1 year										
Δ TSS										
mean (SD)	2.8	0.5	-0.5	6.1 (4.2-8.0)	2.3 (1.5-3.2)	4.3	1.0	1.7	-	-
median (IQR)	0.0 (-0.5-2.5)	0.0 (-1.0-1.0)	-0.5 (-1.5-0.0)	2.5 (0.0-7.0)	0.5 (0.0-3.0)	-	-	-	-	-
Δ ES										
mean (SD)	1.7 (4.4)	0.0 (2.8)	0.4 (2.5)	3.2 (2.1-4.3)	0.9 (0.3-1.4)	-	-	-	-	-
median (IQR)	0.5	0.0	0.0	1.0 (0.0-3.5)	0.0 (0.0-1.0)	-	-	-	-	-
Δ JSN score										
mean (SD)	1.1 (3.1)	0.1 (2.4)	0.5 (2.9)	2.9 (2.0-3.8)	1.5 (0.9-2.1)	-	-	-	-	-
median (IQR)	0.0	0.0	0.0	1.0 (0.0-4.0)	0.0 (0.0-1.7)	-	-	-	-	-
Non-progressors at 1 year, %										
≤ 0 TSS	-	-	-	-	-	-	-	-	-	-
\leq SDC	-	-	-	-	-	75.5 ^d	79.4 ^d	80.8 ^d	-	-
\leq SDD	88.2	95.8	97.2	-	-	-	-	-	-	-
≤ 0.5 TSS	57.0	68.0	80.0	39.0	56.0	-	-	-	45.6 ^h	76.3 ^h

(Supplementary Table 1 Cont'd)

Sharp-van der Heijde score

Patients Population	DMARD IR											TNFi IR		
	J-ETA			BREVACTA		SURROUND D			RA-BUILD			REASSURE		
Intervention ^a	MTX	ETA (10mg biw) + MTX	ETA (25mg biw) + MTX	DMARDs	TCZ + DMARDs	DMARDs	SIR (50mg) + DMARDs	SIR (100mg) + DMARDs	DMARDs	BAR (2mg)	BAR (4mg)	MTX	SEC (75mg) +MTX	SEC (150mg) +MTX
	(n=171) ^e	(n=181) ^e	(n=190) ^e	(n=219)	(n=473)	(n=556)	(n=557)	(n=557)	(n=228)	(n=229)	(n=227)			
Estimated yearly progression	27.8	31.4	25.1	-	-	-	-	-	-	-	-			
Baseline SvdH scores														
TSS														
mean (SD)	43.0 (46.8)	45.2 (38.8)	42.0 (41.5)	60.4 (66.5)	59.0 (65.9)	41.9 (46.7)	41.8 (45.4)	42.5 (49.3)	19.0 (31.0)	26.0 (40.0)	24.0 (40.0)	57.7 (66.8)	55.0 (55.3)	48.1 (51.8)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
range	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ES														
mean (SD)	25.1 (26.3)	26.7 (22.1)	25.2 (23.9)	31.7 (36.6)	30.8 (36.4)	-	-	-	12.0 (19.0)	16.0 (24.0)	15.0 (23.0)	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
range	-	-	-	-	-	-	-	-	-	-	-	-	-	-
JSN score														
mean (SD)	17.9 (21.9)	18.5 (19.1)	16.8 (19.1)	28.7 (31.6)	28.2 (31.1)	-	-	-	7.0 (14.0)	10.0 (18.0)	9.0 (18.0)	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
range	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Change in SvdH at 6 months														
ΔTSS														
mean (SD)	5.1 (0.6) ^c	2.4 (0.5) ^c	1.7 (0.5) ^c	1.2 (2.8)	0.6 (2.7)	2.0	0.4	0.3	0.7 ^f	0.3 ^f	0.2 ^f	-	-	-

median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔES														
mean (SD)	-	-	-	0.7 (1.7)	0.3 (1.4)	-	-	-	0.5 ^f	0.3 ^f	0.1 ^f	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔJSN score														
mean (SD)	-	-	-	0.6 (1.7)	0.4 (1.7)	-	-	-	0.2 ^f	0.0 ^f	0.0 ^f	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Change in SvdH at 1 year														
ΔTSS														
mean (SD)	9.8 (1.2) ^c	5.2 (0.9) ^c	3.3 (0.7) ^c	-	-	3.7	0.5	0.5	-	-	-	-	2.2	1.7
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔES														
mean (SD)	5.4 (0.6) ^c	2.8 (0.6) ^c	2.0 (0.5) ^c	-	-	-	-	-	-	-	-	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔJSN score														
mean (SD)	4.4 (0.7) ^c	2.4 (0.4) ^c	1.3 (0.3) ^c	-	-	-	-	-	-	-	-	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Non-progressors at 1 year, %														
≤ 0 TSS	22.8	41.6	43.6	56.0	60.0	45.5	59.0	62.4	74.2 ^h	71.6 ^h	80.3 ^h	-	-	-
≤ SDC	-	-	-	-	-	-	-	-	83.2 ^h	86.5 ^h	92.9 ^h	-	-	-
≤ SDD	81.9	88.9	94.5	-	-	-	-	-	-	-	-	-	-	-
≤ 0.5 TSS	25.7	45.3	49.2	-	-	-	-	-	77.4 ^h	81.7 ^h	88.9 ^h	-	-	-

(Supplementary Table 1 Cont'd)

Sharp score

Patients Population	MTX naïve												MTX IR			DMARD IR				
Trial Name	US301			MN302		ERA			PREMIER			HOPEFUL 1		DE-019			MN301			
Intervention ^a	PBO	MTX	LEF	MTX	LEF	MTX	ETN (10mg)	ETN (25mg)	MTX	ADA	ADA + MTX	MTX	ADA + MTX	MTX	ADA (40mg) +MTX	ADA (20mg) +MTX	PBO	SSZ	LEF	
	(n=83) ^e	(n=138) ^e	(n=131) ^e	(n=331) ^e	(n=304) ^e	(n=217)	(n=208)	(n=207)	(n=257)	(n=274)	(n=268)	(n=163)	(n=171)	(n=200)	(n=207)	(n=212)	(n=62) ^e	(n=86) ^e	(n=89) ^e	
Estimated yearly progression	3.7	3.5	3.3	6.5	6.7	9.5	8.3	8.7	27.4	26.7	25.6	-	-	6.1	6.5	6.1	8.1	5.7	6.1	
Baseline SvdH scores																				
mTSS																				
mean (SD)	25.4 (31.3)	22.8 (39.0)	23.1 (34.0)	24.6	24.9	12.9 (13.8)	11.2 (14.8)	12.4 (15.8)	21.9 (22.2)	18.8 (19.0)	18.1 (20.1)	13.6 (17.4)	13.6 (22.3)	66.4 (47.4)	72.1 (60.7)	66.4 (56.3)	46.2	41.9	46.3	
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	55.5	48.5	54.5	-	-	-	
range	0.0-104.0	0.0-215.0	0.0-258.0	0.0-229.0	0.0-181.0	0.0-113.0	-	0.0-77.0	-	-	-	-	-	0.5-230.5	1.5-308.5	2.0-280.0	0.0-274.0	0.0-243.0	0.0-209.0	
ES																				
mean (SD)	9.3 (14.2)	8.1 (18.4)	9.0 (19.6)	-	-	7.5 (9.2)	6.1 (9.0)	6.4 (9.0)	13.6 (13.6)	11.3 (11.3)	11.3 (11.3)	7.3 (9.2)	7.5 (11.6)	37.2 (25.8)	41.4 (33.4)	36.7 (31.4)	-	-	-	
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	33.5	30.5	29.5	-	-	-	
range	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5-114.5	1.5-185.0	2.0-169.5	-	-	-	
JSN score																				
mean (SD)	16.1 (20.8)	14.7 (23.3)	14.2 (18.9)	-	-	5.4 (6.1)	5.0 (7.7)	6.0 (8.2)	8.2 (10.7)	7.5 (9.4)	7.1 (9.6)	6.2 (9.4)	6.2 (11.4)	29.2 (24.5)	30.7 (29.2)	29.7 (26.9)	-	-	-	
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	22.0	21.3	22.0	-	-	-	
range	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0-115.5	0.0-138.5	0.0-129.5	-	-	-	
Change in SvdH at 6 months																				
ΔmTSS																				

mean (SD)	-	-	-	-	-	1.1	-	0.6	3.5	2.1	0.8	2.4 (3.2)	1.5 (6.1)	1.3	0.3	0.6	5.9 (10.0)	2.3 (10.1)	1.2 (2.9)
median (IQR)	-	-	-	-	-	-	-	-	1.0	0.5	0.0	1.0	0.0	0.3	0.0	0.0	3.0	0.5	0.0
Δ ES																			
mean (SD)	-	-	-	-	-	0.7	-	0.3	2.4	1.3	0.6	-	-	0.7 (2.4)	0.2 (2.9)	0.3 (2.3)	2.1 (4.1)	0.9 (3.3)	0.6 (1.3)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.0	-	-	-
Δ JSN score																			
mean (SD)	-	-	-	-	-	0.4	-	0.3	1.0	0.8	0.2	-	-	0.6 (2.0)	0.1 (2.2)	0.4 (2.9)	3.8 (7.5)	1.4 (6.9)	0.6 (2.3)
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.0	-	-	-
Change in SvdH at 1 year																			
Δ mTSS																			
mean (SD)	2.2 (4.0)	0.9 (3.3)	0.5 (4.5)	1.6 (13.4)	2.5 (5.4)	1.6	1.4	1.0	5.7	3.0	1.3	3.3	2.6	2.76 (6.8)	0.13 (4.9)	0.9 (5.0)	-	1.4 (2.9)	1.0 (6.1)
median (IQR)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-	-	-	-	-	1.0	0.0	0.5	-	0.5	0.0
Δ ES																			
mean (SD)	0.8 (1.8)	0.5 (1.8)	0.2 (2.2)	0.5 (6.9)	1.0 (2.8)	1.0	1.0	0.5	3.7	1.7	0.8	-	-	1.7 (4.4)	0.0 (2.8)	0.4 (2.5)	-	-	-
median (IQR)	0.0	0.0	0.0	-	-	0.0	0.0	0.0	-	-	-	-	-	0.5	0.0	0.0	-	-	-
Δ JSN score																			
mean (SD)	1.2 (2.7)	0.4 (1.8)	0.3 (2.8)	1.1 (7.2)	1.5 (3.5)	0.6	0.4	0.5	2.0	1.3	0.5	-	-	1.1 (3.1)	0.1 (2.4)	0.5 (2.9)	-	-	-
median (IQR)	0.0	0.0	0.0	-	-	0.0	0.0	0.0	-	-	-	-	-	0.0	0.0	0.0	-	-	-
Non-progressors at 1 year, %																			
≤ 0 mTSS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
\leq SDC	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
\leq SDD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
≤ 0.5 mTSS	-	-	-	-	-	51.0	53.0	63.0	37.0	51.0	64.0	35.4 ^d	62.0 ^d	52.2	68.5	67.8	-	-	-

Others	88.0 ^j	96.0 ^j	97.0 ^j	90.0 ^j	89.0 ^j				83.0 ^j	95.0 ^j	97.0 ^j
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a When the active drug was used at a recommended-standard dose, it was not stated in the table.

b This result was evaluated from all 3 IL-1Ra dosage groups.

c The value was the standard error of mean.

d This was calculated using 26 weeks data

e Statistical analysis was performed using the radiographic data set.

f The value was the least square mean (standard error).

g This was calculated based on 30 weeks data.

h This was calculated based on 24 weeks data.

i Radiographic non-progression at 1 year was defined by erosion score ≤ 0 .

j Radiographic progression was defined by an increase in erosion scores of >3 units.

Δ , changes from baseline; ABA, abatacept; ADA, adalimumab; BAR, baricitinib; bid, two times a day; biw, twice a week; CZP, certolizumab; DMARDs, disease-modifying antirheumatic drugs; DNM, denosumab; ES, erosion score; ETN, etanercept; GOL, golimumab; IFX, infliximab; IL-1RA, interleukin 1 receptor antagonist; IQR, interquartile range; IR, inadequate responder; JSN, joint space narrowing; LEF, leflunomide; mTSS, modified total Sharp score; MTX, methotrexate; PBO, placebo; PEF, peficitinib; RTX, rituximab; SAR, sarilumab; SD, standard deviation; SDC, smallest detectable change; SDD, smallest detectable difference; SEC, secukinumab; SIR, sirukumab; SSZ, sulfasalazine; SvdH, van der Heijde modification of the Sharp score; TCZ, tocilizumab; TGS, total Genant score; TNF, tumor necrosis factor; TOF, tofacitinib; TSS, total Sharp van der Heijde score; UPA, upadacitinib.

Supplementary Table 2. Radiographic outcomes of long-term extension trial

Scoring Method	Genant score											
Patients population	MTX naïve				MTX IR						TNFi IR	
Trial name	IMAGE ¹			AGREE ²		AIM ^{3,4}		LITHE ⁵			REFLEX ⁶	
Intervention ^a	MTX	RTX (2x500mg) + MTX	RTX (2x1000mg)+ MTX	MTX	ABA + MTX	MTX	ABA + MTX	MTX	TCZ (4mg/kg) + MTX	TCZ (8mg/kg) + MTX	MTX	RTX + MTX
Change in Genant score at 2 years												
ΔTGS mean (SEM)	1.9	0.8	0.4	1.8	0.8	3.2	1.6	2.0	0.6	0.4	2.8	1.1
ΔES mean (SEM)	1.3	0.5	0.2	1.4	0.6	1.7	0.8	1.2	0.3	0.2	1.8	0.7
ΔJSN score mean (SEM)	0.6	0.3	0.2	0.4	0.3	1.5	0.7	0.7	0.2	0.2	1.0	0.4
Non progressors at 2 years, %												
≤ 0TGS	37.0	49.0	57.0	43.8	56.8	-	50.0	66.0	75.0	83.0	39.0	57.0
≤ SDC	-	-	-	-	-	-	-	-	-	-	-	-
Change in Genant score at 5 years												
ΔTGS mean (SEM)	-	-	-	-	-	-	0.3 (1.4) ^b	3.0	1.3		5.5 (1.0)	3.2 (0.6)
ΔES mean (SEM)	-	-	-	-	-	-	0.1 (0.7) ^b	1.7	0.7		-	-
ΔJSN score mean (SEM)	-	-	-	-	-	-	0.1 (0.9) ^b	1.3	0.7		-	-
Non progressors at 5 years, %												
≤ 0TGS	-	-	-	-	-	39.1	45.1	34.9	52.7		21.5	32.4

(Supplementary Table 2 Cont'd)

Scoring Method	Sharp-van der Heijde score																					
Patients Population	MTX -naïve											MTX IR										
Trial name	GO-BEFORE ⁷⁻⁹				FUNCTION ¹⁰				ORAL Start ¹¹			ATTRACT ¹²					RAPID 1 ¹³			RAPID 2 ¹⁴		
Intervention ^a	MTX	GOL (100mg)	GOL (50mg) + MTX	GOL (100mg) + MTX	MTX	TCZ (8mg/kg)	TCZ (4mg/kg) + MTX	TCZ (8mg/kg) + MTX	MTX	TOF (5mg bid)	TOF (10mg bid)	MTX	IFX (3mg/kg, q8w) + MTX	IFX (3mg/kg, q4w) + MTX	IFX (10mg/kg, q8w) + MTX	IFX (10mg/kg, q4w) + MTX	MTX	CZP (200mg) + MTX	CZP (400mg) + MTX	MTX	CZP (200mg) + MTX	CZP (400mg) + MTX
Change in Sharp score at 2 years																						
ΔTSS																						
mean (SD)	0.9 (4.2)	2.5 (13.8)	-0.0 (1.9)	-0.2 (2.0)	1.9 (6.2)	1.4 (11.7)	0.2 (2.1)	0.6 (4.8)	2.1	0.6	0.3	12.6 (20.1)	1.0 (7.1)	1.0 (11.7)	1.1 (4.9)	-0.4 (6.1)	-	0.9 (3.8)	0.7 (5.3)	1.0 (2.1)	0.2 (2.9)	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	4.3	0.4	0.5	1.0	0.0	-	-	-	-	-	-
ΔES																						
mean (SD)	-	-	-	-	1.0 (4.0)	0.6 (4.1)	0.1 (1.3)	0.2 (2.0)	1.0	0.2	0.2	6.7 (11.2)	0.3 (4.4)	0.5 (9.1)	0.4 (2.6)	-0.6 (3.9)	-	-	-	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	2.0	0.0	0.1	0.5	0.0	-	-	-	-	-	-
ΔJSN score																						
mean (SD)	-	-	-	-	0.9 (3.3)	0.9 (8.0)	0.1 (0.9)	0.1 (1.4)	1.1	0.4	0.1	5.9 (10.6)	0.8 (3.7)	0.1 (4.8)	0.6 (3.3)	0.2 (3.6)	-	-	-	-	-	-
median (IQR)	-	-	-	-	-	-	-	-	-	-	-	2.0	0.5	0.0	0.0	0.0	-	-	-	-	-	-
Non progressors at 2 years, %																						
≤ 0TSS	56.8	54.0	66.2	67.2	68.0	73.0	83.0	80.0	-	-	-	22.0	43.0	47.0	41.0	54.0	-	-	-	-	-	-
≤ SDC	93.6	92.7	97.7	99.2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
≤ 0.5TSS	-	-	-	-	-	-	-	-	64.9	79.9	83.7	-	-	-	-	-	51.5	72.4	77.3	-	78.3	-
Change in Sharp score at 3 years																						
ΔTSS mean (SD)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.0 (2.5)	0.5 (2.8)	-
Change in Sharp score at 5 years																						
ΔTSS mean (SD)	2.3 (6.7)	1.8 (6.8)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

(Supplementary Table 2 Cont'd)

Scoring Method	Sharp-van der Heijde score																		
Patients Population	MTX IR									DMARD IR						TNFi IR			
Trial name	GO-FORWARD				GO-FORTH ¹⁵			GO-FURTHER ¹⁶		TEMPO ¹⁷			GO-MONO ¹⁸			REASSURE			
Intervention ^a	MTX	GOL (100mg)	GOL (50mg) + MTX	GOL (100mg) + MTX	MTX	GOL (50mg) + MTX	GOL (100mg) + MTX	MTX	GOL (2mg/kg) + MTX	MTX	ETN	ETN + MTX	PBO	GOL (50mg)	GOL (100mg)	PBO + MTX	SEC (75mg) + MTX	SEC (150mg) + MTX	
Change in Sharp score at 2 years																			
ΔTSS																			
mean (SD)	1.2 (4.4)	1.9 (5.8)	0.5 (3.3)	0.5 (3.5)	1.5 (12.0)	2.3 (10.0)	1.6 (7.2)	2.1 (7.4)	0.7 (6.3)	3.3	1.1	-0.6	3.6 (9.4)	3.9 (7.5)	2.6 (6.3)	-	5.58	3.83	
median (IQR)	-	-	-	-	0.0	0.0	0.0	-	-	0.0 (-0.1-2.3)	0.0 (-0.7-1.1)	0.0 (-1.4-0.1)	1.0	1.0	1.0	-	-	-	
ΔES																			
mean (SD)	-	-	-	-	-	-	-	0.4 (4.6)	20.1 (3.7)	2.1	0.4	-0.8	-	-	-	-	-	-	
median (IQR)	-	-	-	-	-	-	-	-	-	0.0 (-0.4-1.5)	0.0 (-0.7-0.5)	0.0 (-1.1-0.0)	-	-	-	-	-	-	
ΔJSN score																			
mean (SD)	-	-	-	-	-	-	-	1.7 (3.9)	0.8 (3.6)	1.2	0.7	0.2	-	-	-	-	-	-	
median (IQR)	-	-	-	-	-	-	-	-	-	0.0 (0.0-0.5)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	-	-	-	-	-	-	
Non progressors at 2 years, %																			
≤ 0TSS	57.1	56.6	63.0	66.7	89.9	83.6	87.3	-	-	-	-	-	37.3	30.6	44.9	-	-	-	
≤ SDC	-	-	-	-	89.9	83.6	87.3	76.1	83.3	85.0	90.0	97.0	21.3	22.2	23.6	-	-	-	
≤ SDD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
≤ 0.5TSS	-	-	-	-	-	-	-	-	-	60.0	68.0	78.0	-	-	-	-	-	-	
Change in Sharp score at 3 years																			
ΔTSS																			
mean (SD)	-	-	-	-	-0.2 (8.1)	4.1 (13.4)	1.70 (5.9)	-	-	5.9	1.6	-0.1	3.9 (9.9)	4.0 (7.7)	2.7 (6.7)	-	-	-	
median	-	-	-	-	0.0	0.0	0.0	-	-	-	-	-	1.5	1.2	1.0	-	-	-	
ΔES mean	-	-	-	-	-	-	-	-	-	3.3	0.4	-0.7	-	-	-	-	-	-	
ΔJSN score mean	-	-	-	-	-	-	-	-	-	2.7	1.2	-0.7	-	-	-	-	-	-	
Non-progressors at 3 years																			
≤ SDC					90.9	79.4	84.2						22.5	22.1	22.4				

(Supplementary Table 2 Cont'd)

Scoring Method	Sharp score											
Patients Population	MTX -naïve									MTX IR		
Trial name	US301			ERA ¹⁹			PREMIER ^{20 21}			DE-019 ²²		
Intervention ^a	PBO	MTX	LEF	MTX	ETN (10mg)	ETN (25mg)	MTX	ADA	ADA+ MTX	MTX	ADA (40mg) +MTX	ADA (20mg) +MTX
Change in Sharp score at 2 years												
ΔmTSS												
mean (SD)	-	1.2 (3.8)	1.6 (4.2)	3.2	-	1.3	10.4	5.5	1.9	-	-	-
median	-	0.0	0.0	0.5	-	0.0	2.3	1.0	0.0	-	-	-
ΔES												
mean (SD)	-	0.6 (1.7)	1.0 (3.1)	1.9	-	0.7	6.4	3.0	1.0	-	-	-
median	-	-	-	0.0	-	0.0	-	-	-	-	-	-
ΔJSN score												
mean (SD)	-	0.6 (2.6)	0.5 (1.7)	1.3	-	0.7	4.0	2.6	0.9	-	-	-
median	-	-	-	0.0	-	0.0	-	-	-	-	-	-
Non progressors at 2 years, %												
≤ 0mTSS	-	-	-	-	51.0	63.0	-	-	-	-	-	-
≤ SDC	-	-	-	-	-	-	-	-	-	-	-	-
≤ SDD	-	-	-	-	-	-	-	-	-	-	-	-
Others	-	80.0 ^c	88.0 ^c	-	-	-	-	-	-	-	-	-
Change in Sharp score at 3 years												
ΔmTSS mean	-	-	-	-	-	-	-	-	-	3.7	0.0	1.0
ΔES mean	-	-	-	-	-	-	-	-	-	1.5	-0.2	0.1
ΔJSN score mean	-	-	-	-	-	-	-	-	-	2.2	0.3	0.9
Change in Sharp score at 5 years												
ΔmTSS mean (SD)	-	-	-	2.8	4.5	3.1	9.7	8.7	2.9	3.9 (9.8)	0.8 (10.6)	2.6 (9.6)

ΔES mean	-	-	-	1.4	2.9	1.6	5.2	4.3	1.0	1.1	-0.1	0.9
ΔJSN score mean	-	-	-	-	1.6	1.5	4.4	4.4	1.9	2.8	0.9	1.8
Non-progressors at 3 years, %												
≤ 0.5mTSS	-	-	-	-	-	-	-	-	-	40.0	58.0	44.0
Change in Sharp at 10 years												
ΔmTSS mean	-	-	-	-	-	-	4.7 ^d	3.9 ^d	3.7 ^d	6.2 ^e	0.7 ^e	-

a When the active drug was used at a recommended-standard dose, it was not stated in the table.

b The value was standard deviation.

c Radiographic progression was defined by an increase in erosion scores only.

d This result corresponded to a change from 3 years to 10 year.

e This change at 10 years was calculated using Sharp-van der Heijde scoring method.

Δ, changes from baseline; BA, abatacept; ADA, adalimumab; CZP, certolizumab; ES, erosion score; ETN, etanercept; GOL, golimumab; IFX, infliximab; IQR, interquartile range; IR, inadequate response; JSN, joint space narrowing; LEF, leflunomide; mTSS, modified total Sharp score; MTX, methotrexate; PBO, placebo; RTX, rituximab; SD, standard deviation; SDC, smallest detectable change; SDD, smallest detectable difference; SEC, secukinumab; SEM, standard error of mean; TCZ, tocilizumab; TGS, total Genant score; TNF, tumor necrosis factor; TOF, tofacitinib; TSS, total van der Heijde modification of the Sharp score.

Supplementary Table 3. Radiographic outcome of tapering trials

Scoring method	Genant score		Sharp-van der Heijde score							
Patients population	MTX IR		MTX naïve							
Trial name	ACT-RAY ²³		PRIZE			OPTIMA ²⁴				
Intervention	TCZ Add-on ^a	TCZ switch ^a	ETN stop + PBO	MTX	ETN + MTX	ADA+MTX ^b			MTX ^b	
						ADA stop + MTX (n=102)	ADA q2w + MTX (n=105)	ADA q2w + MTX ^c	MTX (n=112)	ADA q2w + MTX ^d
Baseline radiographic scores										
TS mean (SD)	36.9 (33.2)	41.2 (40.0)	7.6 (10.5)	8.5 (16.0)	8.1 (13.4)	12.2 (19.4)	10.8 (15.6)	11.3 (18.1)	8.9 (13.8)	11.7 (18.5)
			-	-	-	12.2 (19.3) ^e	10.9 (15.7) ^e	11.6 (18.2) ^e	9.2 (13.8) ^e	13.0 (19.5) ^e
ES mean (SD)			6.4 (7.8)	6.2 (8.8)	6.6 (9.9)	-	-	-	-	-
JSN score mean (SD)			2.3 (5.8)	2.3 (6.5)	1.8 (4.8)	-	-	-	-	-
Change in radiographic score at 1 year										
TS mean (SD)	0.35 (0.35) ^f	0.95 (0.32) ^f	0.4 (0.2) ^g	0.0 (0.2) ^g	0.1 (0.1) ^g	-	-	-	-	-
median (IQR)			-	-	-	-	-	-	-	-
ES mean (SD)	-0.03 ^f	0.26 ^f	0.3 (0.1) ^g	0.0 (0.1) ^g	0.0 (0.1) ^g	-	-	-	-	-
JSN score mean (SD)			0.1 (0.1) ^g	0.0 (0.1) ^g	0.1 (0.1) ^g	-	-	-	-	-
Non progressors at 1 year, %										
≤ SDC	94.4	94.1	-	-	-	-	-	-	-	-
≤ 0.5TSS	-	-	-	-	-	80.6 ^e	89.3 ^e	-	78.0 ^e	-

(Supplementary Table 3 Cont'd)

Scoring method	Sharp-van der Heijde score									
Patients population	NTX naïve		MTX IR		DMARD naïve				TNF user	
Trial name	C-OPERA ²⁵		CAMEO		C-EARLY				ADMIRE	
Intervention	CZP hold +MTX	MTX	ETN+ MTX hold	ETN +MTX	MTX	CZP q2w + MTX	CZP q4w + MTX	CZP stop + MTX	ADA + MTX	ADA stop +MTX
Baseline SvdH scores										
TSS mean (SD)					6.8 (12.7)	3.3 (5.4)	4.5 (8.9)	5.0 (7.4)	-	-
median (IQR)	3.8 (7.4)	3.2 (6.2)	37.9 (55.7)	38.2 (50.1)	2.5	1.8	1.5	2.5	22.5 (11.3-52.5)	42.5 (22-95.3)
range	-	-			0.0-70.0	0.0-34.0	0.0-64.0	0.0-38.0	-	-
ES mean (SD)	-	-	16.8 (29.4)	15.3 (25.0)	-	-	-	-	-	-
JSN score mean (SD)	-	-	21.1 (27.8)	22.9 (26.9)	-	-	-	-	-	-
Change in SvdH score at 1 year										
TSS median (IQR)	-	-	-	-	-	-	-	-	25 (13.8-51.8)	35.5 (18.3-70.8)
ES mean (SD)	-	-	-	-	-	-	-	-	-	-
JSN score mean (SD)	-	-	-	-	-	-	-	-	-	-
Non progressors at 1 year, %										
≤ 0.5TSS					21.7	9.7	15.9	18.9	-	-
Change in SvdH score at 2 years										
TSS mean (SD)	0.7 (5.4)	3.0 (9.7)	0.4 (1.9)	0.0 (1.4)	-	-	-	-	-	-
median (IQR)	-	-			-	-	-	-	-	-
ES mean (SD)	0.3 (2.5)	1.4 (4.4)	0.3 (1.5)	0.0 (1.0)	-	-	-	-	-	-
JSN score mean (SD)	0.4 (4.3)	1.6 (7.2)	0.1 (0.6)	0.0 (0.7)	-	-	-	-	-	-
Non progressors at 2 years, %										
≤ 0.5TSS	84.2	67.5			-	-	-	-	-	-

a If DAS28-ESR was <2.6 at two consecutive assessment visits 12 weeks apart, TCZ was discontinued.

- b The OPTIMA trial was double-period study. For the first 26 weeks (period 1), patients were randomized to ADA plus MTX and placebo (PBO) plus MTX group.
- c At Period 1, patients who received treatment with ADA+MTX but did not reach stable low disease activity (DAS<3.2) (LDA) at weeks 22 and 26 received ADA plus MTX (ADA carry on group).
- d At Period 1, patients who received treatment with PBO+MTX but did not reach stable LDA received at week 22 and 26 received ADA plus MTX (ARA rescue group).
- e This was calculated using 26 weeks data.
- f The value was adjusted mean.
- g Values were mean adjusted change with standard error from double-blind baseline to week 39 for the double-blind phase.

ADA, adalimumab; CZP, certolizumab; DAS28, the 28-joint disease activity score; DMARDs, disease-modifying antirheumatic drugs; ES, erosion score; ETN, etanercept; IQR, interquartile range; IR, inadequate responder; JSN, joint space narrowing; MTX, methotrexate; SvdH, van der Heijde modification of the Sharp score; SD, standard deviation; SDC, smallest detectable change; TCZ, tocilizumab; TS, total score; TSS, total van der Heijde modification of the Sharp score; TNF, tumor necrosis factor.

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Supplementary Figure legends

Supplementary Figure 1. Flow chart of data extraction.

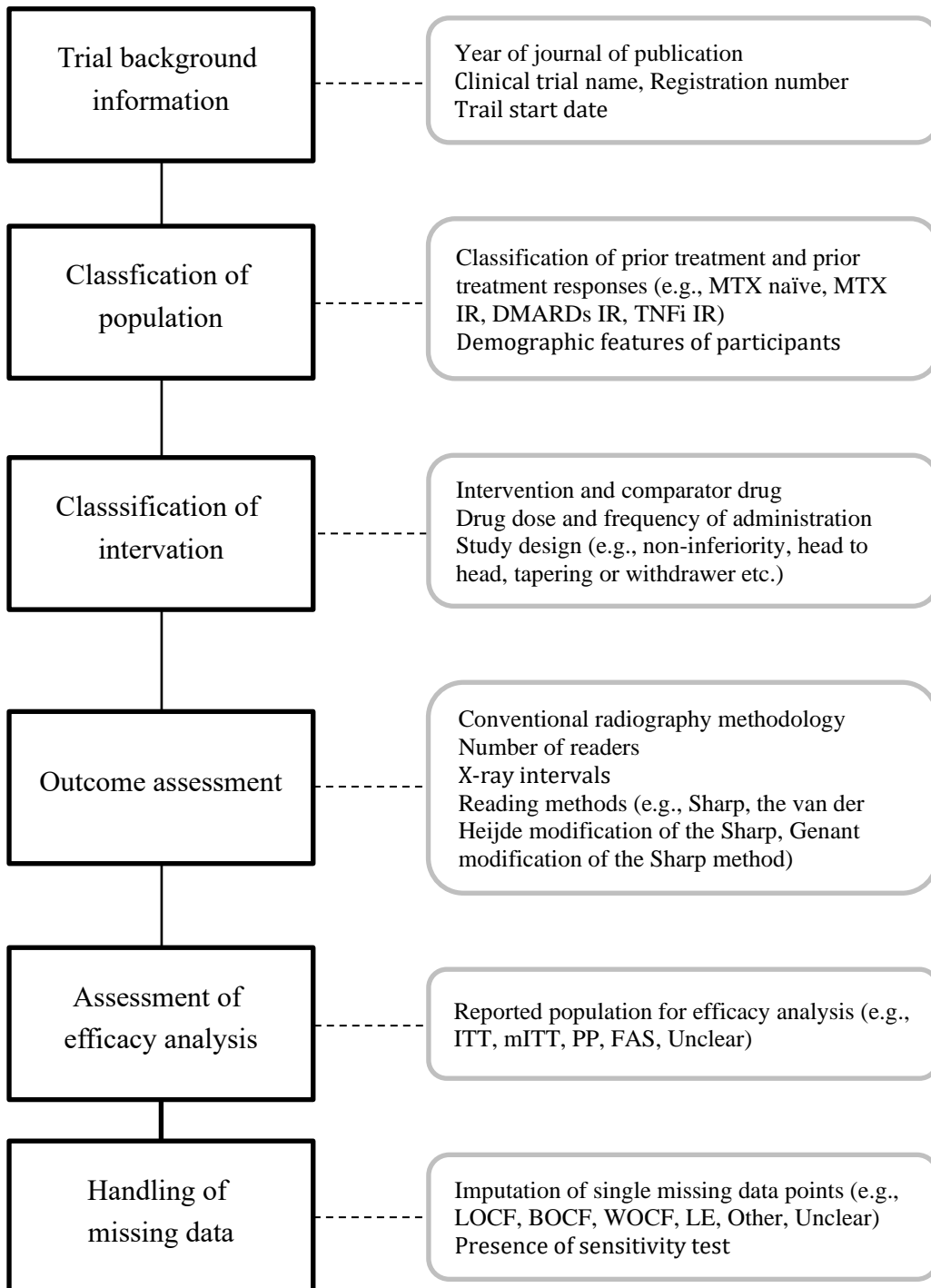
MTX, methotrexate; IR, inadequate responder; DMARDs, disease-modifying antirheumatic drugs; TNF, tumor necrosis factor; ITT, intention to treat; mITT, modified ITT; PP, per protocol; FAS, full analysis set; LOCF, last observation carried forward method; BOCF, baseline observation carried forward; WOCF, worst observation carried forward; LE, Linear extrapolation.

Supplementary Figure 2. Relationship between autoantibody positivity and trial launched year. A scatter plot showed the relationship with trial launched year and (A) RF positivity and (B) ACPA positivity.

RF, rheumatoid factor; ACPA, anti-citrullinated protein antibody.

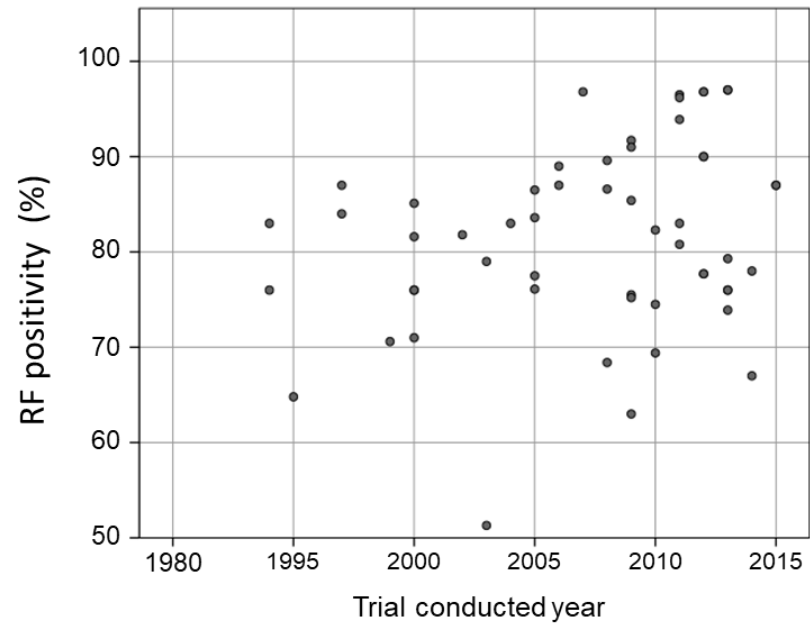
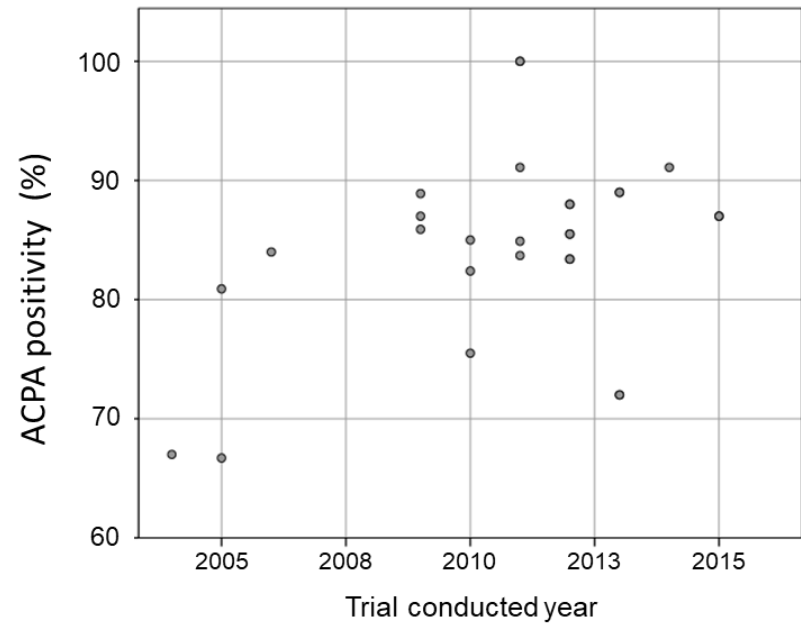
Supplementary Figure 3. Baseline radiographic data (mean SvdH) presented in order of publication separate for patients with early (A) and established RA (B).

RA, rheumatoid arthritis; SvdH, van der Heijde modification of the Sharp.

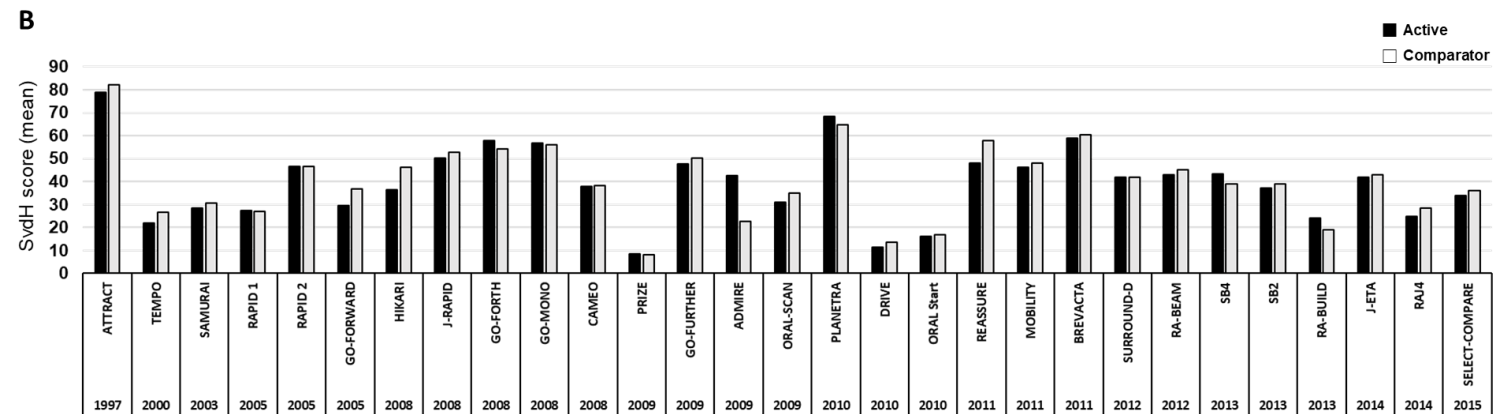
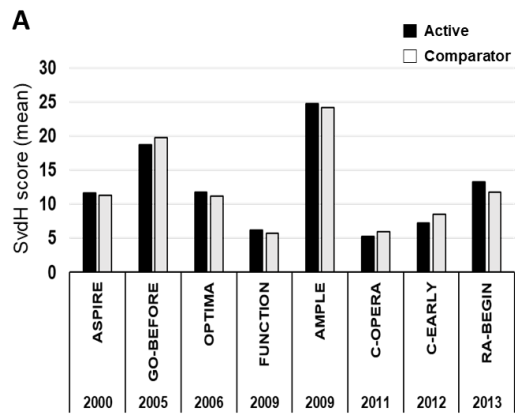


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A**B**

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