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Supplementary material

Supplementary Table 1. Summary of baseline characteristics/covariates for 13 studies used in development of the population PK model.[a]

Variable	Study Number (NCT0)													
	0279760 (n = 8)	**0048581 (n = 50)**	**0048932 (n = 50)**	**0254293 (n = 65)**	**0162266 (n = 162)**	**0162279 (n = 66)**	**0048568 (n = 50)**	**0533897 (n = 162)**	**0547521 (n = 100)**	**0559585 (n = 1408)**	**663702 (n = 123)**	**1001832 (n = 117)**	**2504268 (n = 689)[b]**	**Overall (n = 3050)**
Age, yrs, mean (SD)	39.9 (10.8)	53 (11.6)	52.7 (12.4)	59.9 (11.5)	55.5 (11.6)	50.1 (11.4)	53.8 (12.7)	49.8 (13.4)	54 (10.9)	49.8 (12.9)	54.3 (12.5)	55.5 (12.9)	49.3 (12.8)	50.9 (12.9)
Sex, female, n (%)	7 (87.5)	38 (76)	38 (76)	55 (84.6)	113 (69.8)	48 (72.7)	33 (66)	137 (84.6)	75 (75)	1164 (82.7)	101 (82.1)	86 (73.5)	535 (77.6)	2430 (79.7)
Weight, kg, mean (SD)	72.6 (18.5)	80.7 (20.1)	72.2 (23.4)	82.1 (22.5)	78.2 (19.7)	83.1 (23.1)	76.7 (20.2)	71.3 (18.2)	83.1 (20.6)	71.9 (17.9)	78 (20.2)	55.1 (10.3)	72.2 (16.7)	72.9 (18.8)
Race, n (%)														
White	5 (62.5)	49 (98)	43 (86)	57 (87.7)	143 (88.3)	64 (97)	47 (94)	148 (91.4)	76 (76)	1048 (74.4)	117 (95.1)	0 (0)	484 (70.2)	2281 (74.8)
Black/ African American	0 (0)	1 (2)	2 (4)	8 (12.3)	5 (3.09)	2 (3.03)	1 (2)	3 (1.85)	11 (11)	53 (3.76)	3 (2.44)	0 (0)	27 (3.92)	116 (3.8)
Hispanic/ Latino	2 (25)	0 (0)	0 (0)	0 (0)	12 (7.41)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	14 (0.459)
Asian/ Pacific Islander	0 (0)	0 (0)	5 (10)	0 (0)	2 (1.23)	0 (0)	2 (4)	6 (3.7)	11 (11)	134 (9.52)	1 (0.813)	1 (0.855)	15 (2.18)	177 (5.8)
Other	1 (12.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (3.09)	2 (2)	173 (12.3)	2 (1.63)	0 (0)	89 (12.9)	272 (8.92)
Region, n (%)														
North America	0 (0)	0 (0)	0 (0)	65 (100)	0 (0)	0 (0)	0 (0)	67 (41.4)	71 (71)	545 (38.7)	123 (100)	0 (0)	100 (14.5)	971 (31.8)
South America	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	34 (21)	0 (0)	416 (29.5)	0 (0)	0 (0)	294 (42.7)	744 (24.4)

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Asia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	121 (8.59)	0 (0)	117 (100)	84 (12.2)	322 (10.6)
Europe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	234 (16.6)	0 (0)	0 (0)	164 (23.8)	398 (13)
Rest of world	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	61 (37.7)	29 (29)	92 (6.53)	0 (0)	0 (0)	47 (6.82)	229 (7.51)
SJC, mean (SD)	28 (12.6)	21.7 (10.2)	NA (NA)	15.6 (7.14)	20.1 (8.27)	19.1 (9.54)	22.5 (9.02)	10.7 (5.65)	17.2 (12.1)	19.9 (9.16)	4.76 (6.13)	17.1 (7.16)	13.4 (8.8)	17.1 (9.7)
GFR, mL/min/1.73 m^2, mean (SD)	112 (8.83)	99 (21.6)	94.8 (16.9)	82.5 (20.6)	77.1 (18.7)	71.3 (16.9)	96.4 (20)	96.3 (18.3)	86.8 (17.7)	97.7 (19.8)	88.9 (20.6)	107 (12.9)	101 (16.6)	96.1 (20)
Presence of anti-abatacept antibodies, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	31 (4.5)[c]	31 (1.02)
MTX use, n (%)	0 (0)	42 (84)	0 (0)	65 (100)	162 (100)	0 (0)	50 (100)	162 (100)	86 (86)	1408 (100)	99 (80.5)	117 (100)	1 (0.145)	2192 (71.9)
NSAID use, n (%)	4 (50)	36 (72)	40 (80)	15 (23.1)	138 (85.2)	57 (86.4)	39 (78)	15 (9.26)	7 (7)	128 (9.09)	8 (6.5)	109 (93.2)	350 (50.8)	946 (31)

[a]Values of 0 indicate absence of the relevant variable in the patient population.

[b]AVERT-2 study.

[c]Anti-abatacept antibody values differ from those provided in the Results due sample size differences between analyses.

GFR: glomerular filtration rate; MTX: methotrexate; NCT: National Clinical Trial; NSAID: non-steroidal anti-inflammatory drug; PK: pharmacokinetic; SD: standard deviation; SJC: swollen joint count.

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Supplementary Table 2. Analysis of E–R safety models for time to first infection regardless of seriousness by exposure metric.

Exposure	*P* value
AUC_{ss}	0.840
$C_{avg,ss}$	0.840
$C_{min,ss}$	0.850
$C_{max,ss}$	0.882
$C_{min,ss}$	0.988
AUC_{ss}	0.989
$C_{avg,ss}$	0.996
$C_{max,ss}$	0.998

Degrees of freedom = 1 for all exposure variables. AIC: Akaike information criteria (estimator of prediction error and relative quality of statistical models); AUCss: area under the concentration-time curve at steady state; $C_{avg,ss}$: time-averaged serum concentration at steady state; $C_{max,ss}$: peak serum concentration at steady state; $C_{min,ss}$: trough serum concentration at steady state; E–R: exposure–response.

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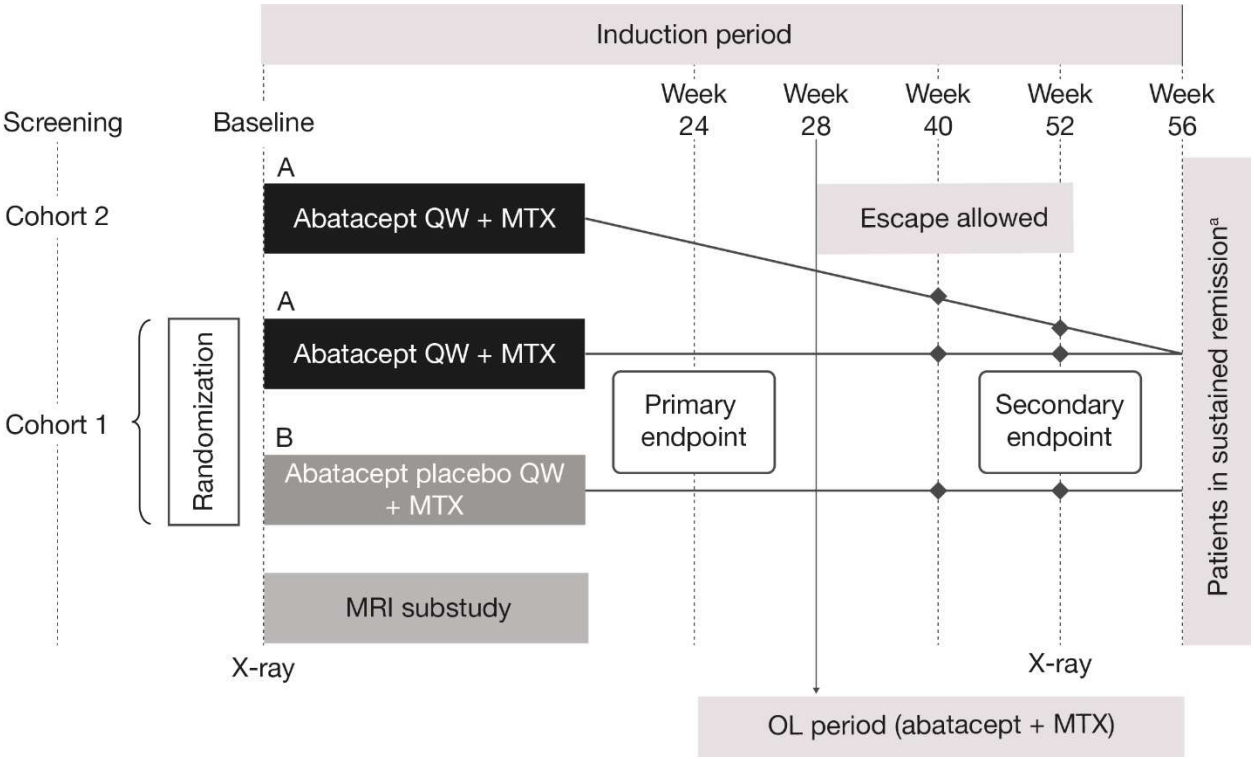
Supplementary Figure 1. Study design.



[a]SDAI ≤3.3 at both weeks 40 and 52.

MRI: magnetic resonance imaging; MTX: methotrexate; OL: open label; QW: once weekly; SDAI: Simplified Disease Activity Index.