Data Supplement

Supplemental Table 1. Treatment emergent adverse events (TEAE) in the long term extension (LTE) study. Numbers of subjects with one or more TEAE (% subjects), total subject-years of exposure from first dose in LTE to last dose + up to 5 half-lives (exposure), and incidence per 100 subject-years of exposure with 95% confidence intervals (Incidence)

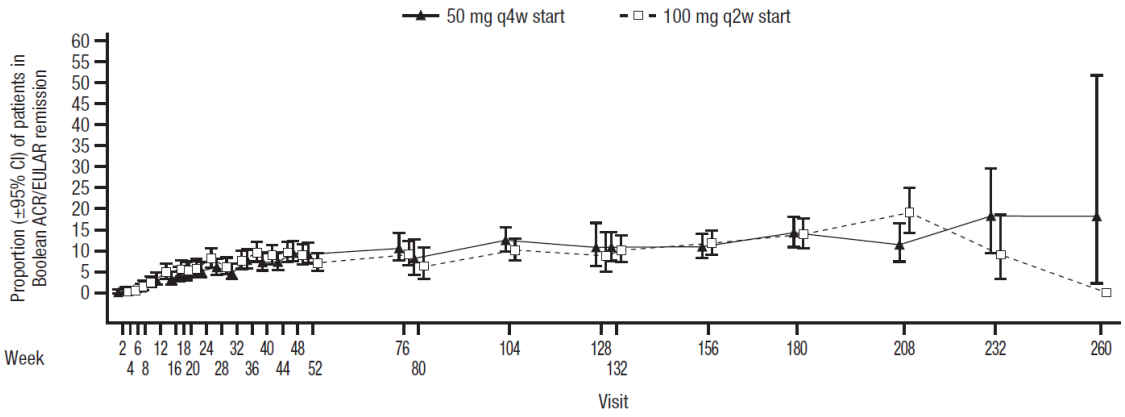
		Placebo → 50 mg q4w	Placebo → 100 mg q2w	50 mg q4w Start	100 mg q2w Start	50 mg q4w combined	100 mg q2w combined	Combined
MI	% subjects	1 (0.3%)	0	5 (0.8%)	3 (0.5%)	6 (0.7%)	3 (0.3%)	9 (0.5%)
	Exposure (PY)	983.5	929.2	2345.2	2414.5	3328.6	3343.7	6672.3
	Incidence (per 100 PY)	0.10 (0.00, 0.57)	0.00 (0.00, 0.32)	0.21 (0.07, 0.50)	0.12 (0.03, 0.36)	0.18 (0.07, 0.39)	0.09 (0.02, 0.26)	0.13 (0.06, 0.26)
Death	% subjects	5 (1.6%)	6 (2.1%)	13 (2.1%)	8 (1.3%)	18 (2.0%)	14 (1.5%)	32 (1.8%)
	Exposure (PY)	986.2	929.2	2352.7	2418.3	3338.9	3347.5	6686.4
	Incidence (per 100 PY)	0.51 (0.16, 1.18)	0.65 (0.24, 1.41)	0.55 (0.29, 0.94)	0.33 (0.14, 0.65)	0.54 (0.32, 0.85)	0.42 (0.23, 0.70)	0.48 (0.33, 0.68)
MACE	% subjects	6 (2.0%)	2 (0.7%)	22 (3.6%)	7 (1.1%)	28 (3.1%)	9 (1.0%)	37 (2.0%)
	Exposure (PY)	982.9	929.1	2324.3	2412.6	3307.2	3341.7	6648.9
	Incidence (per 100 PY)	0.61 (0.22, 1.33)	0.22 (0.03, 0.78)	0.95 (0.59, 1.43)	0.29 (0.12, 0.60)	0.85 (0.56, 1.22)	0.27 (0.12, 0.51)	0.56 (0.39, 0.77)
Stroke	% subjects	3 (1.0%)	2 (0.7%)	7 (1.2%)	3 (0.5%)	10 (1.1%)	5 (0.5%)	15 (0.8%)
	Exposure (PY)	985.7	929.1	2344.7	2416.4	3330.4	3345.5	6675.9
	Incidence (per 100 PY)	0.30 (0.06, 0.89)	0.22 (0.03, 0.78)	0.30 (0.12, 0.62)	0.12 (0.03, 0.36)	0.30 (0.14, 0.55)	0.15 (0.05, 0.35)	0.22 (0.13, 0.37)
Malignancies	% subjects	4 (1.3%)	11 (3.8%)	11 (1.8%)	13 (2.1%)	15 (1.6%)	24 (2.6%)	39 (2.1%)
	Exposure (PY)	980.6	924.2	2345.1	2406.9	3325.7	3331.2	6656.9
	Incidence (per 100 PY)	0.41 (0.11, 1.04)	1.19 (0.59, 2.13)	0.47 (0.23, 0.84)	0.54 (0.29, 0.92)	0.45 (0.25, 0.74)	0.72 (0.46, 1.07)	0.59 (0.42, 0.80)
Malignancies (excluding non-Melanomas)	% subjects	2 (0.7%)	8 (2.7%)	7 (1.2%)	7 (1.1%)	9 (1.0%)	15 (1.6%)	24 (1.3%)
	Exposure (PY)	985.9	927.3	2350.8	2416.5	3336.7	3343.8	6680.4

	Incidence (per 100 PY)	0.20 (0.02, 0.73)	0.86 (0.37, 1.70)	0.30 (0.12, 0.61)	0.29 (0.12, 0.60)	0.27 (0.12, 0.51)	0.45 (0.25, 0.74)	0.36 (0.23, 0.53)
Serious Infections	% subjects	28 (9.2%)	40 (13.7%)	78 (12.9%)	73 (11.8%)	106 (11.6%)	113 (12.4%)	219 (12.0%)
	Exposure (PY)	957.2	891.6	2264.2	2336.8	3221.4	3228.5	6449.9
	Incidence (per 100 PY)	2.93 (1.94, 4.23)	4.49 (3.20, 6.11)	3.44 (2.72, 4.30)	3.12 (2.45, 3.93)	3.29 (2.69, 3.98)	3.50 (2.88, 4.21)	3.40 (2.96, 3.88)
GI Perforations	% subjects	2 (0.7%)	4 (1.4%)	4 (0.7%)	3 (0.5%)	6 (0.7%)	7 (0.8%)	13 (0.7%)
	Exposure (PY)	985.9	927.9	2352.2	2417.3	3338.2	3345.2	6683.4
	Incidence (per 100 PY)	0.20 (0.02, 0.73)	0.43 (0.12, 1.10)	0.17 (0.05, 0.44)	0.12 (0.03, 0.36)	0.18 (0.07, 0.39)	0.21 (0.08, 0.43)	0.19 (0.10, 0.33)
Lower GI Perforations	% subjects	2 (0.7%)	4 (1.4%)	4 (0.7%)	3 (0.5%)	6 (0.7%)	7 (0.8%)	13 (0.7%)
	Exposure (PY)	985.9	927.9	2352.2	2417.3	3338.2	3345.2	6683.4
	Incidence (per 100 PY)	0.20 (0.02, 0.73)	0.43 (0.12, 1.10)	0.17 (0.05, 0.44)	0.12 (0.03, 0.36)	0.18 (0.07, 0.39)	0.21 (0.08, 0.43)	0.19 (0.10, 0.33)
Upper GI Perforations	% subjects	0	0	0	0	0	0	0
	Exposure (PY)	986.2	929.2	2352.7	2418.3	3338.9	3347.5	6686.4
	Incidence (per 100 PY)	0.00 (0.00, 0.30)	0.00 (0.00, 0.32)	0.00 (0.00, 0.13)	0.00 (0.00, 0.12)	0.00 (0.00, 0.09)	0.00 (0.00, 0.09)	0.00 (0.00, 0.04)
Hepatobiliary	% subjects	0	2 (0.7%)	1 (0.2%)	1 (0.2%)	1 (0.1%)	3 (0.3%)	4 (0.2%)
	Exposure (PY)	986.2	928.6	2352.3	2417.9	3338.6	3346.6	6685.1
	Incidence (per 100 PY)	0.00 (0.00, 0.30)	0.22 (0.03, 0.78)	0.04 (0.00, 0.24)	0.04 (0.00, 0.23)	0.03 (0.00, 0.17)	0.09 (0.02, 0.26)	0.06 (0.02, 0.15)
Serious Opportunistic Infections	% subjects	0	0	1 (0.2%)	1 (0.2%)	1 (0.1%)	1 (0.1%)	2 (0.1%)
	Exposure (PY)	986.2	929.2	2352.5	2418.0	3338.7	3347.2	6685.9
	Incidence (per 100 PY)	0.00 (0.00, 0.30)	0.00 (0.00, 0.32)	0.04 (0.00, 0.24)	0.04 (0.00, 0.23)	0.03 (0.00, 0.17)	0.03 (0.00, 0.17)	0.03 (0.00, 0.11)
Serious or Moderate/Severe Systemic Hypersensitivity Reactions, or Serum Sickness	% subjects	1 (0.3%)	2 (0.7%)	2 (0.3%)	2 (0.3%)	3 (0.3%)	4 (0.4%)	7 (0.4%)
	Exposure (PY)	986.0	924.4	2347.8	2416.0	3333.8	3340.4	6674.2
	Incidence (per 100 PY)	0.10 (0.00, 0.57)	0.22 (0.03, 0.78)	0.09 (0.01, 0.31)	0.08 (0.01, 0.30)	0.09 (0.02, 0.26)	0.12 (0.03, 0.31)	0.10 (0.04, 0.22)

Serious Event Pneumonia	% subjects	9 (3.0%)	11 (3.8%)	14 (2.3%)	23 (3.7%)	23 (2.5%)	34 (3.7%)	57 (3.1%)
	Exposure (PY)	976.3	919.5	2338.3	2392.3	3314.6	3311.8	6626.4
	Incidence (per 100 PY)	0.92 (0.42, 1.75)	1.20 (0.60, 2.14)	0.60 (0.33, 1.00)	0.96 (0.61, 1.44)	0.69 (0.44, 1.04)	1.03 (0.71, 1.43)	0.86 (0.65, 1.11)
Serious Events of Demyelination	% subjects	0	0	0	0	0	0	0
	Exposure (PY)	986.2	929.2	2352.7	2418.3	3338.9	3347.5	6686.4
	Incidence (per 100 PY)	0.00 (0.00, 0.30)	0.00 (0.00, 0.32)	0.00 (0.00, 0.13)	0.00 (0.00, 0.12)	0.00 (0.00, 0.09)	0.00 (0.00, 0.09)	0.00 (0.00, 0.04)
Serious Adverse Events of Cellulitis	% subjects	4 (1.3%)	8 (2.7%)	28 (4.6%)	21 (3.4%)	32 (3.5%)	29 (3.2%)	61 (3.4%)
	Exposure (PY)	983.6	921.5	2329.1	2391.1	3312.7	3312.6	6625.3
	Incidence (per 100 PY)	0.41 (0.11, 1.04)	0.87 (0.37, 1.71)	1.20 (0.80, 1.74)	0.88 (0.54, 1.34)	0.97 (0.66, 1.36)	0.88 (0.59, 1.26)	0.92 (0.70, 1.18)
Serious AEs	% subjects	77 (25.2%)	92 (31.6%)	205 (33.9%)	176 (28.4%)	282 (31.0%)	268 (29.5%)	550 (30.2%)
	Exposure (PY)	884.3	808.9	2030.1	2145.8	2914.4	2954.7	5869.1
	Incidence (per 100 PY)	8.71 (6.87, 10.88)	11.37 (9.17, 13.95)	10.10 (8.76, 11.58)	8.20 (7.04, 9.51)	9.68 (8.58, 10.87)	9.07 (8.02, 10.22)	9.37 (8.60, 10.19)

Supplemental Figure 1. (A) Proportion of patients with Boolean-based ACR/EULAR remission from baseline of primary studies to the end of the SIRROUND-LTE study period. (B) Change from baseline in CDAI score by visit from baseline of primary studies to the end of the SIRROUND-LTE study period.

A.



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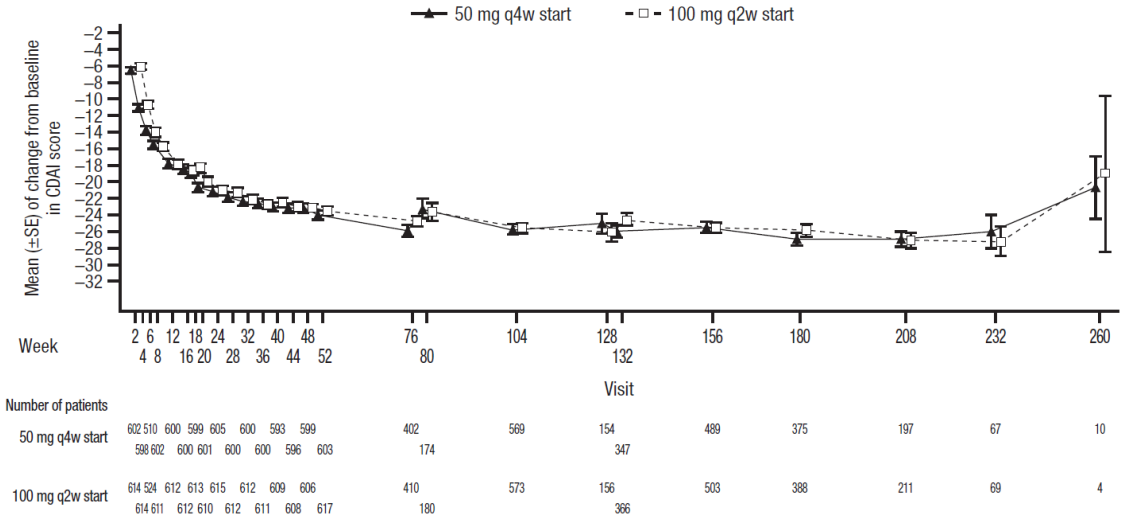

ACR=American College of Rheumatology; CDAI=Clinical Disease Activity Index; EULAR=European League Against Rheumatism; q2w=every 2 weeks; q4w=every 4 weeks; SE, standard error.