

ONLINE SUPPLEMENTARY DATA

Supplementary Table 1. Treatment outcomes for all patients at week 12, by disease duration subgroup*

		Disease Duration and Treatment (n)			
		≤ 2 Years	> 2 to 5 Years	> 5 to 10 Years	> 10 Years
		ETN (225)	ETN (142)	ETN (150)	ETN (291)
		SSZ (56)	SSZ (37)	SSZ (31)	SSZ (51)
Tx		PBO (50)	PBO (28)	PBO (46)	PBO (96)
ASAS20,	ETN	171/225 (76.0)†	99/140 (70.7)†	108/151 (71.5)†	191/289 (66.1)†
<i>n/N (%)</i>	SSZ	28/56 (50.0)	17/37 (45.9)	20/31 (64.5)	28/51 (54.9)
	PBO	22/50 (44.0)‡	4/28 (14.3)‡	14/46 (30.4)‡	26/96 (27.1)‡
BASDAI50	ETN	137/225 (60.9)	89/141 (63.1)	84/151 (55.6)	159/289 (55.0)
<i>n/N (%)</i>	SSZ	19/56 (33.9)	15/37 (40.5)	14/31 (45.2)	17/51 (33.3)
	PBO	10/50 (20.0)	1/28 (3.6)	11/46 (23.9)	15/96 (15.6)
ASDAS $\Delta \geq 2.0$	ETN	81/225 (36.0)	56/141 (39.7)	64/150 (42.7)	112/289 (38.8)
<i>n/N (%)</i>	SSZ	3/56 (5.4)	4/36 (11.1)	3/31 (9.7)	3/50 (6.0)
	PBO	3/50 (6.0)	1/28 (3.6)	3/46 (6.5)	9/96 (9.4)
ASDAS inactive	ETN	61/225 (27.1)	30/141 (21.3)	35/150 (23.3)	62/289 (21.5)
disease	SSZ	3/56 (5.4)	4/36 (11.1)	3/31 (9.7)	3/50 (6.0)
<i>n/N (%)</i>	PBO	3/50 (6.0)	0/28 (0.0)	5/46 (10.9)	9/96 (9.4)
ASDAS-CRP	ETN	-1.7 (-1.9, -1.6)	-1.6 (-1.8, -1.5)	-1.6 (-1.8, -1.5)	-1.6 (-1.7, -1.5)

	SSZ	-0.8 (-1.0, -0.5)	-0.8 (-1.1, -0.5)	-0.9 (-1.2, -0.6)	-0.7 (-1.0, -0.5)
	PBO	-0.6 (-0.9, -0.4)	-0.1 (-0.4, 0.3)	-0.4 (-0.7, -0.1)	-0.4 (-0.6, -0.2)
BASDAI	ETN	-32.5 (-35.8, -29.2)	-29.5 (-33.4, -25.6)	-29.6 (-33.4, -25.8)	-29.0 (-31.6, -26.4)
	SSZ	-17.0 (-22.7, -11.4)	-21.5 (-28.6, -14.3)	-19.5 (-27.1, -11.9)	-18.3 (-24.3, -12.4)
	PBO	-16.2 (-22.1, -10.3)	-4.5 (-12.1, 3.1)	-13.0 (-19.1, -7.0)	-11.1 (-15.5, -6.7)
BASFI	ETN	-25.0 (-28.4, -21.6)	-24.2 (-28.1, -20.2)	-23.1 (-26.9, -19.3)	-21.3 (-23.9, -18.6)
	SSZ	-12.1 (-17.7, -6.4)	-17.3 (-24.5, -10.2)	-16.6 (-24.1, -9.0)	-15.3 (-21.2, -9.4)
	PBO	-12.7 (-18.3, -7.2)‡	2.3 (-4.8, 9.3)‡	-7.1 (-12.7, -1.4)‡	-6.6 (-10.8, -2.4)‡
CRP (mg/L)	ETN	-13.0 (-14.7, -11.4)	-13.3 (-15.2, -11.4)	-11.7 (-13.5, -9.9)	-12.8 (-14.1, -11.5)
	SSZ	-4.9 (-7.9 to -1.9)†‡	-3.5 (-7.2 to 0.2)†‡	-1.7 (-5.8 to 2.3)†‡	1.8 (-1.4 to 5.0)†‡
	PBO	-2.7 (-7.0 to 1.5)	1.7 (-3.7 to 7.1)	2.9 (-1.4 to 7.3)	-2.5 (-5.7 to 0.6)
Modified	ETN	1.0 (0.8, 1.3)†‡	0.9 (0.6, 1.1)†‡	1.0 (0.8, 1.2)†‡	0.6 (0.5, 0.8)†‡
Schober's test	SSZ	0.9 (0.5, 1.3)‡	0.3 (-0.2, 0.8)‡	-0.0 (-0.6, 0.5)‡	0.4 (-0.0, 0.8)‡
	PBO	0.1 (-0.2, 0.5)	0.1 (-0.3, 0.5)	0.1 (-0.3, 0.4)	-0.1 (-0.3, 0.2)
OWD	ETN	-1.2 (-1.6, -0.8)	-0.9 (-1.4, -0.5)	-0.9 (-1.4, -0.5)	-0.8 (-1.1, -0.5)
	SSZ	-0.1 (-0.7, 0.5)	-0.3 (-1.0, 0.4)	-0.5 (-1.3, 0.2)	-0.6 (-1.3, 0.0)

	PBO	-1.0 (-2.0, 0.1)	0.1 (-1.2, 1.5)	-0.5 (-1.6, 0.6)	0.1 (-0.7, 0.9)
PGA	ETN	-33.9 (-36.9, -30.9) ^{†‡}	-28.9 (-32.4, -25.4) ^{†‡}	-30.8 (-34.2, -27.4) ^{†‡}	-29.1 (-31.4, -26.7) ^{†‡}
	SSZ	-22.8 (-28.5, -17.2)	-24.6 (-31.5, -17.7)	-24.1 (-31.7, -16.7)	-23.4 (-29.2, -17.5)
	PBO	-17.9 (-23.6, -12.1)	-5.6 (-13.0, 1.8)	-16.1 (-22.0, -10.2)	-13.6 (-18.0, -9.3)

* All values are adjusted mean change (95% confidence interval) unless otherwise noted.

[†] $p \leq 0.05$ as ordered (trend) using Cochran-Mantel-Haenszel (CMH) test of non-zero correlation for dichotomous outcomes or an ANCOVA model, with baseline of outcome, study, and disease duration as predictors for continuous outcomes.

[‡] $p \leq 0.05$ for disease duration categories analyzed as non-ordered, nominal using CMH test of general association for dichotomous outcomes or an ANCOVA model, with baseline of outcome, study, and disease duration as predictors for continuous outcomes.

Δ = change; ASAS20 = Assessment in Ankylosing Spondylitis improvement of 20%; ASDAS = Ankylosing Spondylitis Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, BASFI = Bath Ankylosing Spondylitis Disease Functional Index; CRP = C-reactive protein; ETN = etanercept; OWD = occiput-to-wall distance; PBO = placebo; PGA = physician global assessment; SSZ = sulfasalazine; tx = treatment.

Supplementary Table 2. Treatment outcomes at week 12 in patients aged ≤ 40 years versus >40 years at diagnosis, by disease duration subgroup*

		Disease Duration by Age Subgroup and Treatment (n)							
		≤ 2 Years		> 2 to 5 Years		> 5 to 10 Years		> 10 Years	
Outcome	Tx	Age ≤ 40 y	Age > 40 y	Age ≤ 40 y	Age > 40 y	Age ≤ 40 y	Age > 40 y	Age ≤ 40 y	Age > 40 y
		ETN (151)	ETN (74)	ETN (99)	ETN (43)	ETN (113)	ETN (37)	ETN (268)	ETN (23)
		SSZ (40)	SSZ (16)	SSZ (27)	SSZ (10)	SSZ (24)	SSZ (7)	SSZ (40)	SSZ (10)
		PBO (31)	PBO (19)]	PBO (19)	PBO (9)	PBO (33)	PBO (13)	PBO (86)	PBO (10)
ASDAS-	ETN	-1.8	-1.5	-1.8	-1.4	-1.8	-1.2	-1.6	-1.3
CRP		(-2.0, -1.7)†	(-1.9, -1.2)	(-2.0, -1.6)†	(-1.7, -1.0)	(-2.0, -1.6)†	(-1.6, -0.9)	(-1.7, -1.5)†	(-1.7, -0.8)
	SSZ	-0.9	-0.4	-0.8	-0.8	-0.9	-0.9	-0.8	-0.3
		(-1.2, -0.6)	(-0.8, -0.0)	(-1.2, -0.5)	(-1.4, -0.2)	(-1.2, -0.5)	(-1.5, -0.3)	(-1.1, -0.6)	(-0.8, 0.2)
	PBO	-0.8	-0.5	-0.3	0.2	-0.4	-0.5	-0.5	-0.5
		(-1.1, -0.4)	(-1.0, -0.1)	(-0.7, 0.2)	(-0.4, 0.8)	(-0.7, -0.1)	(-1.0, 0.0)	(-0.7, -0.2)	(-1.1, 0.0)
BASDAI	ETN	-34.2	-31.8	-31.8	-26.9	-31.9	-25.6	-29.1	-25.4
		(-38.1, -30.4)†	(-39.0, -24.5)	(-36.2, -27.4)†	(-35.5, -18.3)	(-36.1, -27.7)†	(-34.8, -16.5)	(-31.7, -26.4)†	(-35.2, -15.6)
	SSZ	-19.9	-10.2	-20.3	-24.5	-19.6	-19.3	-19.3	-14.4
		(-26.8, -13.0)	(-20.7, 0.3)	(-28.7, -11.9)	(-38.8, -10.3)	(-28.4, -10.9)	(-35.3, -3.3)	(-26.0, -12.6)	(-27.7, -1.1)
	PBO	-20.1	-11.2	-9.0	2.6	-12.9	-15.1	-11.1	-12.9
		(-27.5, -12.7)	(-21.8, -0.6)	(-18.2, 0.2)	(-11.7, 16.9)	(-20.0, -5.8)	(-27.7, -2.6)	(-15.9, -6.3)	(-26.2, 0.5)
BASFI	ETN	-25.7	-26.5	-26.5	-21.5	-24.9	-20.2	-20.5	-23.4

		(-29.6, -21.8)†	(-34.0, -18.9)	(-31.0, -22.0)†	(-30.4, -12.7)	(-29.1, -20.7)†	(-29.6, -10.7)	(-23.3, -17.8)†	(-33.5, -13.2)
	SSZ	-17.1	-0.3	-16.7	-21.0	-15.5	-18.6	-15.5	-13.3
		(-23.5, -10.7)	(-12.0, 11.4)	(-24.6, -8.9)	(-37.0, -5.1)	(-23.7, -7.3)	(-36.3, -0.9)	(-21.8, -9.2)	(-28.3, 1.7)
	PBO	-15.2	-10.0	-2.0	9.9	-7.0	-8.8	-6.4	-11.4
		(-21.9, -8.5)	(-20.8, 0.9)	(-10.3, 6.3)	(-4.4, 24.2)	(-13.4, -0.6)	(-21.6, 3.9)	(-10.8, -2.1)	(-25.4, 2.7)
CRP	ETN	-14.7	-8.0	-14.2	-9.9	-14.2	-3.4	-14.1	-7.1
		(-16.5, -12.9)	(-12.2, -3.9)	(-16.3, -12.2)	(-14.8, -5.1)	(-16.1, -12.3)	(-8.6, 1.8)	(-15.3, -12.9)	(-12.6, -1.5)
	SSZ	-5.9	-1.9	-3.8	-1.4	-2.0	-2.0	0.5	6.2
		(-9.7, -2.2)†	(-6.9, 3.1)	(-8.3, 0.7)†	(-7.9, 5.1)	(-6.8, 2.8)†	(-9.6, 5.7)	(-3.3, 4.2)†	(-0.3, 12.8)
	PBO	-3.0	0.5	3.1	0.2	2.7	5.5	-3.1	-4.3
		(-8.6, 2.6)	(-5.4, 6.5)	(-3.8, 10.1)	(-7.6, 8.0)	(-2.6, 8.1)	(-1.6, 12.5)	(-6.7, 0.6)	(-11.8, 3.1)
Modified	ETN	1.0	1.2	0.9	0.9	1.1	0.7	0.6	0.9
Schober's		(0.7, 1.2)†‡	(0.7, 1.7)	(0.6, 1.2)†‡	(0.3, 1.5)	(0.8, 1.4)†‡	(0.0, 1.3)	(0.4, 0.8)†‡	(0.2, 1.5)
test	SSZ	0.8	1.1	0.4	0.2	0.0	0.1	0.3	0.7
		(0.4, 1.3)	(0.4, 1.8)	(-0.2, 0.9)	(-0.7, 1.0)	(-0.7, 0.6)	(-1.0, 1.2)	(-0.2, 0.8)	(-0.1, 1.5)
	PBO	0.3	-0.1	-0.1	0.6	0.0	0.2	-0.1	0.4
		(-0.1, 0.7)	(-0.7, 0.6)	(-0.5, 0.4)	(-0.3, 1.5)	(-0.3, 0.4)	(-0.6, 1.0)	(-0.4, 0.1)	(-0.4, 1.2)
OWD	ETN	-1.2	-1.5	-0.9	-1.1	-0.9	-1.5	-0.8	-0.7
		(-1.6, -0.7)	(-2.4, -0.6)	(-1.4, -0.4)	(-2.2, -0.1)	(-1.4, -0.4)	(-2.6, -0.4)	(-1.1, -0.5)	(-1.9, 0.5)

	SSZ	-0.3 (-1.1, 0.4)	0.7 (-0.4, 1.9)	-0.3 (-1.2, 0.5)	-0.1 (-1.5, 1.3)	-1.0 (-1.9, -0.1)	0.9 (-0.8, 2.6)	-0.8 (-1.5, -0.1)	-0.2 (-1.6, 1.2)
	PBO	-0.9 (-2.3, 0.6)	-0.9 (-2.1 to 0.3)	-0.3 (-2.1, 1.4)	1.3 (-0.2, 2.9)	-0.6 (-1.9, 0.8)	0.1 (-1.3, 1.5)	0.2 (-0.7, 1.2)	-0.4 (-1.9, 1.0)
PGA	ETN	-35.3 (-38.8, -31.7) ^{†‡}	-31.0 (-37.3, -24.7)	-30.9 (-35.0, -26.8) ^{†‡}	-24.0 (-31.4, -16.6)	-32.6 (-36.5, -28.8) ^{†‡}	-25.6 (-33.5, -17.7)	-29.1 (-31.6, -26.7) ^{†‡}	-28.0 (-36.4, -19.5)
	SSZ	-24.5 (-31.2, -17.9)	-17.5 (-28.9, -6.1)	-22.4 (-30.5, -14.3)	-31.5 (-45.6, -17.3)	-24.8 (-33.4, -16.2)	-22.2 (-38.6, -5.8)	-23.9 (-30.4, -17.3)	-21.4 (-35.1, -7.7)
	PBO	-20.3 (-27.4, -13.2)	-15.2 (-26.2, -4.3)	-8.5 (-17.2, 0.3)	1.5 (-13.2, 16.2)	-16.4 (-23.2, 9.6)	-17.8 (-30.9, -4.7)	-11.9 (-16.5, -7.3)	-20.9 (-34.7, -7.1)

* All values are adjusted mean change (95% confidence interval) unless otherwise noted.

† In the subgroup of patients aged ≤ 40 years at diagnosis, $p \leq 0.05$ as ordered (trend) using the Cochran-Mantel-Haenszel (CMH) test of non-zero correlation for dichotomous outcomes or an ANCOVA model, with baseline of outcome, study, and disease duration as predictors for continuous outcomes

‡ In the subgroup of patients aged ≤ 40 years at diagnosis, $P \leq 0.05$ for disease duration categories analyzed as non-ordered, nominal, using the CMH test of general association for dichotomous outcomes or an ANCOVA model, with baseline of outcome, study, and disease duration as predictors for continuous outcomes.

ASDAS = Ankylosing Spondylitis Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, BASFI = Bath Ankylosing Spondylitis Disease Functional Index; CRP = C-reactive protein; ETN = etanercept; OWD = occiput-to-wall distance; PBO = placebo; PGA = physician's global assessment; SSZ = sulfasalazine; tx = treatment.