

## Supplementary Material

**Table S1.** Characteristics of axial spondyloarthritis patients included in the drug retention analysis at start of first TNFi

Characteristics	Nr-axSpA N=181	r22axSpA N=131	r3+axSpA N=411	All N=723	Overall p value
Male sex, N (%)	80 (44.2)	65 (49.6)	290 (70.6)	435 (60.2)	<0.001
Age, years	37.3 (10.9)	38.6 (10.6)	40.9 (11.7)	39.6 (11.4)	0.006
Disease duration, years	9.0 (9.7)	11.7 (10.0)	15.3 (10.9)	13.0 (10.8)	<0.001
HLA-B27 positivity, N (%)	117 (70.5)	86 (72.9)	300 (80.7)	503 (76.7)	0.02
Elevated CRP, N (%)	67 (39.6)	61 (50.8)	241 (61.6)	369 (54.3)	<0.001
BASDAI	5.9 (1.8)	5.5 (1.9)	5.5 (2.1)	5.6 (2.0)	0.16
ASDAS	3.4 (0.8)	3.3 (0.9)	3.5 (1.0)	3.5 (0.9)	0.02
BASFI	3.8 (2.6)	3.9 (2.3)	4.4 (2.5)	4.1 (2.5)	<0.001
BASMI	1.3 (1.2)	1.7 (1.6)	2.8 (2.2)	2.2 (2.0)	0.03
Current peripheral arthritis, N (%)	77 (43.8)	40 (32.0)	132 (32.7)	249 (35.3)	0.02
Current hip arthritis, N (%)	16 (10.1)	7 (6.2)	62 (16.4)	85 (13.1)	<0.001
Current enthesitis, N (%)	147 (84.0)	98 (77.2)	269 (66.8)	514 (72.9)	<0.001
Current smokers, N (%)	45 (29.0)	38 (33.3)	153 (42.9)	236 (37.7)	0.006
Body mass index	24.9 (4.4)	25.7 (4.9)	25.5 (4.4)	25.4 (4.5)	0.19
Reason of discontinuation					0.15
• ineffectiveness	71 (58.2)	41 (47.1)	92 (43.2)	204 (48.3)	
• adverse event	18 (14.8)	15 (17.2)	52 (24.4)	85 (20.1)	
• remission	10 (8.2)	7 (8.1)	18 (8.4)	35 (8.3)	
• other	23 (18.9)	24 (27.6)	51 (23.9)	98 (23.2)	

Except where indicated otherwise, values are the mean with corresponding standard deviation in brackets. r22axSpA = patients with bilateral grade 2 radiographic sacroiliitis; r3+axSpA = patients with unilateral grade 3-4 radiographic sacroiliitis; ASDAS = Ankylosing Spondylitis Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index; BASMI = Bath Ankylosing Spondylitis Mobility Index; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; HLA-B27 = human leucocyte antigen B27; nr-axSpA = non-radiographic axial spondyloarthritis; TNFi = Tumour Necrosis Factor inhibitor.

**Table S2.** Cox proportional hazards model for analysis of retention of a first TNFi in patients with bilateral grade 2 sacroiliitis (r22axSpA) and in patients with unilateral/bilateral grade 3-4 sacroiliitis (r3+axSpA) versus nr-axSpA.

Variable	HR	95% CI	P
r22axSpA (Ref: nr-axSpA)	0.82	0.57; 1.17	0.27
r3+axSpA (Ref: nr-axSpA)	0.60	0.44; 0.82	0.001
Female sex (Ref. male sex)	1.34	1.03; 1.75	0.03
HLA-B27 neg. (Ref. HLA-B27 pos)	1.29	0.97; 1.72	0.08
Elevated CRP level	0.72	0.56; 0.94	0.01
BASMI	1.06	0.98; 1.15	0.14
BASFI	1.04	0.99; 1.10	0.10
Age	0.99	0.98; 1.01	0.41
Diagnostic delay	1.01	0.99; 1.03	0.33
Peripheral arthritis	0.96	0.74; 1.24	0.76
Enthesitis	0.89	0.67; 1.18	0.40
Current smoking	1.05	0.81; 1.37	0.71
Etanercept (Ref. anti-TNF-antibody)	1.15	0.88; 1.50	0.32
BMI >30 (Ref. BMI <25)	1.14	0.80; 1.63	0.46
BMI 25-30 (Ref. BMI <25)	1.13	0.86; 1.48	0.40

Calculated HR for drug discontinuation in r3+axSpA vs. r22axSpA: 0.73, 95% CI 0.53; 1.02,  $p=0.06$ . Analysis performed in 476 patients (282 events). r22axSpA = patients with bilateral grade 2 radiographic sacroiliitis; r3+axSpA = patients with unilateral/bilateral grade 3-4 radiographic sacroiliitis; BASFI = Bath Ankylosing Spondylitis Functional Index; BASMI = Bath Ankylosing Spondylitis Mobility Index; BMI = Body Mass Index; CI = confidence interval; CRP = C-reactive protein; HLA-B27 = human leucocyte antigen B27; HR = hazard ratio; nr-axSpA = non-radiographic axial spondyloarthritis; Ref = reference; TNF = tumour necrosis factor.

**Table S3.** Characteristics of axial spondyloarthritis patients included in the BASDAI50 response analysis at start of first TNFi (patients with available follow-up visit at 1 year)

Characteristics	nr-axSpA N=143	r22axSpA N=109	r3+axSpA N=343	All N=595	Overall p value
Male sex, N (%)	66 (46.1)	56 (51.4)	245 (71.4)	367 (61.7)	<0.001
Age, years	37.4 (11.)	38.6 (10.7)	40.8 (11.7)	39.6 (11.5)	0.03
Disease duration, years	9.2 (10.1)	11.6 (10.4)	15.2 (10.8)	13.1 (10.8)	<0.001
HLA-B27 positivity, N (%)	98 (74.8)	75 (76.5)	254 (81.9)	427 (79.2)	0.18
Elevated CRP, N (%)	56 (42.4)	53 (53.0)	203 (62.3)	312 (55.9)	0.001
BASDAI	5.9 (1.8)	5.6 (2.0)	5.5 (2.1)	5.6 (2.0)	0.45
ASDAS	3.4 (0.8)	3.4 (0.9)	3.5 (1.0)	3.5 (0.9)	0.11
BASFI	3.6 (2.4)	4.0 (2.3)	4.4 (2.6)	4.1 (2.5)	0.009
BASMI	1.3 (1.2)	1.9 (1.7)	2.8 (2.2)	2.3 (2.0)	<0.001
Current peripheral arthritis, N (%)	60 (43.5)	34 (33.0)	110 (32.6)	205 (35.3)	0.08
Current hip arthritis, N (%)	12 (9.8)	7 (7.7)	52 (16.5)	71 (13.4)	0.04
Current enthesitis, N (%)	113 (82.5)	80 (76.2)	228 (67.7)	421 (72.7)	0.005
Current smokers, N (%)	32 (26.4)	31 (32.3)	129 (43.3)	192 (37.3)	0.003
Body mass index	25.0 (4.4)	25.8 (5.0)	25.3 (4.4)	25.3 (4.5)	0.39

Except where indicated otherwise, values are the mean with corresponding standard deviation in brackets. r22axSpA = patients with bilateral grade 2 radiographic sacroiliitis; r3+axSpA = patients with unilateral grade 3-4 radiographic sacroiliitis; ASDAS = Ankylosing Spondylitis Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index; BASMI = Bath Ankylosing Spondylitis Mobility Index; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; HLA-B27 = human leucocyte antigen B27; nr-axSpA = non-radiographic axial spondyloarthritis; TNFi = Tumour Necrosis Factor inhibitor.

**Table S4.** Association of bilateral grade 2 sacroiliitis (r22axSpA) or grade 3-4 unilateral sacroiliitis (r3+axSpA) with BASDAI50 response after 1 year of treatment with a first TNFi in univariable models and a multivariable analysis.

N	Type of analysis	Variable	OR	95% CI	P
203	Unadjusted	r22axSpA (Ref. nr-axSpA)	1.22	0.67; 2.21	0.57
394	Unadjusted	r3+axSpA (Ref. nr-axSpA)	1.69	1.06; 2.70	0.03
351	Adjusted	r22axSpA (Ref. nr-axSpA)	1.28	0.59; 2.77	0.54
		r3+axSpA (Ref. nr-axSpA)	2.05	1.09; 3.91	0.03
		Female sex (Ref. male sex)	0.40	0.23; 0.68	<0.001
		HLA-B27 neg. (Ref. HLA-B27 pos)	0.55	0.30; 0.98	0.04
		Elevated CRP level	2.67	1.62; 4.47	<0.001
		BASMI	0.77	0.66; 0.90	<0.001
		BASFI	0.92	0.83; 1.02	0.13
		Age	0.99	0.97; 1.02	0.58
		Diagnostic delay	1.00	0.96; 1.03	0.97
		Peripheral arthritis	1.57	0.94; 2.64	0.09
		Enthesitis	1.56	0.90; 2.73	0.11
		Current smoking	0.82	0.49; 1.35	0.43
		ETA (Ref. anti-TNF-Ab)	1.01	0.59; 1.73	0.97
		BMI >30 (Ref. BMI <25)	0.52	0.25; 1.07	0.08
		BMI 25-30 (Ref. BMI <25)	0.77	0.44; 1.32	0.34

r22axSpA = axial spondyloarthritis patients with bilateral grade 2 radiographic sacroiliitis; r3+axSpA = patients with unilateral/bilateral grade 3-4 radiographic sacroiliitis; BASFI = Bath Ankylosing Spondylitis Functional Index; BASMI = Bath Ankylosing Spondylitis Mobility Index; BMI = Body mass index; CRP = C-reactive protein; ETA = etanercept; HLA-B27 = human leucocyte antigen B27; nr-axSpA = non-radiographic axSpA.

**Table S5.** Characteristics of axial spondyloarthritis patients at first spinal radiograph (analysis of spinal radiographic progression)

Parameter	nr-axSpA N=86	r22axSpA N=101	r3+axSpA N=318	All N=505	Overall P value
Male sex, N (%)	39 (45.4)	59 (58.4)	219 (68.9)	317 (62.8)	<0.001
Age, years	39.9 (11.0)	40.3 (11.1)	40.3 (11.1)	40.2 (11.0)	0.94
Disease duration, years	10.2 (9.9)	11.8 (9.4)	14.6 (9.9)	13.3 (10.0)	<0.001
HLA-B27 positivity, N (%)	51 (70.8)	62 (67.4)	244 (85.0)	357 (79.2)	<0.001
Elevated CRP, N (%)	22 (31.0)	22 (27.5)	120 (44.4)	164 (39.0)	0.009
BASDAI	4.6 (2.0)	4.0 (2.3)	4.3 (2.3)	4.2 (2.2)	0.22
ASDAS	2.8 (0.9)	2.6 (1.0)	2.9 (1.1)	2.8 (1.0)	0.13
BASFI	2.8 (2.2)	2.6 (2.4)	3.2 (2.6)	3.0 (2.5)	0.16
BASMI	1.1 (1.4)	1.7 (1.6)	2.4 (2.0)	2.0 (1.9)	<0.001
Presence of syndesmophytes, N (%)	8 (9.3)	19 (18.8)	128 (40.2)	155 (30.7)	<0.001
Number of syndesmophytes	0.1 (0.4)	0.7 (2.3)	2.7 (4.9)	1.9 (4.2)	<0.001
mSASSS	0.9 (1.5)	2.4 (6.5)	8.1 (13.8)	5.8 (11.8)	<0.001
Current peripheral arthritis, N (%)	28 (37.3)	26 (30.6)	78 (28.0)	132 (30.1)	0.29
Current hip arthritis, N (%)	2 (2.8)	6 (7.2)	34 (12.2)	42 (9.8)	0.03
Current enthesitis, N (%)	51 (68.0)	52 (59.8)	146 (52.1)	249 (56.3)	0.04
Current smokers, N (%)	21 (29.2)	20 (23.8)	117 (43.3)	158 (37.1)	0.002
Body mass index	24.9 (4.5)	25.3 (3.8)	25.3 (4.4)	25.2 (4.3)	0.850.85

Except where indicated otherwise, values are the mean with corresponding standard deviation in brackets. r22axSpA = patients with bilateral grade 2 radiographic sacroiliitis; r3+axSpA = patients with unilateral grade 3-4 radiographic sacroiliitis; ASDAS = Ankylosing Spondylitis Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index; BASMI = Bath Ankylosing Spondylitis Mobility Index; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; HLA-B27 = human leucocyte antigen B27; mSASSS = modified Stokes Ankylosing Spondylitis Spinal Score; nr-axSpA = non-radiographic axial spondyloarthritis.

**Table S6.** Association of either bilateral grade 2 sacroiliitis (r22axSpA) or grade 3-4 unilateral/bilateral sacroiliitis (r3+axSpA) with spinal radiographic progression in a multivariate analysis.

Analysis after multiple imputation of missing covariate data (N=505)	Progression defined as $\geq 2$ mSASSS units in 2 years			Progression defined as $\geq 1$ new syndesmophyte in 2 years		
	OR	95% CI	P value	OR	95% CI	P value
r22axSpA vs. nr-axSpA	1.76	0.54; 5.69	0.35	0.88	0.30; 2.55	0.81
r3+axSpA vs. nr-axSpA	2.81	1.00; 7.89	0.05	1.60	0.68; 3.75	0.28
Baseline mSASSS	1.07	1.05; 1.09	<0.001			
Presence of syndesmophytes at BL				9.27	5.33; 16.2	<0.001
ASDAS	1.28	0.97; 1.69	0.09	1.17	0.90; 1.52	0.24
Male sex	1.85	1.04; 3.27	0.04	1.36	0.72; 2.54	0.34
TNFi use prior to radiographic interval	0.61	0.35; 1.06	0.08	0.54	0.32; 0.89	0.02
NSAID use at start of radiogr. interval	0.78	0.39; 1.55	0.47	1.04	0.49; 1.55	0.91
Current smoking	0.94	0.52; 1.69	0.83	0.87	0.48; 1.55	0.63
Length of radiographic interval	1.81	0.95; 3.42	0.07	1.98	1.04; 3.76	0.04
<b>Complete Case Analysis (N=394)</b>						
r22axSpA vs. nr-axSpA	2.67	0.56; 12.7	0.22	1.31	0.33; 5.12	0.70
r3+axSpA vs. nr-axSpA	4.72	1.16; 19.2	0.03	3.05	0.97; 9.63	0.06
Baseline mSASSS	1.07	1.05; 1.10	<0.001			
Presence of syndesmophytes at BL				8.83	4.78; 16.3	<0.001
ASDAS	1.32	0.98; 1.77	0.07	1.23	0.92; 1.64	0.16
Male sex	1.97	1.02; 3.82	0.04	1.63	0.79; 3.34	0.18
TNFi use prior to radiographic interval	0.73	0.40; 1.32	0.30	0.61	0.34; 1.09	0.09
NSAID use at start of radiogr. interval	0.63	0.31; 1.30	0.21	0.86	0.43; 1.73	0.67
Current smoking	0.85	0.47; 1.56	0.61	0.63	0.35; 1.13	0.12
Length of radiographic interval	1.55	0.69; 3.49	0.29	1.67	0.76; 3.68	0.20

Analyses performed in 724 radiographic intervals from 505 patients after multiple imputation of missing data and in 532 intervals from 394 patients in the complete case analysis. r22axSpA = patients with bilateral grade 2 radiographic sacroiliitis; r3+axSpA = patients with unilateral/bilateral grade 3-4 radiographic sacroiliitis; ASDAS = Ankylosing Spondylitis Disease Activity Score; BL = baseline; nr-axSpA = nonradiographic axial spondyloarthritis; NSAID = Non-steroidal anti-inflammatory drug; TNFi = Tumour necrosis factor inhibitor.

**Figure S1.** Variation in sacroiliac joint scoring between primary readers.

		Score of reader 2				
		0	1	2	3	4
Score of reader 1	0	87	32	7	5	0
	1	28	201	73	11	0
	2	4	45	359	78	1
	3	2	8	114	582	29
	4	0	0	0	49	273

Right sacroiliac joint

		Score of reader 2				
		0	1	2	3	4
Score of reader 1	0	74	45	8	4	0
	1	33	204	70	17	1
	2	3	39	357	95	0
	3	2	11	102	570	30
	4	0	0	0	39	282

Left sacroiliac joint

Number of patients presenting at inclusion with the respective sacroiliac joint score (1-4) according to the radiographic item of the modified New York criteria, shown separately for the left and right sacroiliac joint and for reader 1 (y axis) and reader 2 (x axis).