SUPPLEMENTARY MATERIALS

Assessments

For the present analyses, radiographic outcomes were measured as mean change from baseline in modified total Sharp score (mTSS), calculated at Year 2 (Day 729). Radiographic non-progression, defined as a change in mTSS of ≤2.2 based on the smallest detectable change for the patient population at 2 years (trial-specified definition), was analysed in patients achieving remission at Year 2.

Statistical analysis

Disease Activity Score (DAS; C-reactive protein [CRP]) was assessed as a predefined endpoint, using as-observed data for all patients who had completed Year 2. For radiographic assessments in patients with a baseline assessment but missing data at Year 2, the Year 2 assessment was imputed with linear extrapolation based on assessments performed at baseline, at the time of discontinuation and/or Year 1 (Day 365), if at least two of these assessments were available.

American College of Rheumatology (ACR) responses are presented for the intent-to-treat (ITT) population, as well as using as-observed data for all patients who had completed Year 2. DAS28 (CRP), Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), Routine Assessment of Patient Index Data 3 (RAPID3) and Boolean analyses are presented using as-observed data for study completers. Health Assessment Questionnaire–Disability Index (HAQ-DI) is presented for the ITT population.

Discussion

Radiographic assessment is an important outcome in rheumatoid arthritis (RA) trials, particularly the correlation between joint damage over time and disease activity, long-term disability and treatment benefit.[1-4] Findings regarding the use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and the correlation of reduced disease activity with inhibition of radiographic progression are inconsistent. In patients with early RA treated with csDMARDs, radiographic progression, defined as a Larsen score of ≥2 units, has been observed despite a substantial reduction in disease activity (DAS28).[5] However, the present study demonstrates that patients treated with an effective biologic DMARD who achieve remission as defined by the stringent ACR/EULAR/OMERACT criteria (SDAI and Boolean) are more likely to be radiographic non-progressors. The present study also demonstrates that low disease activity (LDA) is sufficient to achieve inhibition of radiographic progression, suggesting that achievement of LDA with radiographic scores could be an acceptable treatment target in some patients.[6]

The radiographic non-progression cut-off used in this study (defined as change in mTSS of ≤2.2) is not considered clinically relevant and this limitation should be taken into account when evaluating the radiographic data.

References

1. Aletaha D, Funovits J, Breedveld FC, et al. Rheumatoid arthritis joint progression in sustained remission is determined by disease activity levels preceding the period of radiographic assessment. Arthritis Rheum 2009;60:1242-9.
2. Bruynesteyn K, Boers M, Kostense P, et al. Deciding on progression of joint damage in paired films of individual patients: smallest detectable difference or change. Ann Rheum Dis 2005;64:179-82.
3. Welsing PM, Landewe RB, van Riel PL, et al. The relationship between disease activity and radiologic progression in patients with rheumatoid arthritis: a longitudinal analysis. Arthritis Rheum 2004;50:2082-93.
4. Stenger AA, van Leeuwen MA, Houtman PM, et al. Early effective suppression of inflammation in rheumatoid arthritis reduces radiographic progression. Br J Rheumatol 1998;37:1157-63.
5. Sanmarti R, Gomez A, Ercilla G, et al. Radiological progression in early rheumatoid arthritis after DMARDS: a one-year follow-up study in a clinical setting. Rheumatology (Oxford) 2003;42:1044-9.
6. Smolen JS, Aletaha D, Bijlsma JW, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis 2010;69:631-7.

Supplementary Table S1 Patients who achieved remission or LDA at Year 1* and sustained it through Year 2 (as observed)

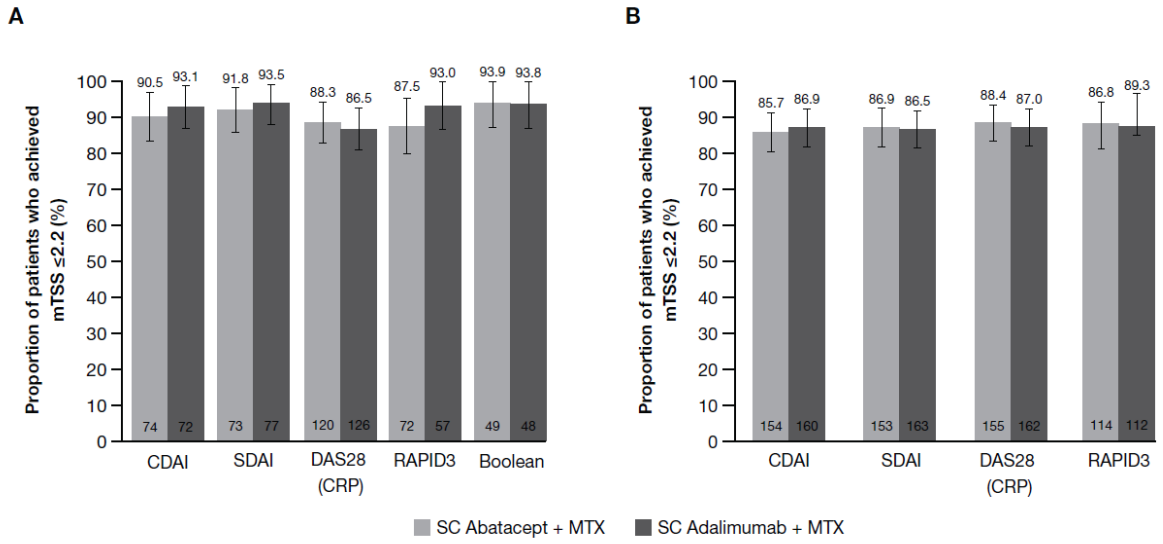
	SC abatacept + MTX (n=318)		SC adalimumab + MTX (n=328)	
	Year 1	**Year 2***	**Year 1**	**Year 2***
Remission				
CDAI	65/277 (23.5)	46/61 (75.4)	64/268 (23.9)	45/62 (72.6)
SDAI	64/275 (23.3)	46/60 (76.7)	66/267 (24.7)	47/64 (73.4)
DAS28 (CRP) <2.6	119/275 (43.3)	87/113 (77.0)	112/268 (41.8)	85/106 (80.2)
RAPID3	76/272 (27.9)	56/69 (81.2)	67/266 (25.2)	48/62 (77.4)
Boolean	37/275 (13.5)	24/33 (72.7)	42/268 (15.7)	27/41 (65.9)
LDA				
CDAI	169/277 (61.0)	138/159 (86.8)	165/268 (61.6)	137/154 (89.0)
SDAI	171/275 (62.2)	139/162 (85.8)	169/267 (63.3)	138/157 (87.9)
DAS28 (CRP) ≤3.2	163/275 (59.3)	131/155 (84.5)	164/268 (61.2)	140/153 (91.5)
RAPID3	122/272 (44.9)	101/113 (89.4)	113/266 (42.5)	85/107 (79.4)

Values shown are n/N (%). N represents the number of patients remaining on treatment with available data at both specified time points.

*Analysis done at specified time points on those patients who achieved remission at Year 1 (as-observed analysis).

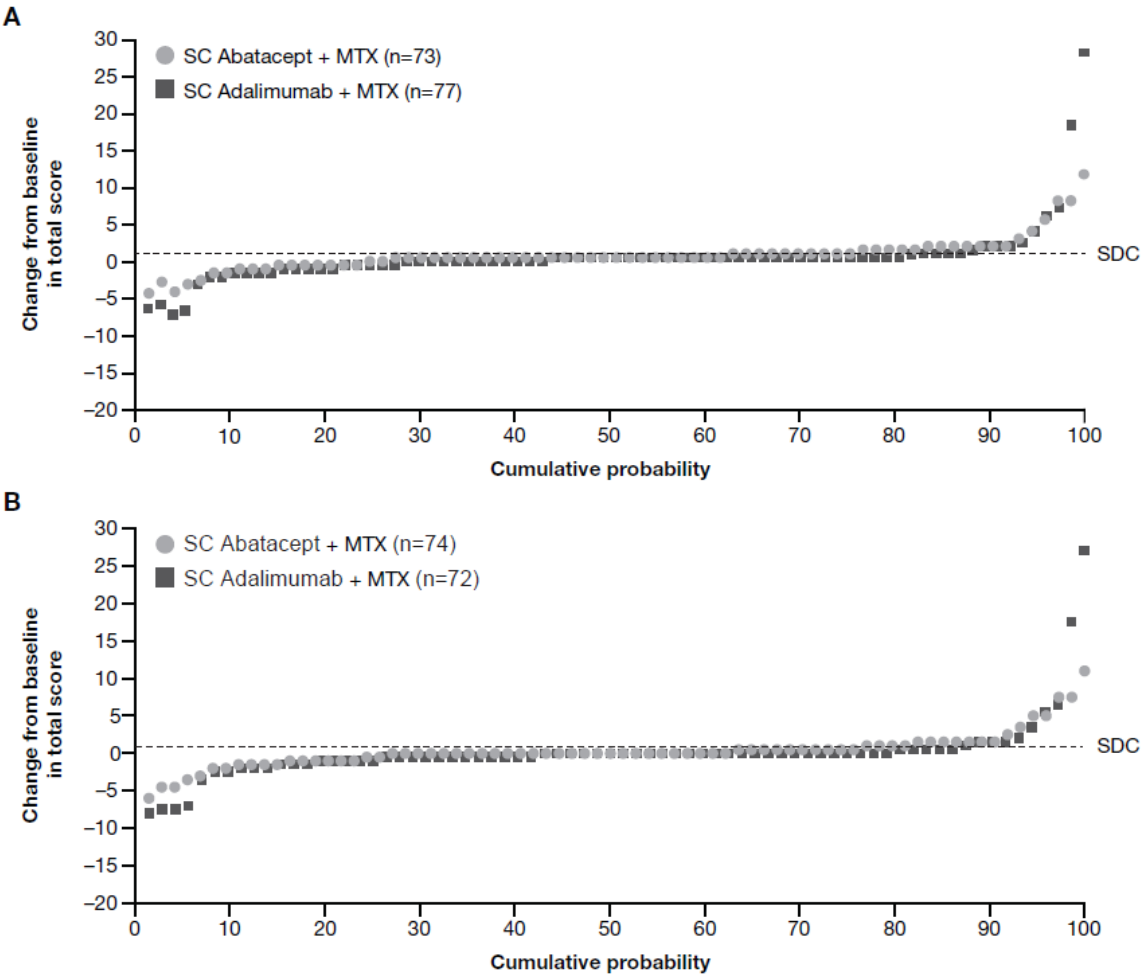
CDAI, Clinical Disease Activity Index; DAS28 (CRP), Disease Activity Score 28 (C-reactive protein); LDA, low disease activity; MTX, methotrexate; RAPID3, Routine Assessment of Patient Index Data 3; SC, subcutaneous; SDAI, Simplified Disease Activity Index.

Supplementary figure S1 Radiographic outcomes in patients who achieved (A) remission or DAS28 (CRP) ≤2.6 and (B) LDA at Year 2 (as observed). All error bars represent 95% confidence intervals. CDAI, Clinical Disease Activity Index; DAS28 (CRP), Disease Activity Score 28 (C-reactive protein); LDA, low disease activity; mTSS, van der Heijde modified total Sharp score; MTX, methotrexate; RAPID3, Routine Assessment of Patient Index Data 3; SC, subcutaneous; SDAI, Simplified Disease Activity Index.

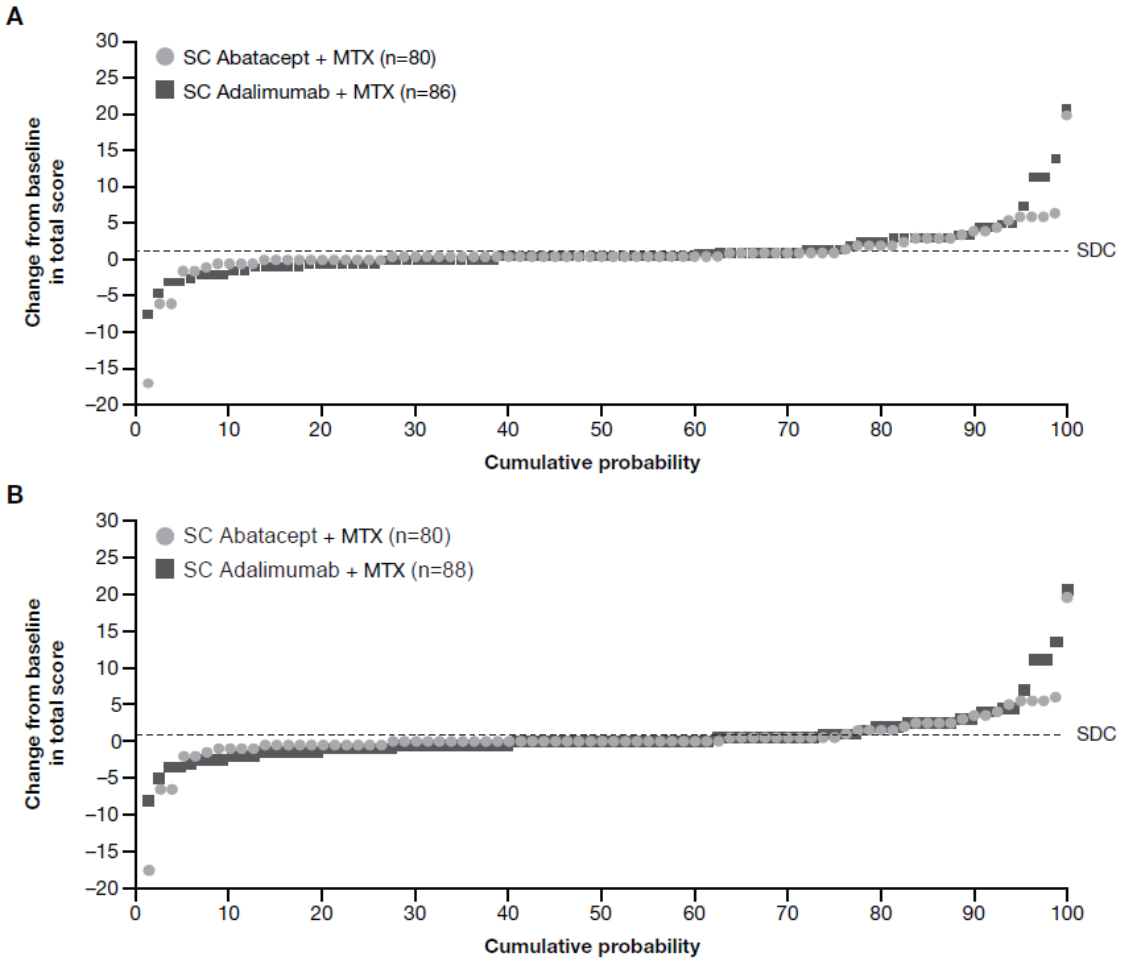


Patients who achieved remission according to more stringent criteria (SDAI, CDAI, Boolean) were more likely to be radiographic non-progressors than those who achieved LDA, as seen in the cumulative probability plots (see supplementary figures S2–4). The cumulative probability plots with the distribution of change in modified total Sharp/van der Heijde scores from baseline to 2 years were similar between the abatacept and adalimumab treatment groups (see supplementary figures S2-4). Similar results were observed for the correlation of DAS28 (CRP) and RAPID3 with radiographic outcomes (see supplementary figure S4).

Supplementary figure S2 Radiographic outcomes in patients achieving remission over 2 years (as observed): (A) SDAI remission; (B) CDAI remission. Trial-specific definition of radiographic non-progression was a change in total score of ≤2.2 (SDC). CDAI, Clinical Disease Activity Index; MTX, methotrexate; SC, subcutaneous; SDAI, Simplified Disease Activity Index; SDC, smallest detectable change.

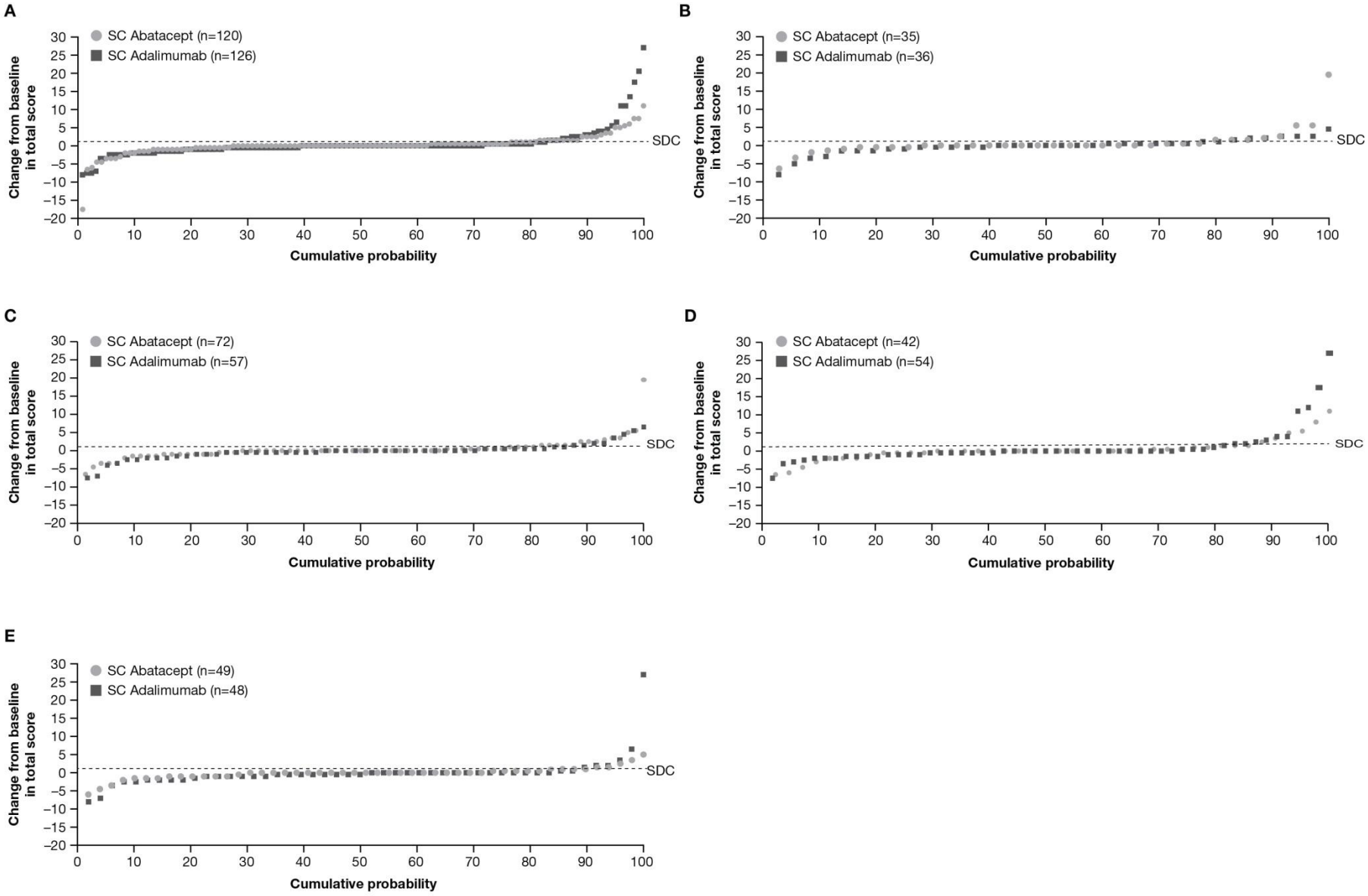


Supplementary figure S3 Radiographic outcomes in patients achieving LDA over 2 years (as observed): (A) SDAI LDA (but not remission); (B) CDAI LDA (but not remission). Trial-specific definition of radiographic non-progression was a change in total score of ≤2.2 (SDC). CDAI, Clinical Disease Activity Index; LDA, low disease activity; MTX, methotrexate; SC, subcutaneous; SDAI, Simplified Disease Activity Index; SDC, smallest detectable change.

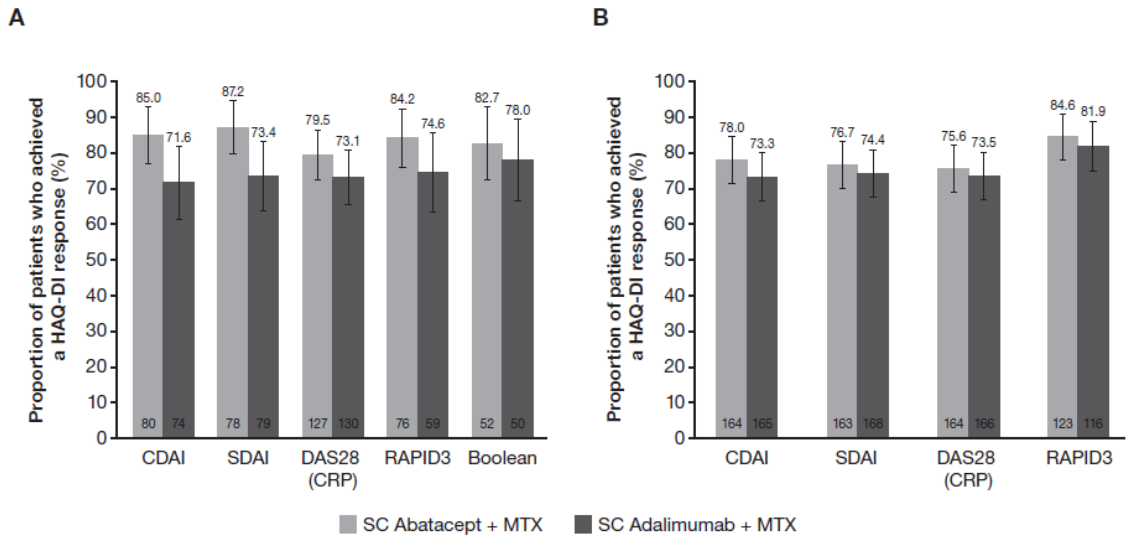


Supplementary figure S4 Radiographic outcomes in patients achieving remission or LDA over 2 years (as observed): (A) DAS28 (CRP) <2.6; (B) DAS28 (CRP) ≤3.2 (but not <2.6); (C) RAPID3 remission; (D) RAPID3 LDA (but not remission); (E) Boolean remission. Trial-specific definition of radiographic non-progression was a change in total score of ≤2.2 (SDC). DAS28 (CRP), Disease Activity Score 28 (C-reactive protein); LDA, low disease activity; RAPID3, Routine Assessment of Patient Index Data 3; SC, subcutaneous; SDC, smallest detectable change.

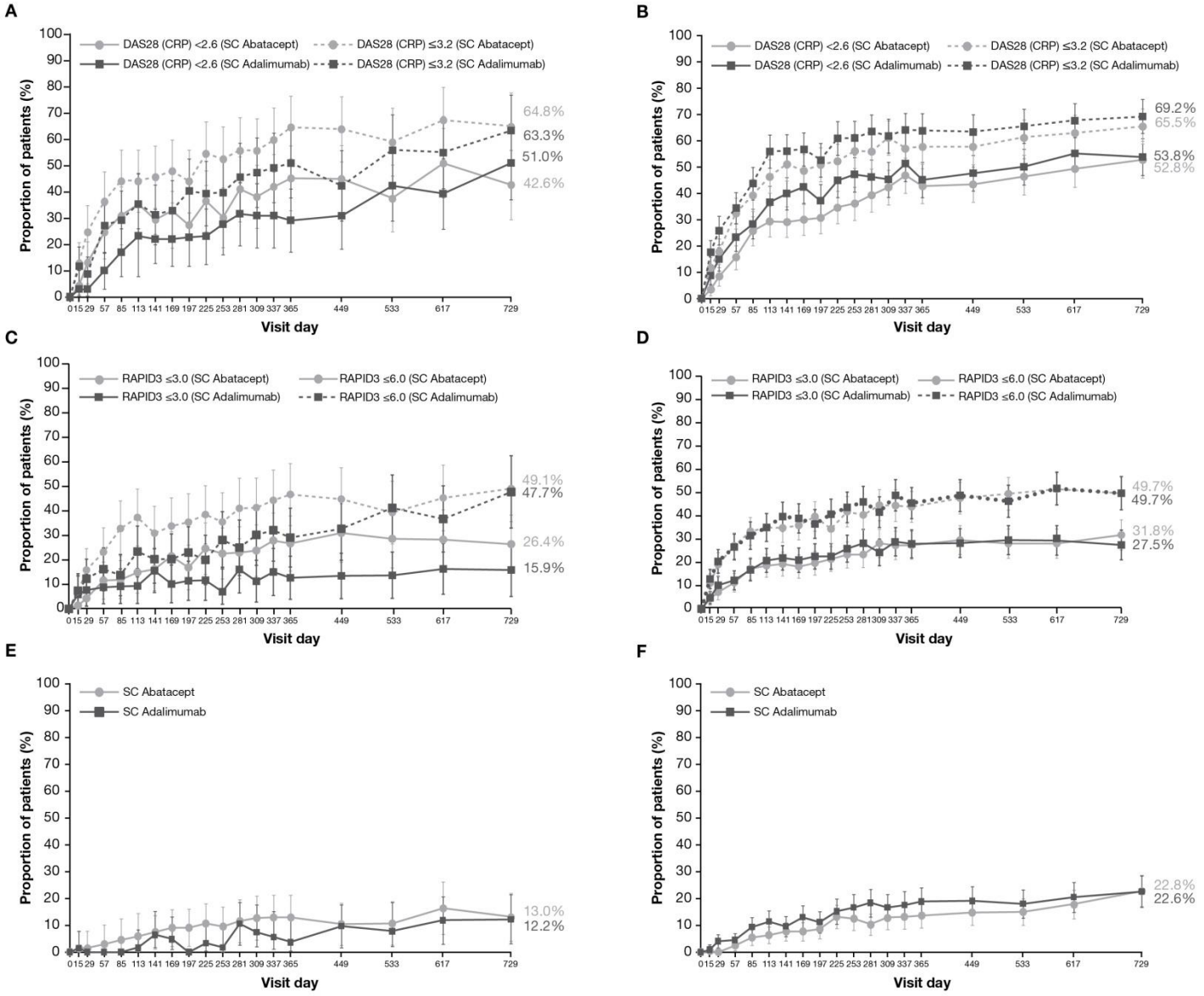
There was no clear discrimination between the remission and the LDA criteria in patients who had achieved a HAQ-DI response.


A
SC Abatacept (n=120)
SC Adalimumab (n=126)
Change from baseline in total score
Cumulative probability
SDC
B
SC Abatacept (n=35)
SC Adalimumab (n=36)
Change from baseline in total score
Cumulative probability
SDC
C
SC Abatacept (n=72)
SC Adalimumab (n=57)
Change from baseline in total score
Cumulative probability
SDC
D
SC Abatacept (n=42)
SC Adalimumab (n=54)
Change from baseline in total score
Cumulative probability
SDC
E
SC Abatacept (n=49)
SC Adalimumab (n=48)
Change from baseline in total score
Cumulative probability
SDC

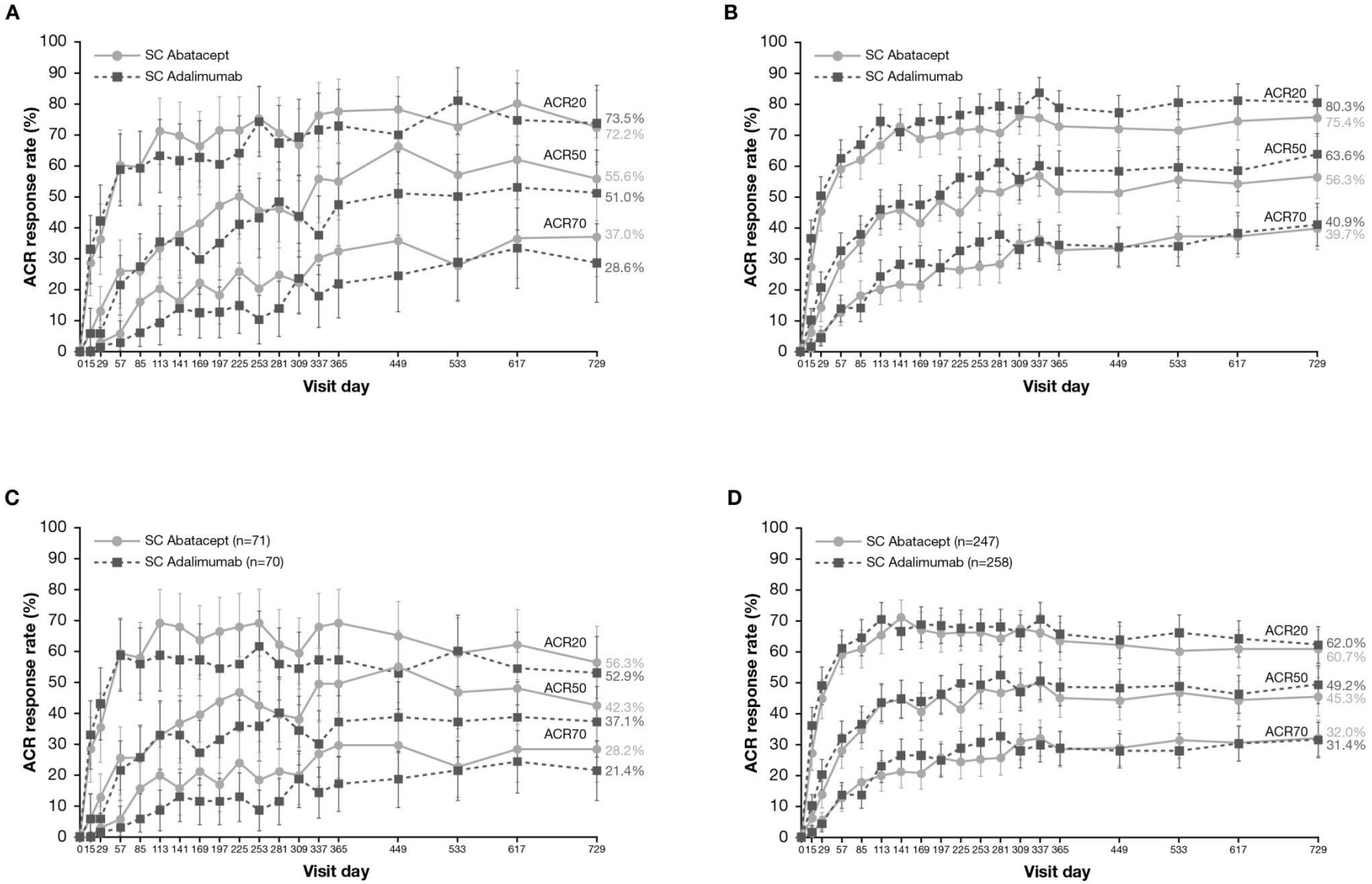
Supplementary figure S5 Physical function in patients who achieved (A) remission or DAS28 (CRP) <2.6 and (B) LDA at Year 2. All patients with baseline and post-baseline measurements were used for this as-observed analysis. HAQ response was defined as an improvement ≥0.3 units. All error bars represent 95% confidence intervals. CDAI, Clinical Disease Activity Index; DAS28 (CRP), Disease Activity Score 28 (C-reactive protein); HAQ-DI, Health Assessment Questionnaire–Disability Index; LDA, low disease activity; MTX, methotrexate; RAPID3, Routine Assessment of Patient Index Data 3; SC, subcutaneous; SDAI, Simplified Disease Activity Index.



Supplementary figure S6 Proportion of patients with DAS28 (CRP) <2.6 or DAS28 (CRP) ≤3.2 over (A) ≤6 months' disease duration or (B) >6 months' disease duration; RAPID3 remission or LDA over (C) ≤6 months' disease duration or (D) >6 months' disease duration; and Boolean remission over (E) ≤6 months' disease duration or (F) > 6 months' disease duration. Number of randomised and treated patients with disease duration ≤6 months: SC abatacept, n=71; SC adalimumab, n=70. Number of randomised and treated patients with disease duration >6 months: SC abatacept, n=247; SC adalimumab, n=258. All error bars represent 95% confidence intervals. DAS28 (CRP), Disease Activity Score 28 (C-reactive protein); LDA, low disease activity; RAPID3, Routine Assessment of Patient Index Data 3; SC, subcutaneous.


A
DAS28 (CRP) <2.6 (SC Abatacept)
DAS28 (CRP) ≤3.2 (SC Abatacept)
DAS28 (CRP) <2.6 (SC Adalimumab)
DAS28 (CRP) ≤3.2 (SC Adalimumab)
Proportion of patients (%)
Visit day
64.8%
63.3%
51.0%
42.6%
B
DAS28 (CRP) <2.6 (SC Abatacept)
DAS28 (CRP) ≤3.2 (SC Abatacept)
DAS28 (CRP) <2.6 (SC Adalimumab)
DAS28 (CRP) ≤3.2 (SC Adalimumab)
Proportion of patients (%)
Visit day
69.2%
65.5%
53.8%
52.8%
C
RAPID3 ≤3.0 (SC Abatacept)
RAPID3 ≤6.0 (SC Abatacept)
RAPID3 ≤3.0 (SC Adalimumab)
RAPID3 ≤6.0 (SC Adalimumab)
Proportion of patients (%)
Visit day
49.1%
47.7%
26.4%
15.9%
D
RAPID3 ≤3.0 (SC Abatacept)
RAPID3 ≤6.0 (SC Abatacept)
RAPID3 ≤3.0 (SC Adalimumab)
RAPID3 ≤6.0 (SC Adalimumab)
Proportion of patients (%)
Visit day
49.7%
49.7%
31.8%
27.5%
E
SC Abatacept
SC Adalimumab
Proportion of patients (%)
Visit day
13.0%
12.2%
F
SC Abatacept
SC Adalimumab
Proportion of patients (%)
Visit day
22.8%
22.6%

Supplementary figure S7 Proportion of patients with ACR20, 50 and 70 responses: (A) ≤6 months' disease duration (as observed) or (B) >6 months' disease duration (as observed); (C) ≤6 months' disease duration (ITT population) or (D) >6 months' disease duration (ITT population). Number of randomised and treated patients with disease duration ≤6 months: SC abatacept, n=71; SC adalimumab, n=70. Number of randomised and treated patients with disease duration >6 months: SC abatacept, n=247; SC adalimumab, n=258. All error bars represent 95% confidence intervals. ACR, American College of Rheumatology; ITT, intent-to-treat; SC, subcutaneous.


A
SC Abatacept
SC Adalimumab
ACR response rate (%)
Visit day
ACR20
ACR50
ACR70
73.5%
72.2%
55.6%
51.0%
37.0%
28.6%
B
SC Abatacept
SC Adalimumab
ACR response rate (%)
Visit day
ACR20
ACR50
ACR70
80.3%
75.4%
63.6%
56.3%
40.9%
39.7%
C
SC Abatacept (n=71)
SC Adalimumab (n=70)
ACR response rate (%)
Visit day
ACR20
ACR50
ACR70
56.3%
52.9%
42.3%
37.1%
28.2%
21.4%
D
SC Abatacept (n=247)
SC Adalimumab (n=258)
ACR response rate (%)
Visit day
ACR20
ACR50
ACR70
62.0%
60.7%
49.2%
45.3%
32.0%
31.4%