Research article

International Journal of Clinical Rheumatology

Long-term results of joint damage in patients with rheumatoid arthritis treated with abatacept: 5-year results of a clinical observational study

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Background: In abatacept treatment for RA, there are no studies investigating the long-term results of joint damage in daily clinical practice. We aimed to investigate the long-term efficacy of abatacept in Japanese patients with rheumatoid arthritis. Methods: We examined 120 patients who received abatacept for 5 years. Joint damage was radiographically analyzed using the van der Heijde-modified total Sharp score. Disease activity score was assessed using the disease activity score in 28 joints-erythrocyte sedimentation rate (DAS28-ESR). The data analyses were used by observed case analysis. Results: Changes in the Sharp score was 0.60 ± 2.03, 0.93 ± 2.40, 1.23 ± 2.92, 1.53 ± 3.38, and 1.71 ± 3.84 at years 1, 2, 3, 4, and 5, respectively. Progression of joint damage did not differ significantly between the Bio-naÃ¯ve and Bio-switch groups and methotrexate [MTX](+) and MTX(MTX(-)) groups. DAS28-ESR at baseline was associated with radiographic progression (p = 0.035). In all patients, the remission rates of DAS28-ESR were 44.6% and 50.0% at years 1 and 5, respectively. These rates were 45.2% and 50.8% in the biological disease-modifying anti-rheumatic drugs (Bio)-naïve¨ve group, and 42.9% and 47.1% in the Bio-switch group, respectively. Moreover, these rates were 45.2% and 52.6% in the MTX(+) group and 43.6% and 47.6% in the MTX(-) group, respectively. The remission rates were not significantly different between the groups at any of time points. Conclusions: we have analyzed the efficacy of abatacept treatment in patient with RA for 5 years in daily clinical practice. The present study suggested that improvement of joint damage, disease activity, and physical function are maintained in the long-term.

Keywords: abatacept ● joint damage ● long-term ● observational study ● rheumatoid arthritis

Introduction

Rheumatoid Arthritis (RA) is associated with joint inflammation and destruction, which leads to pain, swelling, stiffness, and loss of function in joints throughout the body. Gradually, patients with RA experience a diminished quality of life, including disability, which impacts both the activities of daily living and work [1-3]. Although the pathogenic mechanisms of RA remain unknown, the involvement of inflammatory cytokines (e.g., tumor necrosis factor-α, interleukin-1, and interleukin-6), has been established [4]. Activated T cells promote and stimulate monocytes, macrophages, and synovial fibroblasts to produce inflammatory cytokines. Thus, the modulation of T cells could bean effective strategyfor preventing RA progression. T cells require both an antigen-specific and a co-stimulatory signal for complete activation. One of the best characterized pathways for T cell activation is the engagement of CD80/86 on antigen-presenting cells with the CD28 on T cells [5,6]. During normal immune responses, endogenous cytotoxic T-lymphocyte antigen-4 (CTLA-4) down regulates CD28-mediated T cell activation by binding to CD80/86 with higher affinity than CD28 [7,8]. Given theimportant roleof T cells in theimmune responseofpatients with RA, they may be a reasonable therapeutic target for the treatment of RA.

Abatacept is a fully human, soluble fusion protein comprising the extracellular domain of human CTLA-4 linked to the fragment

crystallizable portion of human immunoglobulin G1. This protein functions as a selective modulator of T cell co-stimulation. A combination of abatacept with Methotrexate (MTX) improves signs, symptoms, physical function, quality of life, and disease activity, in patients with active RA despite ongoing therapy with MTX [9,10]. Similarly, in Japan, administration of 10 mg/kg abatacept with MTX significantly improved Disease Activity Score in 28 joints based on C-reactive protein (DAS28-CRP) compared with that reported in the placebo group at week 24 [11]. Moreover, abatacept improved DAS28-CRP and the Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index, and Health Assessment Questionnaire Disability Index (HAQ-DI) compared with those recorded in the placebo group. It has been shown that abatacept suppresses the progression of joint damage, as evaluated using the van der Heijde-modified Total Sharp Score(mTSS), compared with the placebo group at week 52 [12]. Both subcutaneously and intravenously of abatacept demonstrated comparable efficacy and safety [13,14]. In Post-Marketing Surveillance (PMS), the DAS28-CRP and DAS28-Erythrocyte Sedimentation Rate(ESR) at week 24 were significantly lower than those observed at baseline [15]. Several similar results have been reported in daily practice [16-20]. In contrast, there are few long-term results regarding the use of abatacept for the treatment of RA. In the Abatacept in Inadequate Responders to Methotrexate (AIM) trial, the rates of patients who achieved the American College of Rheumatology (ACR) criteria of 20, 50, and 70 at y 1 were maintained for 3 y [21]. Moreover, the results were maintained for 5 y [22]. However, there are no studies investigating the long-term results of joint damage in actual clinical practice. Therefore, we investigated the change in joint damage in Japanese patients with RA treated with abatacept in a clinical observational study over a period of 5 y.

Methods

Patients

In thisstudy, we investigated the clinical course and background characteristics of patients with RA who fulfilled theACRclassification criteria(1987) and/or the ACR/European League Against Rheumatism criteria[23, 24]. A total of 120 consecutive patients who received at least one dose of abatacept were enrolled from January 2011 to October 2014. Patients without baseline data were excluded from analyses. In all patients, RA was poorly controlled for ≥3 months during therapy with Disease-Modifying Antirheumatic Drugs (DMARDs), there by satisfying the existing relevant criteria for the management of RA in the Japanese guidelines for the administration of biologic agents(e.g., more than six tender joints, more than six swollen joints, CRP level of >2.0 mg/dL, and ESR >28 mm/h). Inpatients who did not meetthese criteria, the following additionalcriteriacould bemet: progressive bone erosion, DAS28-CRP >2.7, and DAS28-ESR>3.2.

Abatacept was intravenously administered in patients weighing <60, 60–100, or >100 kg received 500, 750, or 1000 mg every 4 weeks, respectively. The subcutaneous formulation of abatacept was administered 125 mg weekly.

This study was conducted according to the principles of the Declaration of Helsinki, and informed consent was provided by all patients. The Ethics Committee for Clinical Research of Kamagaya General Hospital approved this study (approval number: TGE00888-064).

Assessment of efficacy against joint damage

The joint damage was examined using mTSS. Changes from baseline in joint damage categorized total score (ΔTSS), erosion score (ΔEN), and joint-space narrowing score (ΔJSN) were determined at years 1, 2, 3, 4, and 5. The scores were assessed by two investigators. Structural remission using the ΔTSS was defined as ≤ 0.5 point per year [17,20]. In this study, structural remission was defined as ΔTSS ≤ 2.5 points at year 5, while no radiographic progression was defined as ΔTSS ≤0 point at year 5.

Assessment of efficacy against disease activity

DAS28-ESR was determined at years 1, 2, 3, 4, and 5. DAS28-ESR are divided into four categories: remission, <2.6; low disease activity, 2.6–<3.2; moderate disease activity, 3.2–≦5.1; and high disease activity, >5.1 [25,26].

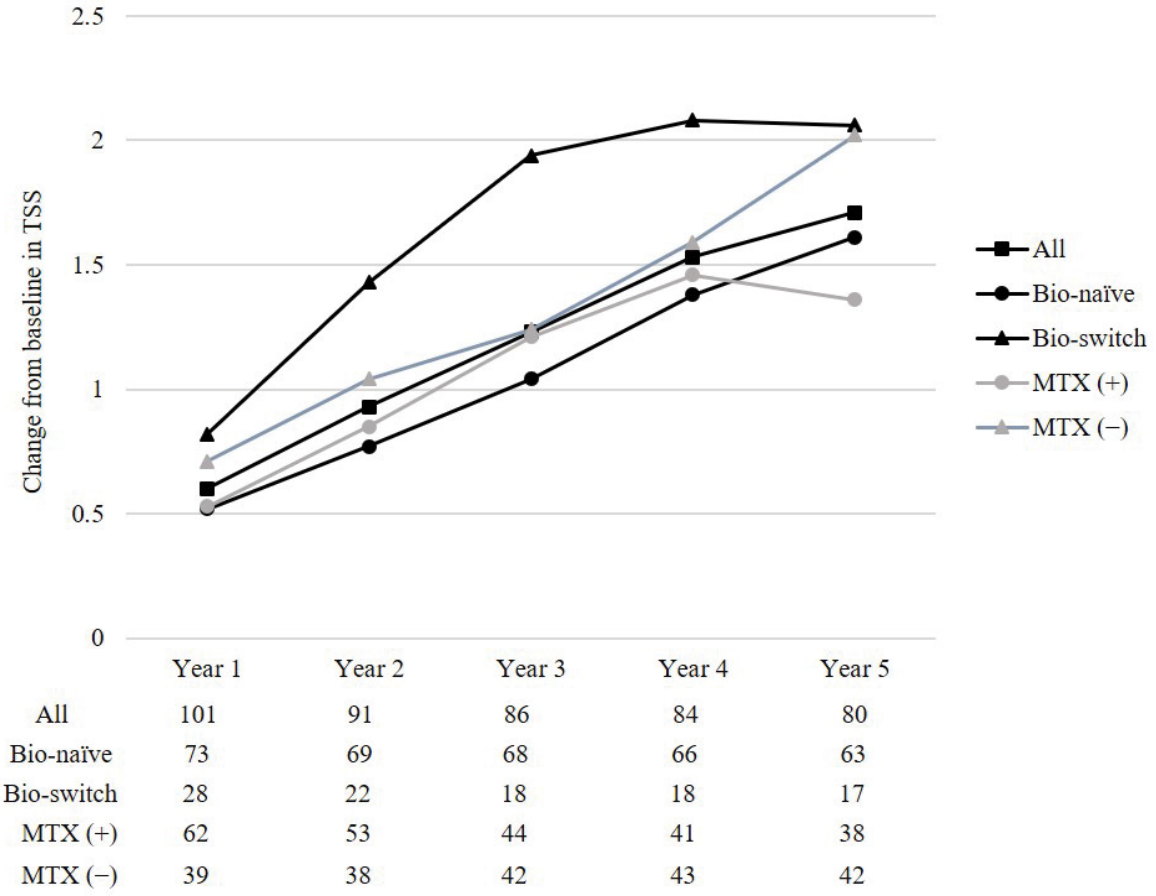
Statistical analysis

The data analyses were used by observed case analysis. Comparisons of the changes in ΔTSS between the Bio-naïve (i.e., patients who received abatacept as their first treatment with a biological DMARD) and Bio-switch (i.e., patients who received treatment with other biological DMARDs prior to abatacept) groups, and MTX(+) (i.e., patients treated with MTX) and MTX(–) (i.e., patients treated without MTX) groups were conducted using paired t-tests. Factors associated with joint damage were analyzed by comparing variables in patients with RA and with or without structural

Table 1. Patient characteristics at baseline.

Variables	All patients (N=120)	Bio-naïve (N=86)	Bio-switch (N=34)	MTX(+) (N=70)	MTX(–) (N=50)
Age, years	66.2 ± 10.3	68.9 ± 8.5	59.2 ± 13.9	63.0 ± 12.2	70.5 ± 7.6
Sex, female, n (%)	102 (85.0)	70 (81.4)	32 (94.1)	62 (88.6)	40 (80.0)
Disease duration, years	9.7 ± 10.3	10.2 ± 11.5	8.3 ± 6.5	7.3 ± 8.6	13.0 ± 11.7
RF positivity, n (%)	92 (76.7)	70 (81.4)	22 (64.7)	51 (72.9)	41 (82.0)
Anti-CCP Ab positivity, n (%)	97 (80.8)	71 (82.6)	26 (76.4)	56 (80.0)	41 (82.0)
Bio-naïve, n (%)	86 (71.7)	86 (100)	0 (0)	51 (72.9)	35 (70.0)
MTX use, n (%)	70 (58.3)	51 (59.3)	19 (55.9)	100 (0)	0 (0)
MTX dose, mg/weeks	7.4 ± 2.5	7.3 ± 2.5	7.6 ± 2.7	7.4 ± 2.5	–
Glucocorticoid use, n (%)	61 (50.8)	43 (50.0)	18 (52.9)	25 (35.7)	36 (72.0)
Glucocorticoid dose, mg/day	4.4 ± 1.7	4.5 ± 1.8	4.3 ± 1.3	4.2 ± 1.9	4.6 ± 1.5
CRP, mg/dL	1.8 ± 2.0	1.7 ± 1.8	1.8 ± 2.3	1.7 ± 2.1	1.8 ± 1.8
MMP-3, ng/mL	216.6 ± 199.3	214.1 ± 194.4	223.0 ± 214.0	206.2 ± 194.1	213.3 ± 207.4
DAS28-ESR	4.61 ± 1.19	4.62 ± 1.16	4.59 ± 1.27	4.59 ± 1.35	4.63 ± 0.92
TSS	53.5 ± 60.4	53.1 ± 64.5	54.5 ± 49.5	47.5 ± 59.1	62.0 ± 61.8
HAQ-DI	0.97 ± 0.76	0.95 ± 0.74	1.03 ± 0.83	0.86 ± 0.68	1.14 ± 0.84

Values are presented as the mean ± standard deviation. Bio-naïve, abatacept of first biological Disease-Modifying Antirheumatic Drug (DMARD); Bio-switch, other biological DMARD treatments prior to abatacept treatment; RF: Rheumatoid Factor; anti-CCP Ab: Anti-Cyclic Citrullinated Peptide Antibody; MTX: Methotrexate; CRP:C-Reactive Protein; MMP-3: Matrix Metalloproteinase-3;DAS28:Disease Activity Score in 28 joints; ESR: Erythrocyte Sedimentation Rate; TSS: Total Sharp Score using van der Heijde-modified total Sharp score; HAQ-DI: Health Assessment Questionnaire Disability Index



	Year 1	Year 2	Year 3	Year 4	Year 5
All	101	91	86	84	80
Bio-naïve	73	69	68	66	63
Bio-switch	28	22	18	18	17
MTX (+)	62	53	44	41	38
MTX (–)	39	38	42	43	42

Figure 1. Change In Total Sharp Score (TSS) using the van der Heijde-modified total sharp score by box and whisker plots for (a) all patients, and the (b) Bio-naïve, (c) Bio-switch, (d) MTX(+), and (e) MTX(–) groups.
Cross bar, mean; error bar, upper and lower limit (1.5 × the interquartile range); upper and lower horizontal line, interquartile range; middle horizontal line, median.

remission and radiographic progression. The variables in the univariate analysis included age, sex, disease duration, Rheumatoid Factor (RF) positivity, anti-cyclic Citrullinated Peptide Antibody(anti-CCP Ab) positivity, Bio-naïve, MTX use, glucocorticoid use, CRP level, matrix metalloproteinase-3 level, DAS28-ESR, TSS, and HAQ-DI at baseline. Stepwise multiple regression analysis was performed to identify factors associated with joint damage.A *p*-value of <0.05 denoted statistical significance. All statistical analyses were performed using the R Statistical Package software, version 3.3.2 (http://www.r-project.org/).

Results

Patient characteristics

A total of 120 patients were enrolled in this study. Table 1 shows the patient characteristics (age, sex, disease duration, RF positivity, anti-CCP positivity, Bio-naïve, MTX use, MTX dose, glucocorticoid use, glucocorticoid dose, CRP, MMP-3, DAS28-ESR, TSS, and HAQ-DI in all groups at baseline.

The rates of MTX use were 58.3%, 61.4%, 58.2%, 51.2%, 48.8%, and 47.5% at baseline, years 1, 2, 3, 4, and 5. The MTX doses (mg/week) were 7.4 ± 2.5, 5.4 ± 2.8, 5.5 ± 2.7, 5.8 ± 2.4, 6.1 ± 2.3, and 6.8 ± 2.4 at baseline, years 1, 2, 3, 4, and 5. The rates of glucocorticoid use were 50.8%, 41.6%, 35.2%, 32.6%, 29.8%, and 33.8% at baseline, years 1, 2, 3, 4, and 5. The glucocorticoid doses (mg/day) were 4.4 ± 1.7, 3.9 ± 1.2, 3.5 ± 1.6, 3.4 ± 1.5, 3.2 ± 1.2, and 2.9 ± 1.1 at baseline, years 1, 2, 3, 4, and 5.

Retention rate

The retention rate was 84.2% at year 1, 75.8% at year 2, 71.7% at year 3, 70.0% at year 4, and 66.7% at year

Table 2. Mean change from baseline in total sharp score in all patients, Bio-naïve, Bio-switch, MTX (+), and MTX (–) groups.

	Year 1	Year 2	Year 3	Year 4	Year 5
All patients	0.60 ± 2.03	0.93 ± 2.40	1.23 ± 2.92	1.53 ± 3.38	1.71 ± 3.84
Bio-naïve group	0.52 ± 1.46	0.77 ± 1.63	1.04 ± 2.12	1.38 ± 2.67	1.61 ± 3.09
Bio-switch group	0.82 ± 3.09	1.43 ± 3.97	1.94 ± 4.92	2.08 ± 5.29	2.06 ± 5.99
MTX (+) group	0.53 ± 1.40	0.85 ± 1.80	1.21 ± 2.69	1.46 ± 3.46	1.36 ± 3.63
MTX (–) group	0.71 ± 2.78	1.04 ± 3.07	1.24 ± 3.18	1.59 ± 3.34	2.02 ± 4.05

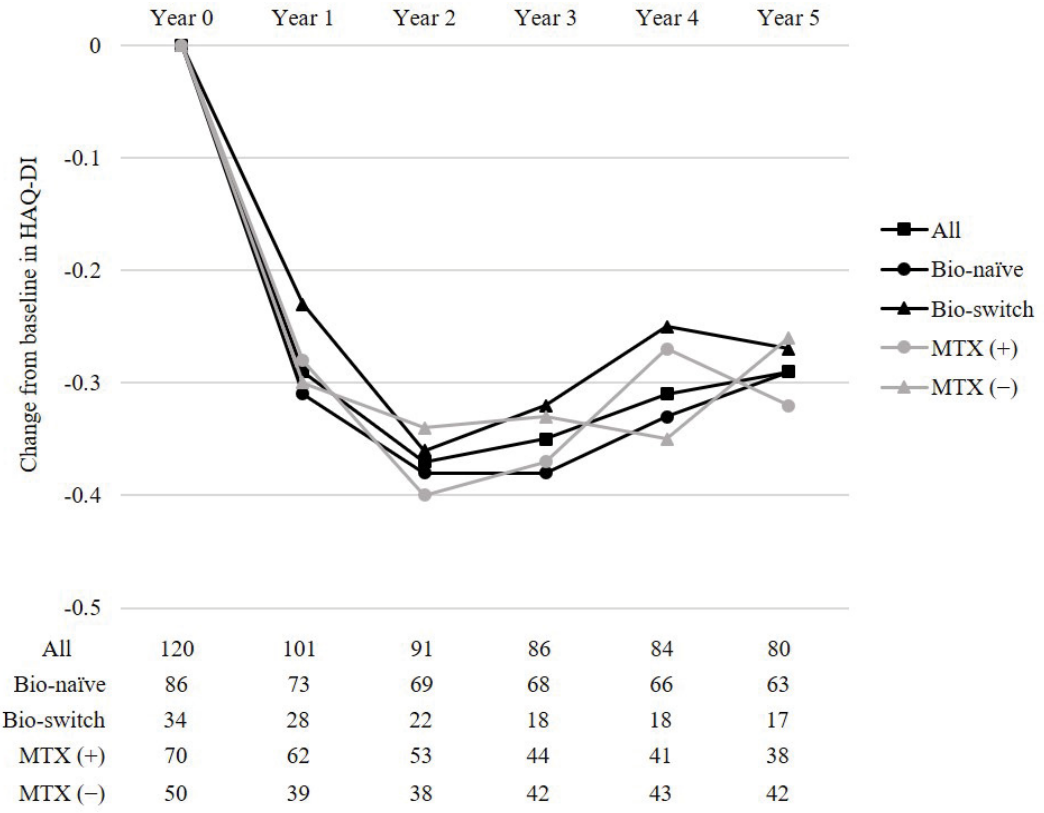


Figure 2. Change in DAS28-ESR for 5 years.

5. The reasons for discontinuation during this 5 year period were lack of efficacy (40%), adverse events (20%), other diseases (10%), change of hospitals (22.5%), and patient hope (7.5%).

Radiographic joint damage

All patients: The ΔTSS was 0.60 ± 2.03, 0.93 ± 2.40, 1.23 ± 2.92, 1.53 ± 3.38, and 1.71 ± 3.84 at years 1, 2, 3, 4, and 5, respectively (Figure 1). The ΔEN was 0.14 ± 0.70, 0.19 ± 0.87, 0.31 ± 0.85, 0.36 ± 1.31, and

Table 3. Comparison between patients without and with radiographic progression for 5 years by univariate analysis.

Variables at baseline	Without progression (n=41)	With progression (n=39)	*p* value
Age, years	66.4 ± 9.4	67.1 ± 9.5	0.745
Sex, female, n (%)	37 (90.2)	48 (87.2)	0.734
Disease duration, years	10.8 ± 12.5	9.2 ± 10.0	0.528
RF positivity, n (%)	29 (70.7)	46 (84.6)	0.183
Anti-CCP Ab positivity, n (%)	31 (75.6)	35 (89.7)	0.142
Bio-naïve, n (%)	30 (73.2)	33 (84.6)	0.227
MTX use, n (%)	26 (63.4)	26 (66.7)	0.817
Glucocorticoid use, n (%)	14 (34.1)	21 (53.8)	0.114
CRP, mg/dL	1.26 ± 1.80	1.89 ± 1.85	0.129
MMP-3, ng/mL	179.1 ± 159.4	256.6 ± 242.5	0.098
DAS-ESR	4.29 ± 1.00	4.85 ± 1.25	0.032
TSS	48.5 ± 63.9	63.2 ± 67.1	0.317
HAQ-DI	0.81 ± 0.70	1.01 ± 0.78	0.229

Values are presented as the mean ± standard deviation. Bio-naïve, abatacept of first biological disease-modifying antirheumatic drug; RF: Rheumatoid Factor; anti-CCP Ab: Anti-Cyclic Citrullinated Peptide Antibody; MTX: Methotrexate; CRP: C-Reactive Protein; MMP-3: Matrix Metalloproteinase-3; DAS28: Disease Activity Score in 28 joints; ESR: Erythrocyte Sedimentation Rate; TSS: Total Sharp Score using van der Heijde-modified total Sharp score; HAQ-DI: Health Assessment Questionnaire Disability Index

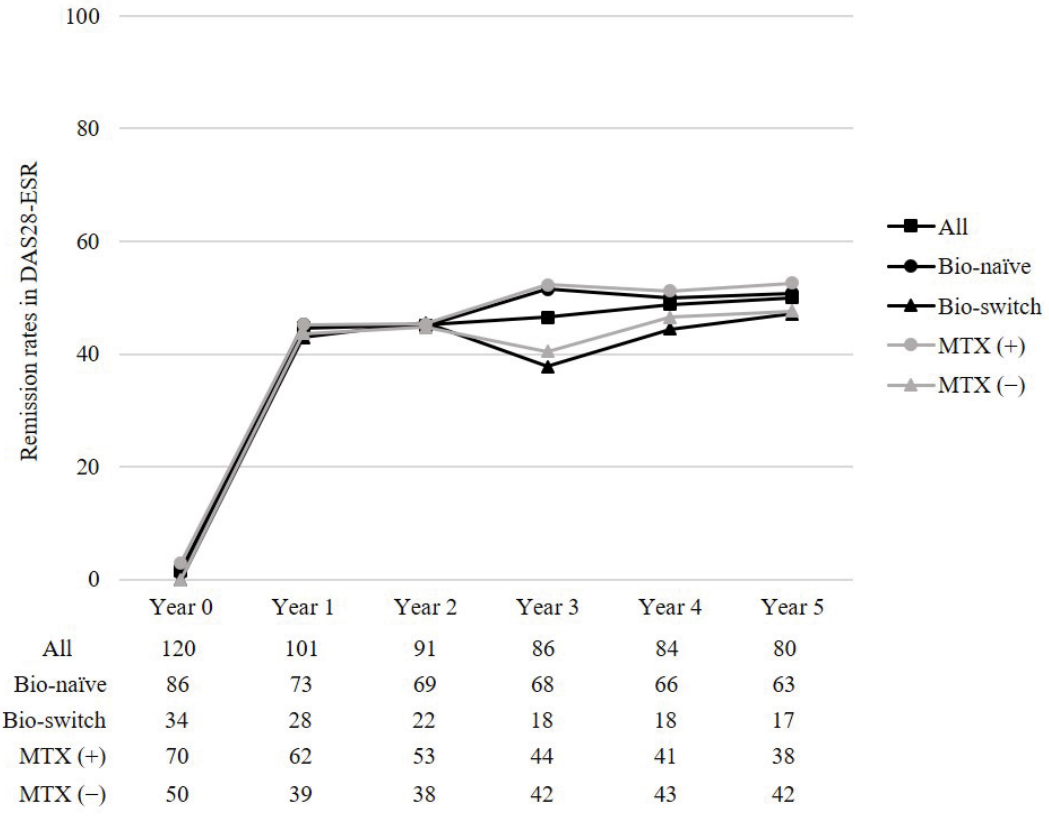


Figure 3. Change in HAQ-DI for 5 years.

0.43 ± 1.48 at years 1, 2, 3, 4, and 5. The ΔJSN was 0.48 ± 1.52, 0.75 ± 1.78, 0.94 ± 2.16, 1.20 ± 2.51, and 1.29 ± 2.91 at years 1, 2, 3, 4, and 5. On the other hand, the ΔTSS using linear extrapolation based on last scores was 0.67 ± 1.97 at 0years to 1 year, 0.48 ± 1.20 at 1yearsto 2 years, 0.45 ± 1.21 at 2years to 3 years, 0.43 ± 1.18 at 3 years to 4 years, 0.42 ± 1.15 at 4 years to 5 years.

Bio-naïve vs. Bio-switch

In Bio-naïve group, the ΔTSS was 0.52 ± 1.46, 0.77 ± 1.63, 1.04 ± 2.12, 1.38 ± 2.67, and 1.61 ± 3.09 at years 1, 2, 3, 4, and 5 (**Figure 1**). In Bio-switch group, the ΔTSS was 0.82 ± 3.09, 1.43 ± 3.97, 1.94 ± 4.92, 2.08 ± 5.29, and 2.06 ± 5.99 at years 1, 2, 3, 4, and 5 (**Figure 1**). There was no difference between these groups in ΔTSS each year (year 1: $p = 0.625$; year 2: $p = 0.453$; year 3: $p = 0.454$; year 4: $p = 0.591$, and year 5: $p = 0.769$).

MTX (+) vs. MTX (–)

In MTX (+) group, the ΔTSS was 0.53 ± 1.40, 0.85 ± 1.80, 1.21 ± 2.69, 1.46 ± 3.46, and 1.36 ± 3.63 at years 1, 2, 3, 4, and 5 (**Figure 1**). In MTX (–) group, the ΔTSS was 0.71 ± 2.78, 1.04 ± 3.07, 1.24 ± 3.18, 1.59 ± 3.34, and 2.02 ± 4.05 at years 1, 2, 3, 4, and 5 (**Figure 1**). There was no difference in these groups in ΔTSS each year (year 1: $p = 0.700$; year 2: $p = 0.733$; year 3: $p = 0.972$; year 4: $p = 0.862$, and year 5: $p = 0.438$).

Factors associated with structural remission and radiographic progression

The structural remission rate at year 5 (ΔTSS ≤ 2.5) was 78.8%. There were no significant factors associated with structural remission.

The rate of no radiographic progression at 5 years (ΔTSS ≤ 0) was 51.3%. The univariate analysis revealed that the following factor was significantly associated with no radiographic progression: DAS28-ESR (**Table 2**). Moreover, the multivariate analysis showed that DAS28-ESR ($p = 0.035$) was a significant factor.

Clinical efficacy

Figure 2 showed the percentage of patients who achieved remission in DAS28-ESR at baseline, and years 1, 2, 3, 4, and 5. In all patients, the remission rates of DAS28-ESR were 44.6 and 50.0% at years 1 and 5. In the Bio-naïve and Bio-switch groups, the remission rates of DAS28-ESR at year 1 and 5 were 45.2% and 42.9%, and 50.8% and 47.1%, respectively. The remission rates were not significantly different between the two groups at any of the time points. In the MTX(+) and MTX(–) groups, the remission rates of DAS28-ESR at years 1 and 5 were 45.2% and 43.6%, and 52.6% and 47.6%, respectively. The remission rates were not significantly different between the two groups at any of the time points.

The HAQ-DI improved in all groups at any of the time points (**Figure 3**). At year 5, the rate of improvement in HAQ-DI ≥ 0.3 was 43.8%. Of note, the rate of deterioration of HAQ-DI ≥ 0.3 was 12.5%. Moreover, the rates of HAQ-DI ≤ 0.5 at baseline and year 5 were 40.0% and 58.8%, respectively.

Discussion

The present clinical observational study evaluated the long-term joint damage and clinical efficacy in Japanese patients treated with abatacept. The radiographic joint damage was suppressed over the 5-year period. Progression of joint damage did not differ between the Bio-naïve and Bio-switch groups, MTX(+) and MTX(–) groups. In the present study, the retention rate was 66.7% at year 5. Similarly to previous reports[11,13,17,19,20,27], the most common reason for discontinuation in this study was lack of efficacy (**Table 3**).

The short-term results in terms of joint damage in patients with early RA who received abatacept plus MTX were 0.65 and 0.19 at 0yearsto 1yearsand 1yearsto 2 years, respectively [28]. In patients with RA who had an inadequate response to MTX, ΔTSS was 0.58 ± 3.22 at year 1[29]. The long-term results in terms of joint damage in patients treated with abatacept in Abatacept in Inadequate Responders to Methotrexate (AIM) trial were 0.80 ± 1.99, 0.41 ± 1.28, 0.37 ± 1.49, 0.34 ± 1.12, and 0.26 ± 1.40 at 0–1, 1–2, 2–3, 3–4, and 4–5 years, respectively, using the Genant-modified Sharp scoring method [22]. These results are similar to those of our study regarding the suppression of joint damage over time; however, they demonstrated greater effectiveness. The AIM trial had differences from the present study. The patients included in the previous report had a mean age of 51.5 years, were Bio-naïve, and all received treatment with MTX (mean dosage: 16.1 mg/week) [30]. In the present study, the mean dosage of MTX was 7.4 mg/week. Based on our results, at this dose of MTX, there was no difference between the MTX(+) and MTX(–) groups in terms of joint damage. In previous reports, factors associated with short-term joint damage during treatment with abatacept were disease duration, CRP, and SDAI at baseline, as well as SDAI remission at month 6 [17,31,32]. In the present study, the only

factor associated with radiographic progression was DAS28-ESR. This result suggests that DAS28-ESR at baseline would be considered a long-term treatment goal for the prevention of radiographic progression in patients treated with abatacept.

In the present study, the remission rates of DAS28-ESR at year 1 and 5 were 44.6% and 50.0%, respectively. In Japanese patients with RA treated with abatacept, the remission rate of DAS28-CRP (<2.6) in subcutaneous and intravenous groups were 63.5% and 62.7% at week 76. The remission rate improved from week 24 to week 76 [14]. In present study, the remission rate of DAS28-CRP (<2.6) at year 1 and 5 were 69.3% and 72.5%. Although the retention rate was slightly different, abatacept had well effectiveness in long-term period. In our previous report, improvement in DAS28-ESR continued from week 24 to year 2 using last observation carried forward analysis [20]. Moreover, the present study showed that improvement in DAS28-ESR continued throughout the entire 5-year period. Similarly, the remission rates of DAS28-ESR were maintained in all patients, as well as in the Bio-naïve, Bio-switch, MTX(+), and MTX(–) groups. In the Bio-switch group of the present study, the remission rate of DAS28-ESR was 44.1% at year 5. The remission rate of DAS28-CRP (<2.6) was 22.3% at year 5 in patients with inadequate response to therapy with an anti-tumor necrosis factor [33]. Although these results differed in remission rates, they were similar in maintenance rates at year 5. Moreover, clinical results of abatacept were also not affected by MTX in the Orencia and Rheumatoid Arthritis (ORA) registry [34]. In PMS of Japan, the reduction rate in DAS28-ESR at week 24 was 22.5%, and MTX was not associated with improvement in DAS28-CRP in patients with moderate disease activity at baseline [15]. The patients examined in the present study had moderate disease activity of mean DAS28-ESR at baseline. Therefore, it is suggested that the clinical results were also not affected by MTX in this study.

Based on the results of the present study, the HAQ-DI improved for up to 2 years, and was maintained at the end of the investigation (5 years). In a previous report, progression of one point in the TSS score was related to 0.013 in HAQ-DI [35]. The remaining functional disability may be attributed to joint damage according to the TSS at baseline and progression of joint damage for 5 years.

This study had several limitations. Firstly, the patients of the present study had moderate disease activity at baseline. Therefore, our results may differ from those of previous randomized controlled trials. However, our data are close to the patient characteristics of daily practice in PMS [15]. We suggest that long-term results are useful in daily practice. Secondly, the data was analyzed using observed case analysis. Therefore, there is a possibility for differences in these results if all patients were able to continue treatment for 5 years. Moreover, this study did not include a control group owing to its clinical observational design. Therefore, the present study could not compare abatacept with other DMARDs.

In conclusion, we analyzed the efficacy of treatment with abatacept in Japanese patients with RA for 5 years in daily clinical practice. The findings of the present study suggested that improvement in joint damage, disease activity, and physical function are maintained in the long-term. Long-term clinical results are important in the treatment of abatacept. These results are useful for the long-term use of abatacept in patients with RA.

Authors' contributions

All authors have contributed to the concept and design of the study, interpretation of the data and revising the manuscript, and have approved the final draft.

Conflict of interest

TM received honoraria for lectures from AbbVie, Astellas, Bristol-Myers, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, Janssen, Mochida, Pfizer, Takeda, and Tanabe-Mitsubishi. KY received honoraria for lectures from AbbVie, Astellas, Ayumi, Bristol-Meyers, Eisai, Hisamitsu, Mochida, and Takeda. KI received honoraria for lectures from AbbVie, Astellas, Bristol-Myers, Chugai, Eisai, Eli Lilly, Janssen, Takeda, Tanabe-Mitsubishi, and UCB. The otfher authors declare that they have no conflicts of interest. The sponsors were not involved in the study design; collection, analysis, and interpretation of data; writing of the article; and/or decision to submit the results for publication.

Funding

None

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