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Original article

Clinical, radiographic and functional effectiveness of tocilizumab for rheumatoid arthritis patients—REACTION 52-week study

Tsutomu Takeuchi[1], Yoshiya Tanaka[2], Koichi Amano[3], Daisuke Hoshi[4], Masao Nawata[2], Hayato Nagasawa[3], Eri Sato[4], Kazuyoshi Saito[2], Yuko Kaneko[1], Shunsuke Fukuyo[2], Takahiko Kurasawa[3], Kentaro Hanami[2], Hideto Kameda[1] and Hisashi Yamanaka[4]

Abstract

Objectives. To evaluate the effectiveness and safety of tocilizumab in RA patients in clinical practice.

Methods. We observed 232 consecutive RA patients who began tocilizumab in three rheumatology centres in Japan for 52 weeks. Clinical, radiographic and functional status and safety were evaluated.

Results. Mean age of the 232 patients was 59.1 years, mean duration of disease was 12.4 years and average DAS using the 28-joint count (DAS-28) was 5.6. Although 62.8% of the patients had been treated previously with anti-TNF biologics, clinical remission at Week 52 was achieved in 43.7%, radiographic non-progression in 62.8% and functional remission in 26.4%. Retention rate at Week 52 was 71.1%, and the same for those with or without previous anti-TNF treatment. Adverse drug reactions leading to tocilizumab discontinuation were observed in 15.5% of patients, the most frequent adverse drug reaction being pneumonia in eight cases. On multivariate logistic regression analysis, DAS-28, HAQ-disability index (HAQ-DI), concomitant MTX and concomitant glucocorticoids (GCs) were predictive variables for clinical remission at Week 52 of tocilizumab treatment. In particular, HAQ-DI was found to be a predictive variable for remission of all three types—clinical, radiographic and functional—at Week 52 of tocilizumab treatment.

Conclusions. In daily clinical practice, tocilizumab exhibited excellent effectiveness in established RA patients, some of whom had failed to respond to previous anti-TNF treatment. Although further detailed safety findings are required, this study provides valuable real-world findings on the management of RA with tocilizumab.

Key words: Rheumatoid arthritis, Tocilizumab, Remission, Joint destruction, Health assessment questionnaire.

CLINICAL SCIENCE

Introduction

Pro-inflammatory cytokines play a fundamental role in the inflammatory processes leading to destructive arthritis in patients with RA [1, 2]. Biological agents against pro-inflammatory cytokines such as TNF-α have dramatically changed the management of patients with RA [1, 2]. It is now recommended to treat RA patients to achieve clinical remission by early and tight control of disease activity with intensive medication [3, 4]. Recent clinical trials have shown that treatment with anti-TNF biologics in combination with MTX in early RA can lead to clinical remission in ~50% of patients [5]; however, the remaining half of the patients are either those not able to achieve clinical

[1]Department of Internal Medicine, Division of Rheumatology, School of Medicine, Keio University, Tokyo, [2]The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, [3]Department of Internal Medicine, Division of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Saitama and [4]Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan.

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Correspondence to: Tsutomu Takeuchi, Department of Internal Medicine, Division of Rheumatology, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan.
E-mail: tsutake@z5.keio.jp

remission or discontinued anti-TNF biologics and switched to other medications [6–8]. A new biological agent, tocilizumab, targeting the IL-6 receptor has recently been approved for use in patients with RA in more than 40 countries around the world, including Japan, drawing attention to the effectiveness and safety of tocilizumab in clinical practice [9–11]. Generally, randomized clinical trials (RCTs) are considered the gold standard for evaluation of the efficacy of newly developed agents. However, RCTs are artificial and may not reflect efficacy and safety in the real rheumatology world.

While we have reported the effectiveness of tocilizumab at Week 24 [12], there is no report that evaluates all efficacy with regard to clinical remission, structural remission and functional remission of tocilizumab comprehensively under daily clinical practice. Hence we undertook the Retrospective Actemra Investigation for Optimal Needs of RA Patients (REACTION 52-week study) to confirm the efficacy and safety of tocilizumab in daily clinical practice.

Patients and methods

Patients

All RA patients included in this study fulfilled the ACR classification criteria [13]. After the approval of tocilizumab in April 2008 in Japan, all patients from three rheumatology centres in Japan (the Division of Rheumatology and Clinical Immunology, Department of Internal Medicine, Saitama Medical Center, Saitama Medical University, Saitama; the First Department of Internal Medicine, School of Medicine, University of Occupational & Environmental Health Japan, Kitakyushu; and the Institute of Rheumatology, Tokyo Women's Medical University) who had started to receive tocilizumab by March 2009 were consecutively registered into this study and were followed up every 4 weeks at the time of infusion. We analysed a total of 232 RA patients who had been observed for 52 weeks from the initial infusion of tocilizumab.

The REACTION study was a retrospective observational study using anonymized information, and conformed to standard tocilizumab treatment proposed by the Japan College of Rheumatology (JCR). Patients' written consent was obtained according to the Declaration of Helsinki.

Tocilizumab treatment and assessment of effectiveness

Tocilizumab was infused every 4 weeks at a dose of 8 mg/kg according to the drug labelling and the tocilizumab therapy guidelines of the JCR [14]. In the JCR guidelines, tocilizumab is recommended for patients who show an inadequate response despite treatment for at least 3 months with the maximum permissible dose of one of the non-biologic DMARDs. Demographic data, including disease duration and concomitant therapy, were collected from the medical charts. The following parameters were evaluated every 4 weeks for 52 weeks following the initial infusion of tocilizumab: tender joint count (TJC) 28, swollen joint count (SJC) 28, patient's global assessment (Pt-GA) of disease activity, physician's global assessment (Ph-GA) of disease activity, ESR, CRP, MMP-3 and HAQ-disability index (HAQ-DI). Disease activity was assessed by the DAS-28 that was calculated according to the authorized formula [15]. Although there were no criteria for measuring CRP, ESR and MMP-3 in this study protocol, these items are approved for monthly monitoring in RA by the Japanese health insurance system. Eventually, ESR, CRP and MMP-3 were performed at each visit in three institutions as routine clinical practice for all patients treated with tocilizumab.

Among the 232 patients in this study, X-ray images of both the hands and feet at 0 and 52 weeks or last observation were available for 149 patients for assessing radiographic damage. The images were read by two independent, well-trained rheumatologists according to the previously reported van der Heijde-modified Sharp (vdH–Sharp) method [16, 17]. Estimated yearly progression was calculated as previously reported [17, 18]. The last observation carried forward (LOCF) method was used in each analysis and radiographic data were extrapolated to 52 weeks. Clinical remission was defined as a DAS-28 of <2.6, structural remission was defined as a change in total vdH–Sharp score of $\leqslant 0.5$ from baseline to Week 52, and functional remission was defined as HAQ-DI of $\leqslant 0.5$, as previously reported [17].

Statistical analysis

The LOCF method was used in each analysis. Baseline variables of RA patients were analysed for association with clinical, structural and functional remissions at Week 52 using Pearson's chi-square test (for categorical variables) and Student's *t*-test (for continuous variables). Univariate logistic analysis was used to screen for potential predictive variables, and a stepwise selection process was used to generate a multivariate regression model for predicting remission at Week 52 of tocilizumab treatment. All statistical analyses were performed with JMP version 8.0.2 statistical software (SAS Institute Inc., Cary, NC, USA).

Results

Demographic data of patients from three institutions

Baseline characteristics of the 232 patients enrolled in this study are shown in Table 1. Mean age was 59.1 years and mean duration of the disease was 12.4 years, indicating that the RA patients in this study were established and advanced. Disease activity was high, as shown by the mean DAS-28 of 5.6 and mean CRP level of 3.1 mg/dl. Notably, MTX and glucocorticoids (GCs) were concomitantly used in 56 and 66% of the patients, respectively, and 62.8% of the patients had previously experienced treatment with anti-TNF biologics.

Changes in DAS-28 and HAQ-DI during 52 weeks of tocilizumab treatment

As shown in Fig. 1, the DAS-28 score significantly decreased from 5.6 (1.3) at baseline to 4.4 (1.5) at Week 4, 3.8 (1.7) at Week 12, 3.3 (1.6) at Week 24 and 3.2 (1.7)

Table 1 Demographic and clinical features of the RA patients (n = 232)

Clinical parameters	Mean (S.D.)	Median (interquartile range)
Age	59.1 (13.3)	61.0 (53.0–68.0)
Gender, female, %	84.3	
Duration, years	12.4 (11.1)	10.0 (4.0–18.0)
Steinbrocker's stages I/II/III/IV, %	7.2/30.5/17.0/45.3	
Steinbrocker's class 1/2/3/4, %	5.0/72.2/22.4/0	
DAS-28	5.6 (1.3)	5.6 (4.9–6.6)
SJC (0–28)	7.7 (5.6)	7 (3–11)
TJC (0–28)	7.9 (6.4)	6 (3–12)
ESR, mm/h	63 (29)	64 (44–85)
CRP, mg/dl	3.1 (2.9)	2.5 (0.9–4.6)
Pt-GA (VAS/100 mm)	56 (24)	54 (40–76)
Concomitant MTX, %	55.6	
Dose of MTX, mg/week	8.6 (3.1)	8.0 (6.0–10.0)
Concomitant GCs, %	66.4	
Dose of GCs, mg/day	5.2 (3.1)	5.0 (3.0–6.0)
Previous anti-TNFs, %	62.8	

at Week 52 ($P < 0.0001$). Disease activity status changed significantly from high disease activity at baseline to clinical remission or low disease activity during treatment with tocilizumab ($P < 0.0001$). Clinical remission was obtained in 14.8% of the patients at Week 4, 27.7% at Week 12, 39.2% at Week 24 and 43.7% at Week 52, indicating that clinical remission was achieved for ~44% of patients and that the rate nearly plateaued at Week 24 in this patient population. Notably, only 14% of the patients showed no response at Weeks 24 and 52. In addition, clinical remission, even when assessed by non-responder imputation methods, was 12.1, 23.3, 34.1 and 39.7% at Weeks 4, 12, 24 and 52, respectively, showing ~3–4% lower than that obtained by the LOCF method. Significant improvements in clinical parameters were observed and the percentage reduction for each parameter at Week 52 compared with at baseline was 63.8% for SJC, 60.5% for TJC, 33.7% for Pt-GA, 70.4% for ESR, 82.6% for CRP and 56.0% for MMP-3.

HAQ-DI similarly decreased significantly from 1.56 (0.80) at baseline to 1.29 (0.87) at Week 52 ($P = 0.0009$). However, improvement in HAQ-DI compared with baseline score (change in HAQ-DI $\geqslant 0.22$) was observed in only 45.6% of patients at Week 52. Although functional remission (HAQ-DI $\leqslant 0.5$) increased significantly from 12.4% at baseline to 26.4% at Week 52, categorical analysis of HAQ-DI did not show any statistical change ($P = 0.1352$).

Effects of medication on clinical and functional response

As shown in Fig. 2, DAS-28 at Week 52 was significantly lower in patients receiving concomitant MTX than in those not receiving it [2.92 (1.46) and 3.45 (1.82), respectively; $P = 0.0336$]. HAQ-DI was also significantly lower in those receiving MTX than in those not receiving it [1.12 (0.83) *vs* 1.55 (0.85); $P = 0.0005$]. In contrast, DAS-28 at Week 52 was significantly higher in patients receiving concomitant GCs than in those not receiving them [3.34 (1.58) *vs* 2.87 (1.79); $P = 0.0037$]. Again, HAQ-DI at Week 52 was also higher in patients receiving GCs than in those not receiving them [1.40 (0.88) *vs* 1.07 (0.82); $P = 0.0071$). However, there was no significant difference in either DAS-28 or HAQ-DI at Week 52 between patients who had or had not received previous treatment with anti-TNF biologics.

Inhibition of radiographic damage by tocilizumab treatment

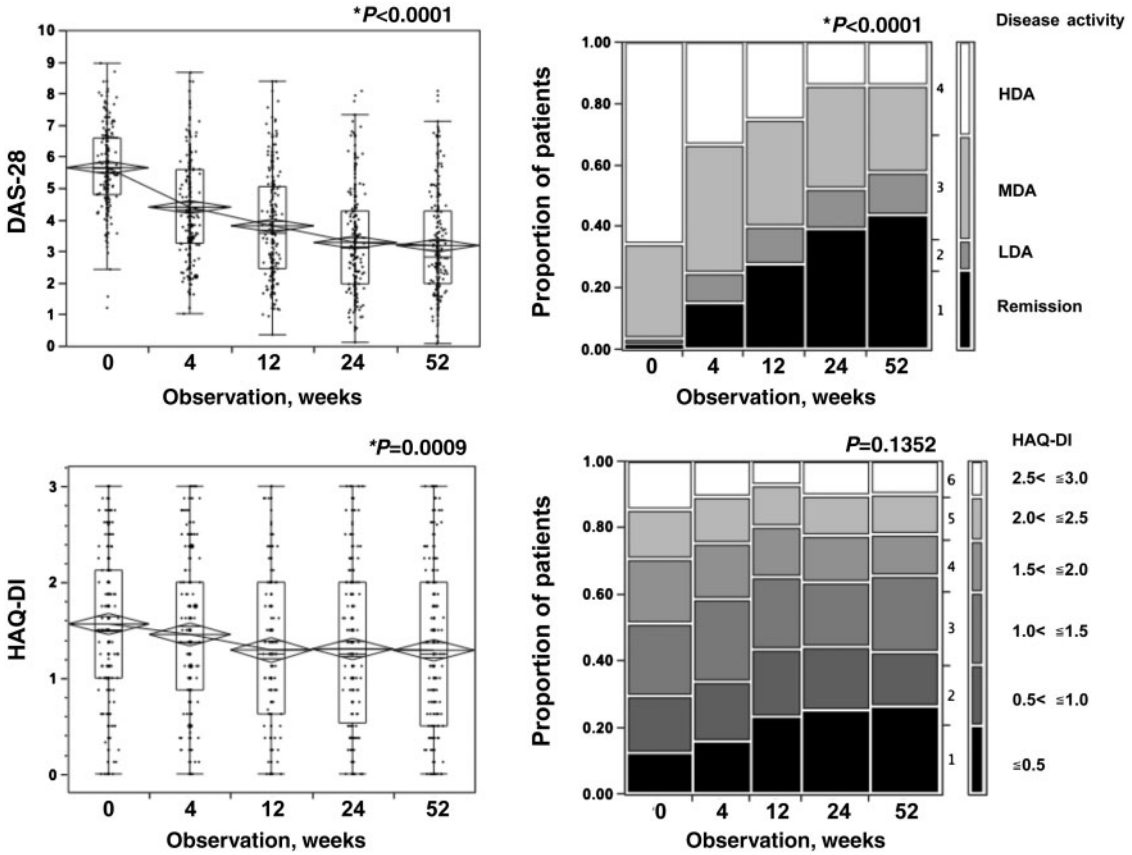
Radiographic damage was evaluated in 149 of the 232 patients. Most baseline parameters as well as clinical and functional response at Week 52 did not differ significantly between the patients who underwent radiographic evaluation ($n = 149$) and those who did not ($n = 83$) (data not shown).

There was no significant difference between total vdH–Sharp score at Week 0 and that after 52 weeks of tocilizumab treatment [140.5 (101.2) *vs* 142.1 (101.3); $P = 0.8916$], and erosion score and joint space narrowing (JSN) score were similarly not significantly changed. The mean change from Week 0 to 52 of tocilizumab treatment was 1.07 (2.87) for total vdH–Sharp score, 0.50 (1.34) for erosion score and 0.58 (1.95) for JSN score, which appears to be clinically sufficient for tocilizumab to inhibit structural damage. As judged by a change in total vdH–Sharp score of $\leqslant 0.5$, 62.8% of the patients showed no radiographic progression (Fig. 3a). For the structural damage, treatment with tocilizumab greatly reduced the estimated yearly progression of the total vdH–Sharp score from 20.8 (22.9) at baseline to 1.1 (2.9) (Fig. 3b). There were no differences in the effect of structural damage among patients with different durations of disease. Interestingly, progression of joint destruction was similar with or without concomitant MTX, GCs or previous use of anti-TNF biologics. Each estimated yearly progression by RA patients treated with or without anti-TNF biologics was dramatically decreased from 18.3 (19.3) at baseline to 0.9 (2.4) at 52 weeks (96% reduction) and 24.8 (27.4) at baseline to 1.4 (3.5) at 52 weeks (94% reduction), respectively.

Retention rate during 52 weeks of treatment with tocilizumab

The retention rate of this study was 92.0% at Week 12, 83.0% at Week 24 and 71.1% at Week 52. Sixty-seven (28.9%) patients discontinued tocilizumab treatment because of adverse events (AEs) (38/67, 56.7%), lack of efficacy (21/67, 31.3%), remission (1/67, 1.5%) and other reasons (7/67, 10.4%). Retention rate was higher for patients with concomitant MTX than for those without it (77.1 *vs* 66.0%), and was lower for those with concomitant GCs than those without (68.7 *vs* 78.4%), while it did not differ between those with or without previous treatment with anti-TNF biologics (72.5 *vs* 70.9%).

Fig. 1 Change in DAS-28 and HAQ-DI scores over 52 weeks of tocilizumab treatment. Upper panels show the change in DAS-28 [left: distribution of the values, mean (S.D.), and median with first and third quartile points of DAS-28; right: categorical distribution of disease activity status]. Lower panels show the change in HAQ-DI [left: distribution of the values, mean (S.D.), and median with first and third quartile points of HAQ-DI; right: categorical distribution of disability status]. HDA: high disease activity; MDA: moderate disease activity; LDA: low disease activity.



Baseline variables predictive of clinical, structural and functional remission at Week 52

Since there are substantial confounding factors contributing to the clinical, radiological and functional responses to tocilizumab treatment, we next searched for independent predictive baseline parameters for clinical, structural and functional remission at Week 52. Based on the results of a univariate logistic regression analysis, age, disease duration, DAS-28, HAQ-DI, dose of MTX and dose of GCs at baseline were selected as significant variables for clinical remission at Week 52; estimated yearly progression of total vdH–Sharp score, HAQ-DI and dose of GCs at baseline were selected as significant variables for structural remission at Week 52; and age, disease duration, DAS-28, total vdH–Sharp score, HAQ-DI and dose of MTX at baseline were selected as significant variables for functional remission at Week 52 (Table 2). Multiple regression analysis showed that DAS-28, HAQ-DI, dose of MTX and dose of GCs at baseline were identified as independent predictive variables for clinical remission at Week 52. Yearly progression of total vdH–Sharp score and dose of GCs were found to be the independent predictive variables for structural remission at Week 52: in addition, although HAQ-DI was not a statistically significant predictive variable, it gave an adjusted odds ratio of 0.624 (Table 3). Finally, baseline HAQ-DI was identified as an independent predictive variable for functional remission at Week 52, with an adjusted odds ratio of 0.582.

Safety

In total, 133 AEs and 26 serious AEs (SAEs) were observed in 58 (25.0%) and 26 (11.2%) of 232 patients, respectively. Most of the AEs were infections and laboratory tests. In the category of SAEs, serious infections were reported in 10 (4.3%) patients, and the most common serious infection was pneumonia (4 points, 1.7%). Skin infection and oesophageal candidiasis were also reported in one patient each as SAEs necessitating discontinuation of tocilizumab treatment. In addition, there were two cases each of cerebral bleeding, malignancy (breast and cervix), liver dysfunction, skin eruption and exacerbation

FIG. 2 DAS-28 and HAQ-DI at Week 52 of tocilizumab treatment in RA patients with or without (**a**) concomitant MTX; (**b**) GCs; (**c**) previous treatment with anti-TNF biologics. Distribution of the values, mean (S.D.) and median with first and third quartile points of each clinical parameter are shown.

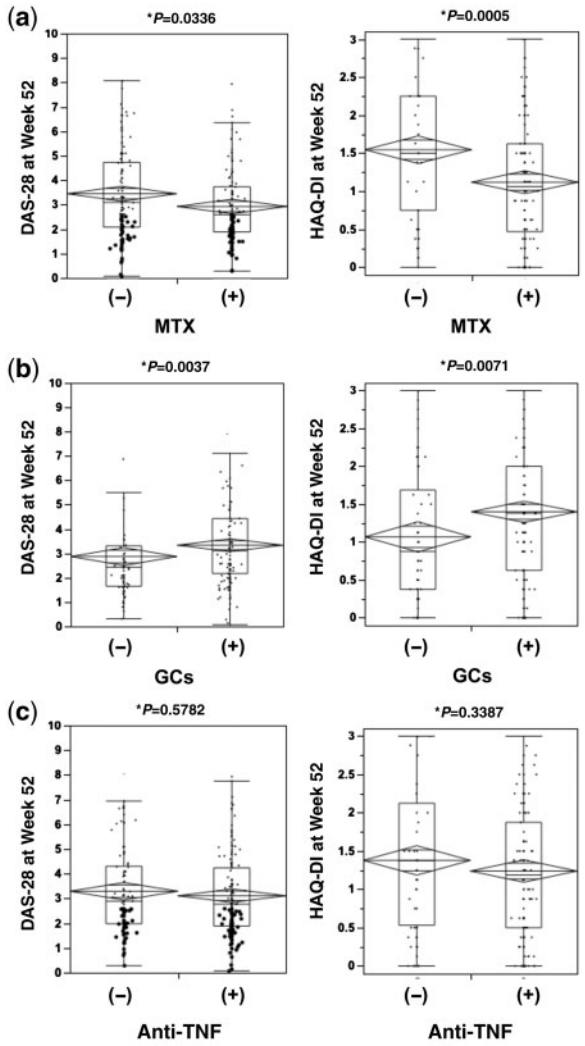
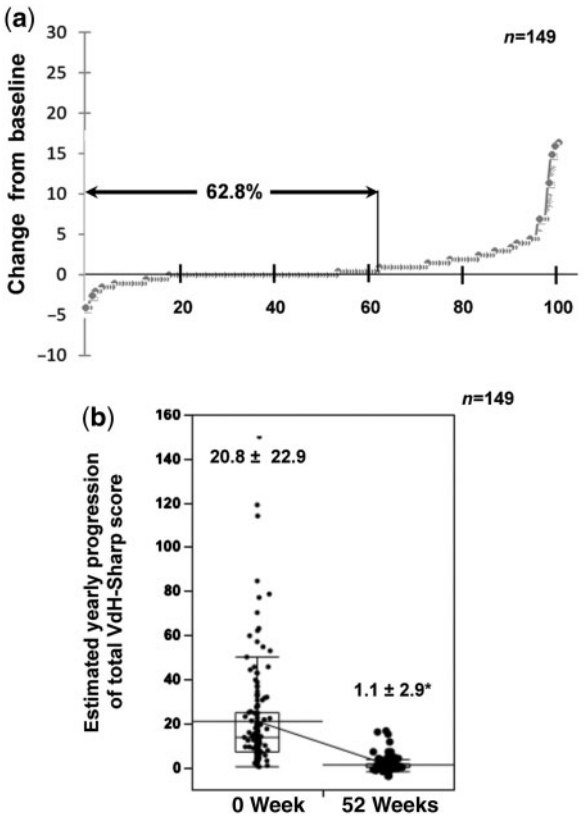


FIG. 3 Effects of radiographic damage before and 52 weeks after tocilizumab treatment by (**a**) the cumulative probability in total vdH–Sharp score and (**b**) estimated yearly progression of total vdH–Sharp score.



of scleroderma, and one case each of acute respiratory failure, myocardial infarction, chest pain, necrotizing pancreatitis and skin ulcer. Gastrointestinal bleeding, gastrointestinal perforation and anaphylaxis were also observed in one patient, leading to discontinuation of further tocilizumab treatment. The most common laboratory abnormalities were increases in lipids, including total, low- and high-density lipoprotein cholesterol in 5 (2.2%) of 232 patients and liver function abnormality, including aspartate aminotransferase (AST) and alanine aminotransferase (ALT) elevation in 7 (3.0%) patients. The elevation of serum bilirubin and cytopenia (white blood cells and platelets decreasing) were also reported in two patients each, leading to discontinuation of tocilizumab treatment.

Discussion

In this study, ~44% of patients with established RA and high disease activity achieved clinical remission at Week 52 of tocilizumab treatment, and radiographic non-progression was observed in >60% of patients. Although it is difficult to compare these results with those of other biologics because the patient background factors in each study differed, the efficacy of tocilizumab might be equivalent to or superior to anti-TNF agents compared with a similar type of study, whose DAS-28-CRP remission rate at Week 52 was 27.6% [19].

The Chugai Humanized Anti-Human Recombinant Interleukin-6 Monoclonal Antibody (CHARISMA) study [20] suggests that tocilizumab in combination with MTX may be superior to tocilizumab monotherapy, suggesting in turn that the rate of clinical remission with tocilizumab plus MTX combination therapy may also be higher as well. The present study clearly showed that clinical and functional remission rates at 52 weeks were significantly higher for RA patients receiving MTX than those without MTX, whereas in marked contrast, remission rates were significantly lower for those receiving GCs than for those not receiving them. These findings were further supported by the observation that the retention rate of tocilizumab

TABLE 2 Logistic regression analysis for the possible association between baseline parameters and clinical, structural and functional remissions at 52 weeks by tocilizumab treatment

Baseline clinical parameters	Clinical remission		Structural remission		Functional remission	
	Chi-square	*P*-value	Chi-square	*P*-value	Chi-square	*P*-value
Age	13.39	0.0003	0.28	0.5966	24.89	<0.0001
Gender	2.81	0.0938	0.04	0.8507	0.17	0.6819
Disease duration	4.68	0.0305	0.63	0.4761	10.11	0.0015
DAS-28	15.74	<0.0001	1.86	0.1726	21.55	<0.0001
MMP-3	1.41	0.2354	1.59	0.2066	2.40	0.1211
Total vdH–Sharp score	0.73	0.3927	0.28	0.5966	4.75	0.0293*
Estimated yearly progression of total vdH–Sharp score	0.90	0.3416	13.18	0.0003	0.43	0.5131
HAQ-DI	24.52	<0.0001	4.21	0.0403	96.42	<0.0001
Comorbidity	0.06	0.8075	0.71	0.3987	0.79	0.3740
Dose of MTX	20.55	<0.0001	0.05	0.8187	6.92	0.0085
Dose of GCs	5.12	0.0237	5.75	0.0165	1.97	0.1609
Previous anti-TNFs	0.32	0.5736	0.44	0.5087	0.12	0.7279

TABLE 3 Multiple logistic regression models for the baseline parameters predictive of clinical, structural and functional remissions at 52 weeks of tocilizumab treatment

Baseline clinical parameters	Clinical remission		Structural remission		Functional remission	
	Adjusted odds ratio (95% confidence interval)	*P*-value	Adjusted odds ratio (95% confidence interval)	*P*-value	Adjusted odds ratio (95% confidence interval)	*P*-value
Duration, years	–	–	–	–	1.022 (0.987–1.061)	0.2295
DAS-28	0.673 (0.500–0.890)	0.0069	–	–	–	–
Estimated yearly progression of total vdH–Sharp score	–	–	0.967 (0.945–0.986)	0.0021	–	–
HAQ-DI	0.569 (0.359–0.886)	0.0141	0.624 (0.381–1.002)	0.0553	0.582 (0.360–0.919)	0.020
Dose of MTX, mg/week	1.134 (1.062–1.214)	0.0002	–	–	–	–
Dose of GCs, mg/day	0.898 (0.809–0.991)	0.0368	0.879 (0.786–0.978)	0.0202	–	–

treatment was higher for patients with MTX than for those without it, and lower for patients with GCs than for those without them. The question might be raised whether concomitant use of MTX and GCs is affected by a number of confounding factors. However, multivariate logistic regression analysis demonstrated that higher doses of MTX and lower doses of GCs, in addition to baseline DAS-28 and HAQ-DI, each independently contributed to achievement by tocilizumab of clinical remission at 52 weeks. The retention rates were not significantly different, and instead were consistent with our findings for DAS-28 and HAQ-DI at Week 52 in patients with and without these medications, suggesting that patients who do not achieve a satisfactory response or who have safety issues should discontinue tocilizumab.

The Study of Active Controlled Monotherapy Used for Rheumatoid Arthritis, An IL-6 Inhibitor (SAMURAI) study demonstrated that, compared with DMARDs, tocilizumab monotherapy significantly inhibited progression of structural damage in Japanese RA patients [21]. In addition, preliminary results reported from the Tocilizumab Safety and the Prevention of Structural Joint Damage (LITHE) study showed that, compared with MTX alone, tocilizumab plus MTX treatment resulted in significantly less progression of joint destruction [22]. In the present study, X-ray images at baseline and at Week 52 of tocilizumab treatment were available for 149 of 232 patients, allowing us to evaluate the radiographic effect of tocilizumab. The radiographic data obtained in this study are consistent with the results of previous clinical trials, and the multivariate logistic regression analysis suggested the new hypothesis that concomitant GCs compromise the inhibition of structural progression by tocilizumab. As stated above, the duration of disease in patients enrolled in this study

was 12.4 years, and estimated yearly progression was significantly high, with 20.8 (1.3) at baseline. Considering the results of the impact on radiographic and clinical response to infliximab therapy concomitant with methotrexate in patients with rheumatoid arthritis by trough serum level in a dose escalating (RISING) study, in which we reported a disease duration of ~8 years and mean estimated yearly progression of 8.1 (9.1) [23], the present study included patients with remarkably severe clinical features with long disease duration and progressive joint destruction. Irrespective of these severe conditions, the 95% inhibitory effect of tocilizumab indicates how powerful its inhibition of joint destruction is. Surprisingly, we found that tocilizumab inhibits the radiographic damage, not only in patients treated without TNF inhibitors, but also in those treated with TNF inhibitors. Although further research is needed, our findings suggest that the pathological condition of RA is dependent on TNF. The good results obtained with tocilizumab are consistent with those of both domestic and foreign studies.

On the other hand, functional remission was achieved in 26.4% of the patients at 52 weeks, which is lower than the clinical remission rate at 52 weeks (43.7%) and that of radiographic non-progression at 52 weeks (62.8%). The longer duration of disease and high HAQ-DI at baseline may be responsible for the lower functional remission rate observed in the present study. Although Nagasawa *et al*. [17] reported that the incidence of HAQ remission (HAQ $\leqslant$ 0.5) after 2 years of treatment with infliximab was 41.6%, it is difficult to compare this result with our own because the methods of statistical analysis used in these two studies differed markedly. Smolen *et al*. [24] analysed the damage-associated HAQ-DI score in the Best Life in RA (BELIRA) trial and seven pivotal clinical trials including anti-TNF biologics, MTX and LEF [24]. According to their report, damage-associated HAQ-DI corresponds to 0.01 per point of total vdH–Sharp score. The total vdH–Sharp score of 140.5 at baseline in this study appears to correspond to a damage-associated HAQ-DI of 1.41, and thus maximum improvement after tocilizumab treatment may be assumed to be an HAQ-DI of 1.56 at baseline minus 1.41, which is 0.15. The real change observed in this study (0.27) was better than that determined based on the above assumption. Considering factors such as the severe baseline HAQ in the present study, our findings suggest that administration of tocilizumab before worsening of HAQ, in the very early stage, might lead to attaining rates of high clinical, structural and functional remission. We should master use of tocilizumab towards achievement of a higher treatment goal in RA patients.

Although the duration of disease in the patients in this study was long and 60% of the patients had used anti-TNF agents previously, the incidences of SAEs and serious infections were comparable with those in the RISING study, in which the incidences of SAEs and serious infections were 11.6 and 5.2%, respectively [23]. These results indicate that attention must be paid to the onset of serious infections, including pneumonia, during tocilizumab treatment as well as with anti-TNF agents. Most of the laboratory test abnormalities in this study were transient and not associated with SAEs. These findings indicate that the safety profile of tocilizumab was acceptable in actual clinical practice.

In conclusion, the REACTION study showed that clinical remission could be achieved in ~40% of patients and radiographic non-progression could be achieved in ~60%. Tocilizumab was well tolerated over 52 weeks, and the most frequent adverse drug reaction was pneumonia. Although functional remission was obtained in 28% of the patients at Week 52, it was confirmed that higher remission rates may be attained with earlier administration of tocilizumab before worsening of HAQ. Additionally, the multivariate logistic regression model that we used provided insights into how the use of tocilizumab can be improved in clinical practice.

Rheumatology key messages

- The REACTION study showed the clinical, structural and functional response to tocilizumab in RA patients in real-world clinical practice.
- A multivariate logistic model provided insights into how the use of tocilizumab can be further improved.

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