Baseline low Modified Health Assessment Questionnaire (MHAQ) predicts the state of remission estimated by Clinical Disease Activity Index and MHAQ at 1 year in tocilizumab-treated rheumatoid arthritis patients

Sirs,
The objectives of this study were to explore the baseline variables that predict the state of remission at 1 year as estimated by the Clinical Disease Activity Index (CDAI) and the Modified Health Assessment Questionnaire (MHAQ) in tocilizumab (TCZ)-treated rheumatoid arthritis (RA) patients. RA patients who received 8 mg/kg of TCZ every 4 weeks were consecutively enrolled in this study from April 2008 to March 2011 at the nine rheumatology centres of Nagasaki Prefecture, Japan. A total of 110 RA patients who had been observed for 1 year from the initial TCZ infusion were examined in this retrospective observational investigation. The last observation carried forward (LOCF) method by intent-to-treat (ITT) analysis was used for the evaluation of the patients' CDAI and MHAQ scores. The median age, disease duration, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), CDAI and MHAQ at entry were 61.3 years old, 9.7 years, 1.6 mg/dL, 48 mm/hr, 23.9, and 0.8, respectively. Anti-cyclic citrullinated peptide antibodies (ACPA) were positive in 90.2% of the patients and rheumatoid factor (RF) was positive in 88.6%. The retention rate of TCZ at 1 year was 85.5%. The median CDAI score decreased significantly from 25.2 at baseline to 10.5 at 1 year ($p<0.0001$ *vs.* baseline), and CDAI remission (CDAI ≤2.8) was achieved in 13.6% of the patients at 1 year. The median MHAQ score decreased significantly from 0.9 at baseline to 0.6 at 1 year ($p<0.01$ *vs.* baseline), and MHAQ remission (MHAQ score <0.3) was achieved in 38.0% of the patients at 1 year. We attempted to identify the baseline variables that predict the state of CDAI remission and MHAQ remission at 1 year through a multiple regression analysis, and we selected the most appropriate model on the basis of Akaike's information criteria. NPAR1WAY and REG in the SAS system®, version 9.2 were used for the calculations. The baseline variables of age, gender, disease duration, Steinblocker classification, concomitant use of methotrexate or glucocorticoids, previous TNF inhibitors use, tender joint counts, swollen joint counts, patient's global assessment, evaluator's global assessment, positivity of ACPA, positivity of RF, matrix metalloproteinase-3 concentrations, CRP concentrations, ESR, Disease Activity

Score (DAS) 28-ESR, CDAI, Simplified Disease Activity Index (SDAI) and MHAQ were selected for the evaluation. As shown in Table I, the logistic regression analysis revealed that shorter disease duration and low MHAQ were predictive of CDAI remission at 1 year. In addition, low MHAQ score was predictive of MHAQ remission at 1 year. The MHAQ was developed as a short version of the HAQ and has been used to assess function in patients with RA (1). Takeuchi *et al.* revealed that low HAQ at baseline is a predictive variable for three types of remission (DAS28, radiographic and HAQ) at 1 year of TCZ treatment (2). In other words, the CDAI may be a more accurate disease activity score than the DAS28 in RA patients treated with TCZ (3-5), since TCZ directly inhibits the increases of CRP and ESR whereas the CDAI does not contain these acute-phase reactants (6). Accordingly, the present study's results showed that low MHAQ at baseline is the only variable to predict the remission state of CDAI and MHAQ at 1 year of TCZ-treatment in RA patients. In addition, shorter disease duration is predictive of CDAI remission at 1 year. In conclusion, we have identified characteristics of patients who achieved remission following TCZ treatment in clinical practice. We suggest that TCZ therapy for RA patients be initiated early, before the progression of functional disability.

S. KAWASHIRI[1,2]
Y. UEKI[3]
K. MIGITA[4]
H. NAKAMURA[2]
K. AOYAGI[1]
A. KAWAKAMI[2]

[1]*Department of Public Health, and*
[2]*Unit of Translational Medicine, Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan;*
[3]*Sasebo Chuo Hospital, Center for Rheumatic Disease, Sasebo, Japan;*
[4]*Department of General Internal Medicine, NHO National Nagasaki Medical Center, Omura, Japan.*

Address correspondence and reprint requests to:
Shin-ya Kawashiri, MD, PhD, Department of Public Health, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan.
E-mail: shin-ya@hotmail.co.jp

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Table I. Logistic regression analysis to estimate the remission of CDAI and MHAQ at 1 year by baseline variables in RA patients treated by TCZ.

CDAI remission				
	Odds ratio	95% CI		*p*-value
Duration of disease ≥5 years	0.16	0.04	0.63	<0.01
MHAQ	0.27	0.07	0.99	<0.05
MHAQ remission				
	Odds ratio	95% CI		*p*-value
RF	0.25	0.05	1.20	0.08
MHAQ	0.22	0.06	0.85	<0.01

CDAI: Clinical Disease Activity Index; MHAQ: Modified Health Assessment Questionnaire; RA: rheumatoid arthritis; TCZ: tocilizumab; RF: rheumatoid factor; CI: confidence interval.

References
1. MASKA L, ANDERSON J, MICHAUD K: Measures of functional status and quality of life in rheumatoid arthritis: Health Assessment Questionnaire Disability Index (HAQ), Modified Health Assessment Questionnaire (MHAQ), Multidimensional Health Assessment Questionnaire (MDHAQ), Health Assessment Questionnaire II (HAQ-II), Improved Health Assessment Questionnaire (Improved HAQ), and Rheumatoid Arthritis Quality of Life (RAQoL). *Arthritis Care Res* (Hoboken) 2011; 63: S4-13.
2. TAKEUCHI T, TANAKA Y, AMANO K *et al.*: Clinical, radiographic and functional effectiveness of tocilizumab for rheumatoid arthritis patients – REACTION 52-week study. *Rheumatology* (Oxford) 2011; 50: 1908-15.
3. KAWASHIRI SY, KAWAKAMI A, IWAMOTO N *et al.*: Disease activity score 28 may overestimate the remission induction of rheumatoid arthritis patients treated with tocilizumab: comparison with the remission by the clinical disease activity index. *Mod Rheumatol* 2011; 21: 365-9.
4. FUNAHASHI K, KOYANO S, MIURA T, HAGIWARA T, OKUDA K, MATSUBARA T: Efficacy of tocilizumab and evaluation of clinical remission as determined by CDAI and MMP-3 level. *Mod Rheumatol* 2009; 19: 507-12
5. KANEKO A, KIDA D, SAITO K, TSUKAMOTO M, SATO T: Clinical results for tocilizumab over one year in the clinical setting as assessed by CDAI (clinical disease activity index): CRP at week 12 and MMP-3 at week 24 are predictive factors for CDAI. *Rheumatol Int* 2012; 32: 3631-7.
6. ALETAHA D, NELL VP, STAMM T *et al.*: Acute phase reactants add little to composite disease activity indices for rheumatoid arthritis: validation of a clinical activity score. *Arthritis Res Ther* 2005; 7: R796-806.