Predictors of Biological Antirheumatic Drug Discontinuation in Patients with Rheumatoid Arthritis while in Remission

To the Editor:

I read the paper by Yoshida, *et al*[1] involving 2 cohort studies from the United States and Japan to determine the predictors of discontinuation of biological disease-modifying antirheumatic drugs (bDMARD) in patients with rheumatoid arthritis (RA) while in remission over 5 years, defined by the Clinical Disease Activity Index (CDAI) ≤ 2.8. The authors used Cox regression models, and the percentages of discontinuation of bDMARD were 10.0% and 11.8% from 6263 patients in the United States and from 744 patients in Japan. Shorter RA duration was significantly associated with higher rates of discontinuation in both cohorts. In addition, methotrexate (MTX) use and lower CDAI were significantly associated with higher rates of discontinuation in the United States. I have some concerns about this study.

First, there was a trend of increase in HR of women in Japan and of glucocorticoid use in the United States. Although these independent variables did not reach the level of significance, there was a discrepancy between the 2 cohorts. Several different baseline settings of the 2 cohorts exist and I understand that the comparison of the study results should be made with caution. In addition, the magnitude of the baseline study differs between the 2 cohorts, and more stable estimates would be observed in the US cohort. Predictors of bDMARD discontinuation in Japan should be confirmed by further study.

Relating to the first query, the same authors reported precise information on the failure rate after discontinuation[2]. The bDMARD-free remission failure rate was estimated to be 67.4% at 1 year and 78.3% at 2 years, and lower CDAI within the remission range was associated with fewer failures. The guideline for the treatment of RA by bDMARD was recently revised in Japan, and MTX usage for the treatment of RA in Japan has been improved in the clinical setting. Taken together, the treatment of RA for the next 10 years in Japan would be dramatically changed.

Second, tumor necrosis factor (TNF) inhibitor occupies 91.5% and 78.8% of bDMARD in the United States and Japan cohorts, respectively. The type of bDMARD did not contribute significantly to the discontinuation of bDMARD in both cohort studies, and the review of TNF inhibitor discontinuation study presented some difficulties for conducting metaanalysis, partly because of the heterogeneous inclusion criteria[3]. Yoshida, *et al*[4] discussed the same factors, and there is a need for more cohort studies for conducting metaanalyses of bDMARD discontinuation.

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