Dr. Wiland, *et al,* reply

To the Editor:

We thank Prof. Bannwarth for his insight into the potential influence of methotrexate (MTX) dosing in the PRIZE clinical trial[1]. The objective of the PRIZE study was to compare sustained remission rates after 39 weeks of reduced medication in patients with rheumatoid arthritis who had first achieved remission after 52 weeks' treatment with a combination of etanercept (ETN), 50 mg subcutaneously (SC) once a week, and MTX, orally 10–25 mg once a week. The MTX dose was optimized for combination therapy with the standard dose of ETN, with induction of remission as the goal. The primary analysis was a comparison of sustained remission rates between patients switched to a reduced dose of ETN (25 mg, with the MTX dose and route of administration kept constant) versus patients switched to placebo. Serving as a standard therapy control, a third cohort discontinued ETN and continued MTX, again with the dose and route of administration kept constant. A secondary endpoint was comparison of the reduced-dose ETN and MTX combination (ETN/MTX) with standard oral MTX monotherapy. After 39 weeks of treatment, the remission rates in the ETN/MTX and placebo groups were 63% and 23%, respectively ($p < 0.001$; pairwise comparison). The remission rate in the MTX monotherapy group was 40% ($p < 0.009$; pairwise comparison with ETN/MTX)[2].

Analysis of patient-reported outcomes (PRO) was described in our recent article and showed a similar pattern[3]. The placebo group showed worsening of PRO compared with the ETN/MTX group. The MTX group also showed greater worsening of PRO than the ETN/MTX group, but not as much as the placebo group. We agree with Prof. Bannwarth that we cannot exclude the possibility that switching to SC MTX rather than continuing oral MTX would have prevented or lessened PRO worsening in the MTX group. However, the study was designed to examine differences between reduced dose ETN/MTX therapy, oral MTX monotherapy, and placebo. The study design necessitated keeping the MTX route of administration constant throughout the study; thus the effect of different MTX regimens on sustained remission cannot be estimated.

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