

Patients with Rheumatoid Arthritis in Remission While Receiving Etanercept Plus Methotrexate Therapy May Require Adjustment of Dosing Regimen When Switched to Methotrexate Monotherapy

To the Editor:

I read with interest the article by Wiland, *et al*¹ reporting on patients with early moderate to severe rheumatoid arthritis who achieved remission while receiving etanercept (ETN) 50 mg once weekly (QW) plus methotrexate (MTX). They experienced significant worsening in patient-reported outcome (PRO) measures when switched to placebo or MTX monotherapy, but experienced only slight, generally nonsignificant worsening after tapering the ETN dose to 25 mg QW. Because the dose of MTX used in this study was not specified, I wonder whether patients switched to MTX monotherapy actually received an optimal dosing regimen.

According to the study protocol, MTX was administered orally at an initial dose of 10 mg per week (minimum required dose)². Then, MTX dose was adjusted at the investigator's discretion during the first 8 weeks of the open-label induction phase with a maximum dose set at 25 mg per week². It may therefore be assumed that patients switched to MTX monotherapy might not have been given the optimal dosing regimen for MTX inasmuch as systemic exposure of oral MTX was shown to plateau at doses \geq 15 mg QW, whereas subcutaneous MTX demonstrated a linear systemic exposure over doses ranging from 10 to 25 mg QW³.

Finally, I stress that the study by Wiland, *et al*¹ cannot exclude the possibility that an adequate dosing regimen of MTX might have prevented worsening in PRO in the subgroup of patients switched to MTX monotherapy.

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J Rheumatol 2017;44:2; doi:10.3899/jrheum.160815