

## RHEUMATOID ARTHRITIS

**An alternative to methotrexate?**

Daily oral treatment with T-614, a member of the methanesulfonanilide family of cyclo-oxygenase 2 inhibitors, might be an alternative to weekly methotrexate therapy for rheumatoid arthritis (RA). Following successful safety trials in Japan and China, the potential of T-614 as a disease-modifying therapy was recently investigated in patients with RA from 12 Chinese centers.

**“Elevated plasma alanine transferase levels were ... the most frequent adverse effect”**

Lu *et al.* randomized 489 patients to one of three study arms: 25 mg per day T-614 for 4 weeks followed by 50 mg per day T-614 for 20 weeks; 50 mg per day T-614 for the entire 24-week study duration; or 10 mg per week methotrexate for the first 4 weeks, then 15 mg per week methotrexate for the remaining time. Previous use of DMARDs, including methotrexate, was permitted, but only if therapy had been discontinued 4 weeks before the study began. However, patients were excluded if they had

discontinued therapy with  $\geq 15$  mg per week methotrexate owing to an inadequate response or toxic effects. Although the investigators acknowledge the exclusion criteria could have biased the results, most of the patients in their study had previously received  $< 10$  mg per week methotrexate and only 15% had received previous DMARD therapy. They reason, therefore, that “these criteria could not actually exaggerate the efficacy and safety of T-614 itself, but instead raise the threshold to assess the non-inferiority of T-614”.

After 24 weeks of treatment, similar numbers of patients in the T-614 50 mg per day and methotrexate groups demonstrated 20% improvement in symptoms according to the American College of Rheumatology (ACR20) criteria (63.8% versus 62.0%). Fewer patients in each group achieved ACR50 and ACR70 responses, but the numbers were again comparable across the two groups. In addition, decreased levels of rheumatoid factor and IgA, IgG and IgM led the authors to suggest that “the immunomodulatory effect on B lymphocytes may have a role in the mechanism of action of T-614”.

Elevated plasma alanine transferase levels were, by far, the most frequent adverse effect in both groups, although notably fewer patients in the T-614 50 mg per day group had this complication compared with the methotrexate-treated patients. Lu *et al.* are not the first to observe increased plasma levels of liver enzymes in patients taking T-614, suggesting that monitoring liver enzyme levels might be warranted. In addition, T-614 treatment was associated with a higher incidence of mild adverse effects (rash and allergy) than methotrexate therapy, whereas patients in the latter group reported a greater incidence of gastrointestinal symptoms than T-614 treated patients.

These results further confirm the efficacy of T-614 and suggest that this agent could become a viable alternative to the current “gold standard” for the treatment of RA.

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**Original article** Lu, L.-J. *et al.* Multicenter, randomized, double-blind, controlled trial of treatment of active rheumatoid arthritis with T-614 compared with methotrexate. *Arthritis Rheum.* 61, 979–987 (2009).