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Tocilizumab Versus Methotrexate in Moderate to Severe Rheumatoid Arthritis

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Introduction

Rheumatoid arthritis (RA) patients have elevated serum and synovial fluid levels of interleukin-6 (IL-6) that correlates with disease activity. Tocilizumab, an anti-IL-6 receptor antibody, has shown efficacy in moderate to severe, active RA that has failed to respond to disease-modifying antirheumatic drugs (DMARDs). MTX, the most commonly used DMARD, is the background drug used in clinical trials to compare with other newer therapies.

Aims

This study compared tocilizumab monotherapy versus MTX monotherapy in treatment of active RA in those who had not previously failed MTX or biologic treatment.

Methods

RA patients with moderate to severe disease (> 3 mo) who had not received MTX 6 months before randomization or had not failed tumor necrosis factor (TNF)- α inhibitors were eligible for the study. Patients were randomly assigned to receive MTX orally (7.5 mg escalating to 20 mg tablets weekly plus placebo intravenously every 4 weeks; $n = 262$), tocilizumab intravenously (8 mg/kg every 4 weeks plus placebo tablets weekly; $n = 268$), or both placebos for the first 8 weeks followed by tocilizumab plus placebo for the remaining 16 weeks (8 mg/kg every 4 weeks plus placebo tablets weekly; $n = 82$). Intention to treat (ITT) and per-protocol population were used in analysis. The 24-week primary end point was the American College of Rheumatology (ACR) 20% improvement criteria (ACR20) response rate.

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Jones G, Scbba A, Gu J, et al.: Comparison of tocilizumab monotherapy versus methotrexate monotherapy in patients with moderate to severe rheumatoid arthritis: the AMBITION study. *Ann Rheum Dis* 2009 Mar 17 (Epub ahead of print).

Disclosure

Dr. Moreland has been a consultant for Roche, Pfizer, Centocor, and UCB. No further potential conflicts of interest relevant to this article were reported.

Rating: •Of importance.

Results

At 24 weeks, more patients achieved ACR20 response (ITT, 69.9% vs 52.5%; $P < 0.0001$) and more patients were in remission (Disease Activity Score using 28 joint counts [DAS28] < 2.6 ; 33.6% vs 12.1%) in the tocilizumab group than in the MTX group. Tocilizumab had superior ACR20 response as early as week 2 (ITT, 24.1% vs 10.2%) and this increased over time. More patients in the tocilizumab group reached ACR 50% improvement criteria (44.1% vs 33.5%; $P = 0.0023$) and ACR 70% improvement criteria (28% vs 15.1; $P = 0.0002$) response. Incidence of serious adverse events was higher in the tocilizumab group than in the MTX group (3.8% vs 2.8%; $P = 0.50$).

Discussion

The results of this double-blind, randomized, double-dummy, parallel-group study demonstrate that tocilizumab monotherapy is superior to MTX monotherapy regardless of previous MTX use. This is the first biologic that has been shown to be superior to MTX monotherapy.

Comments

Targeted biologic agents have changed the outcome of RA and have made the past decade an exciting period for clinical research and patient care. Because these newer agents have generally not shown significant clinical differences when used as monotherapy, they usually have been given in conjunction with conventional DMARDs [1]. Tocilizumab has already shown efficacy for those with active RA who have failed MTX and TNF- α inhibitors [2]. A head-to-head trial of TNF- α inhibitors and IL-6 antagonists will aid clinicians in choosing treatment. This study is interesting in that it is the first to demonstrate biologic monotherapy superiority to MTX for moderate to severe RA. Regulatory authorities are currently reviewing this new biologic for the treatment of RA. No long-term studies yet completed allow us to determine long-term adverse events.

References

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