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Methotrexate Versus Combination Methotrexate and Etanercept for Rheumatoid Arthritis

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Introduction

Some rheumatoid arthritis (RA) patients still experience disability despite newer targeted therapies. Early aggressive treatment combinations can improve outcomes by inducing remission, including halting radiographic progression and preventing joint damage. Biologic agents have made clinical remission a realistic goal for early RA and now a primary end point in most clinical trials. Disease-modifying antirheumatic drugs (DMARDs) alone may not stop radiographic progression of disease in all patients. Previous studies have shown that combining DMARDs such as methotrexate (MTX) with biologic agents can prevent joint damage by stopping structural progression in some patients.

Aims

This study compared MTX versus combination MTX and etanercept in treatment of early RA, using clinical and radiographic remission as outcome measures.

Methods

MTX-naïve patients with early (3–24 mo of disease), moderate to severe RA were eligible for the study if they had not previously received tumor necrosis factor- α inhibitors and had not taken DMARDs or corticosteroid injections 4 weeks before the baseline visit. Patients were randomly assigned to receive MTX orally plus placebo (7.5 mg tablets plus two placebo injections weekly; $n = 263$) or MTX orally plus etanercept (7.5 mg tablets plus two 25 mg injections weekly; $n = 265$). The 52-week co-primary end points were the proportion of patients in remission (Disease Activity Score using 28 joint counts [DAS28] < 2.6) and the change in the modified total Sharp score (mTSS) from baseline.

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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.

Emery P, Breedveld FC, Hall S, et al.: Comparison of methotrexate monotherapy with a combination of methotrexate and etanercept in active, early, moderate to severe rheumatoid arthritis (COMET): a randomized, double-blind, parallel treatment trial. *Lancet* 2008, 372:375–382.

Rating: • Of importance.

Results

Baseline characteristics showed that 92% of all patients had severe disease (DAS28 > 5.1). At 52 weeks, more patients achieved DAS28 remission in the combined-treatment group than in the MTX group (50% vs 28%) and more patients had radiographic nonprogression in the combined treatment group than in the MTX group (80% vs 59%). There was greater improvement in health assessment questionnaire disability index in the combined-treatment group (61% vs 44%). Significantly more patients in the combined-treatment group reached American College of Rheumatology (ACR) 20% improvement criteria (86% vs 67%), ACR 50% improvement criteria (71% vs 49%), and ACR 70% improvement criteria (48% vs 28%) response. Serious adverse events were similar in both groups.

Discussion

The results of this double-blind, randomized, placebo-controlled, parallel-group, multicenter study demonstrate that combination therapy with etanercept and MTX was more effective in achieving remission than MTX alone during the first year in early severe RA.

Comments

MTX is the most commonly used DMARD for moderate to severe RA [1]. As monotherapy, MTX, has shown to be effective in RA as this and other studies have demonstrated radiographic nonprogression after 1 year of treatment in a significant subset of RA patients [2]. This study showed that, of 528 patients available for assessment, 205 patients (39%; both treatment groups) achieved clinical remission after 1 year. The combination of etanercept and MTX demonstrated higher efficacy than MTX alone in achieving clinical remission, radiographic nonprogression, functional status, and prevention of work disability. This study validates previous reports which stated that initial combination therapy results in earlier functional improvement and less radiographic damage at 52 weeks than MTX monotherapy [3]. The current challenge is to discover biomarkers or predictors that indicate which patients with early RA require MTX monotherapy versus early treatment with combination therapy.

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