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Certolizumab Pegol in Active Rheumatoid Arthritis

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Introduction

The treatment of rheumatoid arthritis (RA) has changed since the introduction of tumor necrosis factor (TNF)- α inhibitors as these medications in combination with methotrexate (MTX) have improved signs and symptoms compared with MTX monotherapy. Individual patient response and adverse effects to a certain TNF- α inhibitor can be variable. A novel TNF- α inhibitor, certolizumab pegol (CZP), may avoid Fc-mediated effects and be useful as an additional therapy to MTX in patients with active RA.

Aims

This study compared two dosage regimens of lyophilized CZP plus MTX versus placebo plus MTX in patients with active RA who had an inadequate response to MTX alone.

Methods

RA patients with active disease who had received MTX for 6 months (stable dose of 10 mg/wk for 2 mo before baseline) and who had not received any biologic therapy within 6 months of baseline were eligible for the study. Patients were randomly assigned to three groups (2:2:1). Two groups received subcutaneous CZP at an initial dosage of 400 mg at week 0, 2, and 4, with subsequent dosage of CZP plus MTX (200 mg every 2 wk plus MTX weekly; $n = 393$) or CZP plus MTX (400 mg every 2 weeks plus MTX weekly; $n = 390$). The third group received placebo plus MTX (saline every 2 weeks plus MTX weekly; $n = 199$). Treatment failures were withdrawn (week 16) and had an option for an open-label extension phase (CZP 400 mg every 2 weeks). The co-primary end points were the American College of Rheumatology 20% improvement criteria (ACR20) response rate (week 24) and the change in modified total Sharp score (mTSS) from baseline (week 52).

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Keystone E, van der Heijde D, Mason D Jr, et al.: Certolizumab pegol plus methotrexate is significantly more effective than placebo plus methotrexate in active rheumatoid arthritis: findings of a fifty-two-week, phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. *Arthritis Rheum* 2008, 58:3319–3329.

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

Significantly more patients in the two CZP groups (64.9% with 200 mg and 70.3% with 400 mg) completed 52 weeks of treatment compared with the placebo group (21.6%). At 24 weeks, more patients achieved ACR20 response rates for the groups taking 200 mg and 400 mg of CZP plus MTX (58.8% and 60.8%) compared with placebo plus MTX (13.6%). At week 52, the change in mTSS from baseline was less in the group receiving 200 mg of CZP (0.4 Sharp units) and 400 mg of CZP (0.2 Sharp units) than in the placebo group (2.8 Sharp units). Most adverse events were mild to moderate.

Discussion

The results of this double-blind, randomized, placebo-controlled, parallel-group, multicenter study demonstrate that CZP plus MTX significantly reduced signs and symptoms of active RA and inhibited the progression of structural damage compared with placebo in patients who had inadequate response to MTX and continued to take MTX.

Comments

RA patients who failed to achieve an adequate or sustained response to MTX have been shown to respond to combination therapy with TNF- α inhibitors and MTX [1,2]. This trial demonstrates that this novel TNF- α inhibitor has similar efficacy as others for active RA. Gastroenterology data show that CZP can be effective for those who lose response to infliximab [3]; however, no clinical trials compare CZP with other TNF- α inhibitors for rheumatic disease or other inflammatory conditions. This study and others suggest that CZP should be considered if DMARDS and other TNF- α inhibitors fail to treat active RA [4,5]. At the time of this writing, regulatory authorities are reviewing CZP as a potential therapy for RA.

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