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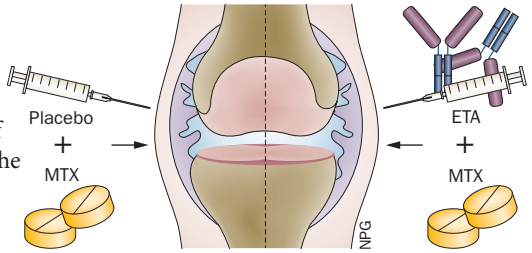
RHEUMATOID ARTHRITIS

ETA and MTX versus MTX alone in early inflammatory arthritis



The results from the EMPIRE trial, now published in *Annals of the Rheumatic Diseases*, show that a combination of methotrexate (MTX) and the anti-TNF agent etanercept (ETA) is nonsuperior to MTX monotherapy in patients with newly diagnosed early inflammatory arthritis, but clinical responses were achieved faster in the combination therapy group.

In this 78-week multicentre, randomized, placebo-controlled superiority trial, 110 patients with early clinical synovitis who had not previously been treated with DMARDs were assigned 1:1 to receive MTX and ETA, or MTX and placebo, for 52 weeks. Subcutaneous injections of ETA (50 mg) or placebo were administered once weekly until 52 weeks, or until the primary endpoint of no tender and no swollen joints (NTSJ) had been achieved for 26 weeks. MTX was started at 10 mg weekly and escalated as appropriate. Patients who achieved NTJS for 12 weeks after stopping ETA/placebo injections were weaned off MTX.

Paul Emery, the lead researcher on the study, explains, "The aim of the study was to compare good standard clinical practice—that is MTX with dose escalation if patients had ongoing disease activity, therefore incorporating a treat-to-target type approach—with optimal therapy using MTX and a biologic agent, in this study, ETA."

At week 52, no statistically significant difference in the primary endpoint (NTJS) was seen between the two treatment groups: 32.5% and 28.1% (adjusted OR 1.32 [0.56–3.09]; $P=0.522$) for the combination therapy and the monotherapy groups, respectively. In addition, the two treatment groups achieved similar secondary endpoint results (including DAS44-CRP and NTJS at 78 weeks).

As Emery points out, "The results highlight the importance of early treatment. Approximately a third of patients in both groups had no tender or swollen joints at 12 months—akin to the 2010 ACR/EULAR rheumatoid arthritis remission criteria; radiographic nonprogression was also high."

Exploratory analyses of DAS28-CRP responses were performed. "Earlier remission was seen with MTX and ETA than with MTX monotherapy," says Emery. At week 2, a DAS28-CRP <2.6 was achieved in 38.5% and 9.2% (adjusted OR 8.87 [2.53–31.17], $P=0.001$) of the combination and the monotherapy groups, respectively.

Ronald van Vollenhoven, who was not an author on this study, comments, "The results of this very interesting trial were somewhat unexpected and disappointing: although the patients on both MTX and ETA improved more rapidly, in the longer term there was no sustained benefit to having received the more intensive therapy." He continues that, "The major question remains whether starting with strong biologic treatments can be justified. Does this approach have any long-term benefit even if the treatment is later stepped down?"

Jenny Buckland

Original article Nam, J. L. *et al.* A randomised controlled trial of etanercept and methotrexate to induce remission in early inflammatory arthritis: the EMPIRE trial. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2013-204882