



OP-0149 CLINICAL REMISSION AND INHIBITION OF RADIOGRAPHIC PROGRESSION WITH COMBINATION ETANERCEPT-METHOTREXATE THERAPY VERSUS MONOTHERAPY IN ACTIVE, EARLY RHEUMATOID ARTHRITIS: 2-YEAR RESULTS FROM THE COMET TRIAL

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Background: Management strategies in rheumatoid arthritis (RA) are changing, with recognition of the importance of earlier treatment and benefits of potent biologic agents. Although traditional DMARDs are often effective in reducing disease activity, they may not be optimal to halt radiographic progression of joint damage.¹⁻³ Treatment efficacy is increasingly determined by both clinical and radiographic evidence of disease control.

Objectives: Assess how continuation of and alterations to the original etanercept-plus-methotrexate combination therapy and methotrexate monotherapy regimens affected clinical and radiographic outcomes in the second yr of the COMET trial.

Methods: Subjects were randomized at baseline; those who completed 1 yr of treatment with combination or methotrexate monotherapy entered yr 2 (n=411). The original combination group either continued combination (EM/EM; n=111) or received etanercept monotherapy (EM/E; n=111) in yr 2; the original methotrexate monotherapy group either received combination (M/EM; n=90) or continued monotherapy (M/M; n=99). Efficacy endpoints included clinical remission (DAS28<2.6) and radiographic non-progression (change in mTSS <=0.5) at yr 2. LOCF data from the yr-2 mITT population were analyzed; an NRI analysis was also performed on clinical remission from yr-1 and yr-2 mITT populations.

Results: Yr-2 LOCF analyses included 398 subjects for clinical and 360 for radiographic endpoints; the combined yr-1 and -2 NRI analysis included 528 subjects. At yr 2, the % of subjects achieving clinical remission was significantly greater in the continued combination therapy and delayed combination therapy groups than in the continued methotrexate monotherapy group (P<0.01; LOCF). In the NRI analysis, clinical remission was observed in significantly greater %s of subjects in the EM/EM, EM/E, and M/EM groups than in the M/M group (P<0.05). Radiographic non-progression was achieved by a significantly greater % in the continued combination group compared with all other groups (P<0.01; LOCF). No new safety signals or between-group differences in serious adverse events were seen.

Table:

Clinical and Radiographic Outcomes by Treatment Group at Year 2

Endpoint	% of Subjects EM/EM	EM/E	M/EM	M/M
Clinical Remission (LOCF)	57* (n=108)	50 (n=108)	58* (n=88)	35 (n=94)
Clinical Remission (NRI)	46† (n=131)	38‡ (n=134)	37‡ (n=133)	24 (n=130)
Radiographic Nonprogression (LOCF)	90** (n=99)	75 (n=99)	75 (n=79)	68 (n=83)

*P<0.01 vs M/M; †P<0.001 vs M/M; ‡P<0.05 vs M/M; **P<0.01 vs all other groups

Conclusion: Sustained combination therapy was consistently superior to continuous methotrexate monotherapy in providing clinical remission and radiographic non-progression over 2 years, without significant additional risk. Although delayed combination therapy was significantly more effective than methotrexate monotherapy with regard to clinical remission, it was not more effective in inhibiting progression of joint damage.

References: 1. Grigor C, et al. *Lancet*. 2004;364:263-9.
2. Allaart CF, et al. *Clin Exp Rheumatol*. 2006;24(6 suppl 43):S77-82.
3. Brown AK, et al. *Arthritis Rheum*. 2008;58:2958-67.

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