21. One-Year Results from the Canadian CAMEO Study: A Trial of Etanercept and Methotrexate versus Etanercept Alone in Rheumatoid Arthritis.

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Introduction: Combination therapy with a biologic and methotrexate (MTX) usually yields better outcomes than biologic monotherapy in rheumatoid arthritis (RA). However, some patients are intolerant to MTX, or prefer fewer medications if doing well. As well, some data suggest monotherapy with etanercept (ETN) may be sufficient. The objective of this open label trial was to determine if withdrawing MTX after 6 months of combination ETN+MTX, in MTX inadequate responders, is as effective as continuing ETN+MTX.

Methods: TNF inhibitor naïve, RA patients with active disease (≥ 3 swollen joints, DAS28 ≥ 3.2) despite stable MTX therapy (≥ 15 mg/wk, or 10 mg/wk if intolerant) for more than 12 weeks were enrolled. Combination therapy with ETN (50 mg/wk sc)+MTX was initiated for 6 months, followed by randomization of the patients to either continue with ETN+MTX or switch to ETN monotherapy for an additional 18 months. The primary endpoint was to show non-inferiority of ETN vs. ETN+MTX, based on the change in DAS28-ESR, 6 months after randomization (non-inferiority margin in delta DAS28-ESR (-0.6)), with pre-specified analyses of subsets by disease activity (DAS28 < 3.2 vs. DAS28 ≥ 3.2).

Results: 205 patients were randomized into two treatment groups. From 6 to 12 months, DAS28 was maintained in patients on ETN+MTX (D DAS28 [95% CI] = 0.04 [-0.2, 0.3]) and increased slightly in patients on ETN monotherapy(D DAS28 [95% CI] = 0.5 [0.3, 0.7]). The primary endpoint of non-inferiority was not achieved with an adjusted difference between ETN and ETN+MTX of -0.4 [-0.7, -0.12]. However, if a low disease activity (LDA) was achieved (DAS28 < 3.2) at 6 months, the change in DAS28 from 6 to 12 months was similar for ETN+MTX (D DAS28 [95% CI] = 0.57 [0.3, 0.8]) and ETN (D DAS28 [95% CI] = 0.7 [0.3, 1.0]). Conversely, for patients on ETN+MTX with DAS28 ≥ 3.2 at 6 months, disease activity continued to improve from 6 to 12 months (D DAS28 [95% CI] = -0.4 [-0.7, -0.1]), while for patients on ETN monotherapy it had slightly worsened at 12 months (D DAS28 [95% CI] = 0.4 [0.1, 0.7]).

Conclusion: Patients who achieve DAS28 <3.2 by 6 months on ETN+MTX have similar disease activity at 12 months, whether they continue or stop MTX. It is possible to discontinue MTX in the subset of patients who reach LDA, while it is preferable to continue MTX in those who do not achieve LDA.