Efficacy and Safety of Tocilizumab in Monotherapy, an Anti-Il-6 Receptor Monoclonal Antibody, in Patients with Active Rheumatoid Arthritis: Results from a 24 Week Double-Blind Phase III Study

The efficacy and safety of tocilizumab, an anti-IL-6 receptor monoclonal antibody, was examined as a monotherapy in patients with active RA who had inadequate responses to MTX. In this Japanese study, RA patients previously treated with MTX received either tocilizumab 8 mg/kg every 4 weeks + a MTX placebo (tocilizumab group) or a tocilizumab placebo + MTX 8 mg/week (MTX group) for 24 weeks. Study endpoints included ACR20, 50, and 70 improvement rates, DAS28, EULAR response, and the numeric index of ACR response (ACR-N) area under the curve (AUC) at 24 weeks.

There were 61 patients in the tocilizumab group and 64 patients in the MTX group. After 24 weeks of treatment, ACR20 (80.3% vs 25.0%, $p<0.001$), ACR50 (49.2% vs 10.9%, $p<0.001$), and ACR70 (29.5% vs 6.3%, $p<0.001$) response rates were significantly higher in the tocilizumab group than in the MTX group. Consistent improvements were observed in the EULAR response criteria as well as ACR-N AUC index.

Fewer patients withdrew from the tocilizumab group (n = 7) compared with the MTX group (n = 31) indicating a greater tolerance for tocilizumab. The safety profiles of the two groups were similar. The most common adverse event was nasopharyngitis in both groups (tocilizumab 18.0% and MTX 10.9%).

This study indicates that tocilizumab is an efficacious and safe treatment in RA patients with inadequate response to MTX.

Concomitant Aspirin Use Reduces the Risk of Acute Myocardial Infarction in Users of Cyclooxygenase-2 Selective and Some Non-Selective Non-Steroidal Anti-Inflammatory Drugs

This study examined the ability of concomitant use of aspirin to off-set the risk of acute myocardial infarction (MI) in patients being treated with cyclooxygenase-2 (COX-2) selective and non-selective NSAIDs. The protocol was based on the increased risk of MI reported with the use of these agents. The hypothesis was based on studies that suggest that inhibition of thromboxane by aspirin may reverse the imbalance resulting from selective inhibition of COX-2-mediated prostacyclin formation.

Data was derived from a California Medicaid database of patients diagnosed with OA or RA. Patients were matched as to age, gender, and length of drug exposure. From this database, 15,343 cases of acute MI (8% fatal) were identified. Adjusted risk ratios (95% CI) of acute MI were 1.31 (1.20 - 1.43) with rofecoxib, 1.13 (1.04 – 1.19) with celecoxib, 1.08 (0.97 – 1.19) with ibuprofen, 1.65 (1.27 – 2.15) with indomethacin, 1.52 (1.14 – 2.03) with meloxicam, and 1.47 (1.03 – 2.11) with sulindac. Concomitant use of aspirin reversed MI risk with rofecoxib to 1.03, with celecoxib to 0.88, with meloxicam to 0.53, and with sulindac to 0.77. The risk was partially reversed with indomethacin to 1.21, but unchanged with ibuprofen (1.20).

The authors concluded that COX-2 selective and NSAIDS contribute to an increased risk of MI probably due to the inhibition of prostacyclin formation. This risk can be reduced by concomitant aspirin use. It was suggested that the incomplete reversal of risk with NSAIDS may be due to the pharmacodynamic interference of these NSAIDS with the binding of aspirin to platelet COX-1. It