RISK FACTORS FOR MAJOR ADVERSE CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH THE INTERLEUKIN-6 RECEPTOR INHIBITOR TOCILIZUMAB

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Background: Inflammation plays a key role in modulating cardiovascular (CV) risk. Rheumatoid arthritis (RA) patients treated with the interleukin-6 receptor inhibitor tocilizumab have marked reductions in C-reactive protein but modest increases in lipid parameters. The relative contributions of inflammation and lipids to CV risk in this population have not been fully defined.

Methods: Data were compared from RA patients with (n = 50) and without (n = 3936) major adverse cardiovascular events (MACE) in tocilizumab phase 3 trials. Univariate Cox proportional hazards modeling was used to evaluate MACE risk factors at baseline, after 24 weeks of tocilizumab treatment and changes from baseline to 24 weeks with time to MACE as the time variable; multivariate Cox proportional hazards models were fit to obtain best prediction of time to MACE.

Results: Univariate modeling showed baseline age, prior cardiac disorders, statin use, RA disease activity score (DAS28), total cholesterol/high-density lipoprotein ratio, apolipoprotein-B and apolipoprotein-B/apolipoprotein-A1 ratio as predictive of MACE on tocilizumab. Baseline age, history of prior cardiac disorders, DAS28, and total cholesterol/high-density lipoprotein ratio were robust predictors of MACE in multivariate modeling. Post-treatment decreases in inflammation markers and lipid increases up to week 24 did not predict future MACE. However, higher levels of RA disease activity measures: swollen joints (hazard ratio [HR] [95% CI]=1.092 [1.051-1.136], p<0.0001) and DAS28 (HR=1.351 [1.118, 1.633], p=0.0018) at week 24 were associated with increased risk of future MACE.

Conclusion: Baseline traditional CV risk factors (age and lipid/atherogenic indices) as well as RA disease activity measures are predictive of MACE in RA patients on tocilizumab. Lipid increases observed on tocilizumab therapy do not appear to confer increased CV risk, whereas reductions in RA disease activity lowered CV risk. Taken together, these data suggest that efforts aimed at aggressive screening and treatment of traditional CV risk factors combined with lowering of RA disease activity may be a means of lowering risk of MACE in this population.