Liver Enzymes Elevated With Two RA Biologics

BY SHERRY BOSCHERT

SAN FRANCISCO — Patients being treated for rheumatoid arthritis with infliximab or adalimumab—but not etanercept—were more likely to have elevated levels of liver enzymes, compared with patients on nonbiologic disease-modifying antirheumatic drugs, analyses of data on 6,861 patients found.

Most elevations in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels with any of the treatments were transient, however, and unlikely to lead to discontinuation. Abnormal levels of ALT or AST were rare, Dr. Vibeke Strand and her associates reported in a poster presentation at the annual meeting of the American College of Rheumatology. Elevations were defined as test results above the upper limit of normal, and abnormal levels were results more than double the upper limit of normal.

After researchers controlled for the effects of other factors, the risk of elevated or abnormal liver enzyme levels was 58% higher in 1,449 patients on infliximab (Remicade) and 35% higher in 849 patients on adalimumab (Humira), but no different in 1,383 patients on etanercept (Enbrel), compared with 4,147 patients on oral DMARDs, with or without a tumor necrosis factor (TNF) inhibitor.

The investigators performed six analyses of data from the Consortium of Rheumatology Researchers of North America. Patients with normal transaminase levels at baseline were divided into three cohorts—prevalent TNF inhibitor users, patients initiating TNF inhibitor therapy, and patients on concomitant TNF inhibitor and methotrexate therapy—and their liver enzyme levels were compared with those of nonbiologic DMARD users. The study excluded patients with psoriatic arthritis.

The risk of elevated liver enzyme levels was significantly higher with infliximab in all three cohorts (a 36%-69% increase) and was higher with adalimumab in two cohorts (a 35%-44% increase). The risk of abnormal enzyme levels was significantly higher with infliximab in two cohorts (a 40%-47% increase) and was higher with adalimumab in one cohort (a 32% increase).

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Assuming that enzyme levels normalized in patients for whom there were no follow-up data, 17% of 1,210 elevations persisted at the next visit, and 7% of 143 abnormalities persisted. Among patients with elevated enzyme levels, 4% discontinued a TNF inhibitor and 11% discontinued a nonbiologic DMARD. Among patients with abnormalities found on liver function tests, 6% discontinued a TNF inhibitor and 24% discontinued a DMARD.

"Use of TNF inhibitors does not appear to be associated with clinically meaningful hepatic events in most patients," concluded Dr. Strand of Stanford (Calif.) University. The results suggest that recommendations for monitoring nonbiologic DMARD therapy could safely guide clinicians in deciding when to reduce or discontinue TNF inhibitor therapy based on liver enzyme levels, she added.

Dr. Strand is also a biopharmaceutical consultant and has received consulting fees and other compensation from Amgen (which comarkets etanercept with Wyeth), Abbott (which markets adalimumab), and Centocor (which markets infliximab). Some of her associates in the study were employees of Amgen and others were consultants or speakers for these companies or received research funds from them. Dr. Strand and her coinvestigators also had associations with multiple other pharmaceutical companies.

The cohorts and comparison group had mean ages of 56-62 years, and 73%-80% were female. ■