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Risk of Herpes Zoster in Patients with Rheumatoid Arthritis Treated with Anti-TNF-Alpha Agents.

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CONTEXT: The risk of bacterial infection is increased in patients treated with drugs that inhibit tumor necrosis factor alpha (TNF-alpha). Little is known about the reactivation of latent viral infections during treatment with TNF-alpha inhibitors.

OBJECTIVE: To investigate whether TNF-alpha inhibitors together as a class, or separately as either monoclonal anti-TNF-alpha antibodies (adalimumab, infliximab) or a fusion protein (etanercept), are related to higher rates of herpes zoster in patients with rheumatoid arthritis.

DESIGN, SETTING, AND PATIENTS: Patients were enrolled in the German biologics register RABBIT, a prospective cohort, between May 2001 and December 2006 at the initiation of treatment with infliximab, etanercept, adalimumab, or anakinra, or when they changed conventional disease-modifying antirheumatic drug (DMARD). Treatment, clinical status, and adverse events were assessed by rheumatologists at fixed points during follow-up. MAIN

OUTCOME MEASURES: Hazard ratio (HR) of herpes zoster episodes following anti-TNF-alpha treatment. Study aims were to detect a clinically significant difference (HR, 2.0) between TNF-alpha inhibitors as a class compared with DMARDs and to detect an HR of at least 2.5 for each of 2 types of TNF-alpha inhibitors, the monoclonal antibodies or the fusion protein, compared with conventional DMARDs.

RESULTS: Among 5040 patients receiving TNF-alpha inhibitors or conventional DMARDs, 86 episodes of herpes zoster occurred in 82 patients. Thirty-nine occurrences could be attributed to treatment with anti-TNF-alpha antibodies, 23 to etanercept, and 24 to conventional DMARDs. The crude incidence rate per 1000 patient-years was 11.1 (95% confidence interval [CI], 7.9-15.1) for the monoclonal antibodies, 8.9 (95% CI, 5.6-13.3) for etanercept, and 5.6 (95% CI, 3.6-8.3) for conventional DMARDs. Adjusted for age, rheumatoid arthritis severity, and glucocorticoid use, a significantly increased risk was observed for treatment with the monoclonal antibodies (HR, 1.82 [95% CI, 1.05-3.15]), although this risk was lower than the threshold for clinical significance. No significant associations were found for etanercept use (HR, 1.36 [95% CI, 0.73-2.55]) or for anti-TNF-alpha treatment (HR, 1.63 [95% CI, 0.97-2.74]) as a class.

CONCLUSION: Treatment with monoclonal anti-TNF-alpha antibodies may be associated with increased risk of herpes zoster, but this requires further study.