Biologic therapy for rheumatoid arthritis not significantly linked with increased malignancy risk

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Although there are concerns regarding the potential development of malignancies in patients with rheumatoid arthritis who are receiving treatment with biologic response modifiers (BRMs), pooled results from more than 60 randomized controlled trials did not find a statistically significant increased risk of any type of cancer with use of BRMs for at least 6 months compared with traditional disease-modifying antirheumatic drugs or with placebo, according to the results of a meta-analysis published in the September 5 issue of *JAMA*.

"Rheumatoid arthritis (RA) is a systemic inflammatory polyarthritis that can lead to significant morbidity, joint deformity, and impaired quality of life and affects approximately 1 percent of the general population. Treatment with traditional disease-modifying antirheumatic drugs (DMARDs) reduces disease activity, retards joint destruction, and improves patients' quality of life. However, in many patients with active disease, traditional DMARDs fail or are not tolerated. Biologic response modifiers provide clinically important improvement in patients not responding to traditional DMARDs by targeting specific immune pathways, reducing inflammation, and leading to better control of symptoms and structural damage. In 2010, published data from European and U.S. registries reported that 25 percent to 56 percent of patients with RA used BRMs," according to background information in the article.

The authors add that because these biologic agents interfere with the immune system, concerns exist regarding their safety, specifically with respect to infections and malignancies. "Since 2005, conflicting data have existed associating tumor necrosis factor (TNF) inhibitors with an increased risk of developing certain types of malignancies."

Maria A. Lopez-Olivo, M.D., Ph.D., of the University of Texas MD Anderson Cancer Center, Houston, and colleagues conducted a study to evaluate the risk of developing any type of malignancy in patients with RA receiving treatment with BRMs. The authors searched the medical literature to identify randomized controlled trials that included the BRMs abatacept, adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab, and tocilizumab. Studies were selected that compared the safety of any BRMs used in RA patients with placebo and/or any traditional DMARDs with a minimum of 24 weeks of follow-up.

The researchers identified 63 RCTs with 29,423 patients for inclusion in the analysis. No statistically significant increased risk of developing malignancy was observed. Of the 29,423 patients, 211 developed a malignancy during the trial (0.72 percent): 23 of 3,615 patients in the BRM monotherapy group (0.64 percent), 123 of 15,989 patients in the BRM combination therapy group (0.77 percent), and 65 of 9,819 patients in the control group (0.66 percent).

"Of the 211 malignancies, 118 were solid tumors (i.e., adrenal, bladder, breast, cholangiocarcinoma, fibrosarcoma, gastrointestinal, hepatic, leiomyosarcoma, liposarcoma, lung, ovarian, pancreatic, prostate, renal, testicular, thyroid, tongue, uterine), 48 were skin cancers (i.e., basal cell, squamous cell, and 4 melanomas), 14 were lymphomas, 26 were not specified, and 5 were hematologic nonlymphoma (i.e., multiple myeloma, leukemia)," the authors write.

No statistically significant risk was observed for specific cancer sites. Anakinra plus methotrexate showed lower odds compared with methotrexate alone.

"Overall, our findings do not support an increased risk of malignancy for patients with RA receiving BRMs in RCTs of at least 24 weeks' duration. Additional systematic reviews of observational studies are needed to establish risk in the longer term. Although the findings suggest that BRMs may be generally safe with respect to risk of malignancy in the short term, the risk of recurrence in patients with RA with history of cancer or cancer risk factors remains unknown," the authors conclude.

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