Update
2/1/2009: RISKS OF MALIGNANCY AND SERIOUS INFECTIONS WITH BIOLOGIC TREATMENTS FOR RHEUMATOID ARTHRITIS

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Related To: Chapter 94, Rheumatoid Arthritis

Biologic approaches to treatment of rheumatoid arthritis have greatly improved care of this disease over the past decade, providing a quality of life for many patients that was not achievable with older agents. However, as drugs such as infliximab and etanercept came into general use, clinicians began to see an increase in the number of patients with certain types of cancers and in the frequency of serious infections among those with rheumatoid arthritis. This recognition has led to much research into the relationship among rheumatoid arthritis, treatment with biologic agents, and the occurrence of cancers and serious infections.

A recently published article reviews the literature on this topic. Hudson and Suissa, writing in *Future Rheumatology*,[1] provide an excellent assessment of current knowledge about the risks of infection and malignancy with therapies for rheumatoid arthritis. Based on their assessment that these risks are very difficult to quantify and attribute to drug therapy, the authors make these bottom-line recommendations:

- Prescribers should stay informed about this topic as research progresses and keep mindful the great benefits of therapy as compared with the small chance of malignancy or serious infections
- The patient should be an active partner in the decision-making process, especially when the best course of action is uncertain.
- As evidence accumulates about these medications and their effects on the body, no one perfect study will answer all the concerns. Instead, several rigorous trials performed in diverse populations will be needed to address the complex questions incrementally.

Compared with the general population, patients with rheumatoid arthritis have a higher frequency of malignancies and serious infections, even with no drug therapy, the authors explain. This complicates the determination of whether medications further increase this risk, and currently available data are inconsistent as to whether patients develop malignancies during therapy with newer biologic agents. Complicating the picture even more is the knowledge that patients with more severe rheumatoid arthritis symptoms are more likely to be given these agents and treated with higher doses of the drugs. Thus, patients with more severe disease—who may also be at greater risk of disease-produced malignancy—are also more likely to receive the newer agents, especially the anti-tumor necrosis factor (anti-TNF) agents such as infliximab. Thus, when malignancy does occur, sorting out whether the drug or the disease is causative or whether susceptible patients have been channeled to drug therapy can be a very difficult process.

The same set of problems applies to the occurrence of serious infections. Some studies have shown no increase in infections with use of biologic agents, while others have indicated that this risk doubles when these drugs are used. Channeling bias may again be in play. For one infectious disease—tuberculosis—risks are increased in those treated with anti-TNF agents. Still though, the absolute risks are small: 7 per 100,000 patient-years with etanercept and 53 per 100,000 patient–years with infliximab.

Hudson and Suissa noted in conclusion the real need for more data but also the difficulties with obtaining reliable estimates of risk with this disease and these drugs. They added that several of the newer biologic agents work through different mechanisms of action, making it necessary for researchers to design studies in a way that permits meaningful analysis. Further, they added that other biologic agents are in the pipeline that counteract rheumatoid arthritis through still other mechanisms. These include CD20 and interleukin-6 antagonists. The authors concluded: “Obtaining better estimates of uncommon risks with anti-TNF drugs in [rheumatoid arthritis] will be challenging, although pharmacoepidemiologic studies using large administrative databases, patient registries and postmarketing surveillance systems have the potential to produce important information on safety outcomes with these new drugs.”

REFERENCE

1. Hudson M, Suissa S. Perspective on the risks of infection and malignancy with rheumatoid arthritis therapy. Future Rheumatol. 2008;3(5):445–449.