



## PIC QUESTION OF THE WEEK: 08/01/05

**Q:** A 62-year-old woman with a history of breast cancer and rheumatoid arthritis is now a candidate for treatment with a TNF blocker. What are the risks of malignancy related to such therapy in this woman?

**A:** The labeling of all tumor necrosis factor (TNF) antagonists contains a general warning regarding the potential risk of lymphoma and malignancy associated with their use. Data varies among the drugs and one must consider that the risk for lymphoma is influenced by the disease being treated. For example, patients with rheumatoid arthritis, Crohn's disease, and psoriasis, especially those with highly active disease, are at greater risk of developing lymphoma than the general population. Although absolute numbers were small, patients with rheumatoid arthritis or Crohn's disease treated with infliximab (Remicade®) during clinical trials had a five-fold higher rate of lymphoma than the general population. Twenty three other patients developed non-cutaneous (breast, colorectal, melanoma) malignancies; however, this number was similar to what was expected in the general population. In post-marketing studies, malignancies such as non-Hodgkin's lymphoma and Hodgkin's disease have been reported with infliximab. Pre-marketing trials identified a three-fold increase in the rate of lymphoma in patients treated with etanercept (Enbrel®). The number and type of common malignancies such as breast, colon, lung, and prostate cancer were similar to that observed in the general population. Reports of lymphoma during clinical trials of adalimumab (Humira®) were five-fold higher than expected in the general population. There do not appear to be any published studies on the risk of using TNF antagonists in patients with a history of malignancy or those who continue treatment with TNF antagonists after diagnosis of malignancy. A relatively recent evaluation of published studies on the topic concludes that there is a small, but real risk of developing non-Hodgkin's lymphoma when using TNF blockers. A Swedish study also concluded that these agents may be associated with an increased risk of lymphoma, but there was no evidence they enhanced overall tumor risk. Even though the exact risk of developing lymphoma or other malignancies secondary to use of TNF blockers has not been established, this complication of treatment must always be considered.

### References:

- Sandborn WJ, Loftus EV. Balancing the risks of infliximab in the treatment of inflammatory bowel disease. *Gut* 2004;53:780-2.
- Geborek P, Bladstrom A, Turesson C, et al. Tumour necrosis factor blockers do not increase overall tumour risk in patient with rheumatoid arthritis, but may be associated with an increased risk of lymphomas. *Ann Rheum Dis* 2005;64:699-703.

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