TNF Blocker Risk-Benefit Analysis Proves Favorable

BY BRUCE JANCIN

BUDAPEST, HUNGARY — More than 100 psoriasis patients treated with adalimumab, etanercept, or infliximab experienced marked clinical improvement for every patient who developed a serious adverse event, according to a risk-benefit analysis of the major randomized trials of the tumor necrosis factor antagonists.

In the resultant rank ordering of TNF blockers in terms of efficacy, infliximab came out on top. The number of patients with moderate to severe chronic plaque psoriasis who needed to be treated (NNT) with infliximab instead of placebo in order for one additional patient to achieve at least a 75% reduction in their Psoriasis Area and Severity Index (PASI 75) score was 1.4, Dr. Stephen J. Rozzo said at the annual meeting of the European Society for Dermatological Research.

The NNT for a PASI 75 with adalimumab at 40 mg every other week was 1.6. Etanercept brought up the rear in terms of efficacy, with a NNT of 2.3 when dosed at 50 mg twice weekly and 3.2 with 50 mg once weekly. Infliximab was dosed at 5 mg/kg at weeks 0, 2, and 6, and then every 8 weeks.

If the efficacy data from the trials and their open-label extensions are viewed from another angle, 74% of infliximab-treated patients achieved PASI 75, as did 64% on adalimumab, 44% on twice-weekly etanercept, and 31% on once-weekly etanercept, according to Dr. Rozzo of Abbott Laboratories in Abbott Park, Ill.

The safety analysis was more complex. No agent had a consistently better safety profile than did the others, and there was a good deal of overlap in terms of adverse event rates.

"There was no consistent pattern to these rates," according to Dr. Rozzo.

As a generalization, however, the numbers needed to harm (NNH) were more than 100-fold greater than the NNTs for all three TNF antagonists.

Infliximab had the highest associated risk of nonmelanoma skin cancer, with an NNH of 99 for this end point in the placebo-controlled trials. In contrast, the NNH for nonmelanoma skin cancer was 270 with once-weekly etanercept, 324 with twice-weekly etanercept, and 470 with adalimumab.

As a generalization, the numbers needed to harm were more than 100-fold greater than the numbers needed to treat for adalimumab, etanercept, and infliximab.

The NNH for one additional serious infectious adverse event was 99 for infliximab, 148 for once-weekly etanercept, 183 for twice-weekly etanercept, and 291 for adalimumab, he said.

There were no cases of tuberculosis, other opportunistic infections, or demyelinating disorders for any of the TNF antagonists during the placebo-controlled portion of the clinical trials.

The long-term safety analysis was based upon nearly 7,400 psoriasis patients who were exposed to one of the TNF antagonists for an average duration of almost 11 months. This analysis concluded that the risk of serious infections was 0.015 cases per patient-year of exposure to adalimumab, 0.014 per patient-year for various dosages of etanercept, and 0.018 per patient-year for infliximab. The risk of nonmelanoma skin cancer was 0.007 per patient-year for adalimumab, 0.010 per patient-year for etanercept, and 0.017 per patient-year for infliximab.

Mean baseline body weights of participants ranged from 88.9 kg to 92.7 kg, suggesting a high prevalence of obesity.

Dr. Rozzo indicated that the NNTs and NNHs generated in this evidence-based assessment need to be taken with a grain of salt, as they were obtained from clinical trials that did not involve head-to-head comparisons among biologics. Moreover, the duration of the placebo-controlled portions varied from study to study. For these reasons, he did not perform any tests of statistical significance for the differences in results. The assessment was sponsored by Abbott. ■

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