No Boost From Infliximab
Prendisone from page 1

At that time point, there was no significant difference between the infliximab and placebo groups in proportion of relapse-free subjects, at 35% and 56%, respectively, Dr. Hoff- man said. There also was no difference between groups in the proportion of patients who were able to taper to 10 mg of prednisone per day, or in mean cumulative dose of prednisone, which was 3,051 mg in the infliximab group and 3,117 mg in the placebo group. Moreover, there were no differences between days to first re- lapse, with a median of 97 days in the infliximab group and 85 days in the placebo group. Accordingly, the study was stopped at 34 weeks rather than at the planned 54-week point, he said.

Safety also was monitored throughout. No severe adverse events were seen, and infections were limited to the upper respiratory tract. This experience would lead me to believe that although TNF is found in abundance in the biopsies of patients with GCA, there must be other pathways and mediators that play even more important roles in the pathogenesis,” he said. The study was sponsored by Cen- tococ, and Dr. Hoffman disclosed that he has received research grants and consulting fees from the company.

Etanercept Ups Cancer Risk In Wegener’s Granulomatosis

San Diego — Adding etanercept to standard immunosuppressive treatment in Wegener’s granulomatosis does not increase efficacy and may increase the risks for developing solid tumors, according to Dr. John H. Stone.

Most patients with Wegener’s granulo- matosis achieve remission if treated with glucocorticoids and cyclophosphamide, but flares are common, adverse effects are troublesome, and no successful long-term maintenance reg- imen as yet exists. Moreover, the use of cyclophosphamide car- ries with it a risk of cancer induction, and patients with this vasculitis already are at elevated risk for malignancy.

The Wegener’s Granulomatosis Etanercept Trial (WGET) was a randomized study comparing standard treatment plus the TNF-α inhibitors etanercept, 25 mg twice weekly, or placebo in 180 patients from eight centers. Standard treatment in the trial consisted of glucocorticoids plus cyclophosphamide for patients with severe disease, and glucocorticoids plus methotrexate for those with limited dis- ease.

Cyclophosphamide was given in doses of 2 mg/kg per day, adjusted for renal dysfunction. Patients who reached remission in 3-6 months could be switched to methotrexate or, if their creatinine was elevated, to azathioprine, Dr. Stone said.

Methotrexate was given in doses up to 25 mg/week, continued for 12 months after remission was achieved, and then tapered at a rate of 2.5 mg/month.

Azathioprine, used in only a small number of patients, was given in doses of 2 mg/kg per day. This was decreased by 25 mg/month after 12 months of remission.

“There were no differences at all in any of the major efficacy parameters, including sus- tained remission,” Dr. Stone said at the annual meeting of the American College of Rheumatology.

Only 49.4% of patients in the combined groups achieved and maintained disease re- mission throughout the trial, he said.

But there was one important difference be- tween the etanercept and placebo groups: During the trial’s 2-year follow-up period, there were six solid malignancies, all in the etanercept group, said Dr. Stone of the Johns Hop- kins Vasculitis Center, Baltimore, who chaired WGET.

There were two cases of colon cancer, one in a patient initially ran- domized to placebo, and a second severe flare. This patient was subsequently treated with infliximab for 14 months and was diagnosed with disseminated renal cell carcinoma.

The third was a cholangiocarcinoma in a pa- tient in the placebo group who had not received any cyclophosphamide during the trial.

“Flares per person-year were 1.40 for OC users and 1.44 for placebo patients.

Serious adverse events requiring hospitalization occurred in 15 pa- tients on OCs and 13 placebo pa- tients.

Thrombosis occurred in two OC users and three women on placebo.

Two OC users had abnormal liver function tests, and one developed hypertension.

None of these events occurred among women on placebo.

Seven women on OCs had to dis- continue treatment, and 12 women on placebo withdrew from the study (N. Engl. J. Med. 2005;353:2550-8).

In an accompanying editorial, Dr. Bonnie L. Bermas of Brigham and Women’s Hospital in Boston com- mented that the study “supports the use of combined oral contracep- tives by those with inactive or mod- erately active, stable disease.”


Oral Contraceptives Safe in Women With Stable SLE

By Martha Kerr

O
right oral contraceptive does not increase the number or sever- ity of flares of inactive or mild, sta- ble systemic lupus erythematosus, according to investigators with the Safety of Estrogens in Lupus Ery- thematosus—National Assessment (SELENA): Oral Contraceptives tri- al.

Dr. Michelle Petri, of Johns Hop- kins University, Baltimore, and her associates randomized 183 women with inactive (76%) or stable active (24%) disease to receive either place- bo or an oral contraceptive (OC).

The OC regimen used involved a 35-mcg triphasic ethinyl estradiol plus norethindrone 0.5-1.0 mg for 12 weeks rather than at the planned 54-week point, he said.

Safety also was monitored throughout. No severe adverse events were seen, and infections were limited to the upper respiratory tract. This experience would lead me to believe that although TNF is found in abundance in the biopsies of patients with GCA, there must be other pathways and mediators that play even more important roles in the pathogenesis,” he said. The study was sponsored by Cen- tococ, and Dr. Hoffman disclosed that he has received research grants and consulting fees from the company.

Using the database from WGET, which was unlocked when the database was unlocked.

Also important was the fact that the data were collected in the context of a clinical tri- al. “We know that postmarketing studies are very good at detecting rare events but not so good at detecting events that are common. Most of these cancers, such as those of the colon and breast, are very common, so the likeli- hood of detecting them in any setting other than a clinical trial would be quite small,” he said.

The lack of efficacy and the heightened risk of malignancy seen in the trial also have po- tential implications for the use of other TNF blocking agents in Wegener’s granulomatosis;

In rheumatoid vasculitis, where patients might have received etanercept previously and now require cyclophosphamide; and in patients with systemic lupus erythematosus, many of whom have been previously treated with cy- clophosphamide and may be being given an anti-TNF drug, he said.

Ongoing follow-up from WGET, which was funded by the National Institutes of Health, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, is underway. Dr. Stone stated that he had no financial con- flicts to disclose.

Data on age- and gender-specific incidence rates for invasive solid malignancies in the Sur- veillance, Epidemiology, and End Results (SEER) Program suggest that a total of 1.92 solid tumors could be expected in this cohort. The standardized incidence ratio in the trial therefore was 1.12, which was highly statisti- cally significant, he said.

Three additional cancers were seen in the 6 months after the study (N. Engl. J. Med. 2005;353:2551-61). One was prostate cancer in a 70-year-old man in the etanercept group; he had not received any cy- clophosphamide during the trial. A second was in a patient initially ran- domized to placebo, who dropped out after a second severe flare. This patient was subsequently treated with infliximab for 14 months and was diagnosed with dis- seminated renal cell carcinoma.

The third was a cholangiocarcinoma in a pa- tient in the placebo group who had not received any cyclophosphamide during the trial.

There were no differences between the groups in terms of the percentage of patients who had received cyclophosphamide before the trial, who had ever used daily cyclophosphamide, in the mean duration of daily cy- clophosphamide therapy, or in the maximum daily cyclophosphamide dose.


Aortic root dilatation and aneurysm formation resulted from giant cell arteritis disease process.