Natalizumab Takes Crohn's Remission Past 2 Years

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BERLIN — Treatment with natalizumab maintained remission in selected patients with severe Crohn's disease for more than 2 years, in an open-label extension study with 87 patients.

"The data show that if a patient [with Crohn's disease] goes into initial remission [on natalizumab treatment], the patient is likely to maintain the remission," often without the need for steroid treatment, Dr. Remo Panaccione said at the 14th United European Gastroenterology Week.

Of the 905 patients with severely active Crohn's disease who entered the study, about 30% achieved and maintained remission over the 27-month study period. But natalizumab's efficacy was greater in the subset of patients who responded initially. In the 87 patients who achieved and maintained remission on natalizumab during the initial 15 months of therapy, 86% remained in remission during the next 12 months of treatment, said Dr. Panaccione, a gastroenterologist at the University of Calgary (Alta.).

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Natalizumab is a humanized monoclonal antibody that inhibits leukocyte adhesion and migration into inflamed tissue. The new study used patients who had been enrolled in the first and second rounds of the International Efficacy of Natalizumab in Active Crohn's Therapy (ENACT) trial, ENACT-1 and ENACT-2. Both studies, as well as the subsequent open-label extension, were sponsored by Biogen Idec and Elan Pharmaceuticals, which produce and market natalizumab (Tysabri).

The drug was off the U.S. market for more than a year, starting in early 2005, because a fatal case of progressive multifocal leukoencephalopathy was linked to its use. But marketing resumed earlier this year with the indication of monotherapy for relapsing multiple sclerosis. Under the revised approval, natalizumab prescribers must first register with Elan.

In the first ENACT study, 56% of Crohn's disease patients responded, and 37% had remission after three doses of 300 mg natalizumab, given by an intravenous infusion every 4 weeks. These rates were slightly above those for the placebo group. The second study began with 339 of the natalizumab-treated patients from the first study who had responded to the drug. They were randomized to placebo or ongoing natalizumab infusions, every 4 weeks, for another 48 weeks.

The primary end point was the rate of a sustained response after 36 weeks of treatment, which was 61% in patients treated with natalizumab and 28% in the placebo group, a statistically significant difference. Remission rates at week 36 were 44% with natalizumab treatment and 26% without, also a significant difference (N. Engl. J. Med. 2005;353:1912-25).

The current study included 87 patients who completed ENACT-2 and were in remission 15 months after they started their natalizumab regimen. After treatment with another six doses over the next 24 weeks, 81 patients (93%) remained in remission. After the next six doses, or 48 weeks after the new study began, 75 patients (86%) remained in remission.

Most of the patients in remission were maintained without treatment with a corticosteroid. The average Crohn's Disease Activity Index score for the 87 patients remained at less than 90. Included in the extended-treatment group were 22 patients who were previously treated with a biologic drug that cut the activity of tumor necrosis factor–α (such as infliximab); 11 of these patients also failed prior treatment with an anti-TNF drug. These subgroups maintained their remission on natalizumab about as well as the overall study group did.

In these 87 patients, the overall safety profile was good. There was an 18% rate of drug-attributable, serious adverse effects, and five patients (6%) stopped treatment because of an adverse effect. The most common adverse effects were nasopharyngeal (21%), headache (20%), and exacerbation of Crohn's disease (15%). Four patients had serious infections. None developed an immune reaction to natalizumab. ■