No PML Seen With Natalizumab Since Summer '06

BY AMY ROTHMAN SCHONFELD
Contributing Writer

CHICAGO — No new cases of progressive multifocal leukoencephalopathy were reported among 36,700 patients with multiple sclerosis treated with natalizumab since the summer of 2006.

Similarly, no drug-related deaths have been reported. And the incidence of adverse events (AEs) has been low, despite the fact that many patients have been using the drug for longer than 1 year to treat multiple sclerosis (MS), said Dr. Carmen M. Bozic, vice president for drug safety at Biogen Idec Inc., which markets natalizumab as Tysabri.

"The TOUCH [prescribing program], TYGRIS [safety study], and pregnancy registry will constitute the largest long-term follow-up undertaken by any sponsor for a single therapy for multiple sclerosis," said Dr. Bozic at the annual meeting of the American Academy of Neurology.

Hepatic events occurred in less than 1/1,000 patients and were mostly reversible, she said. Less than 20% discontinued the drug.

The JC virus (JCV), which lies dormant in about 80% of adults whether they have MS or not, causes PML. When Dr. Bozic examined data from 2,370 MS patients who had undergone JCV testing, 5 had detectable plasma levels of JCV, including 3 from the placebo group.

At the time of the presentation, 2,752 physicians were registered with TOUCH and 17,863 patients were receiving natalizumab. About 18% previously had been treated with natalizumab, with a median of seven infusions. About 5,600 patients were treated for at least 1 year. Four percent were treatment naive, 65% switched from another disease-modifying therapy, 13% switched from other therapies, and a few were "returning quitters."

As of February 2008, about 2,100 patients were enrolled in the TYGRIS study. The incidence of serious adverse events was 2.6%. The most frequent adverse events were hypersensitivity reactions (0.6%) and infections (0.6%), the latter being "garden variety" upper respiratory infections, she said. There were no reports of PML. Two deaths unrelated to treatment were documented.

Thirty-six pregnant patients were enrolled in the pregnancy registry, with 20 ongoing pregnancies. There were no reports of adverse pregnancy outcomes.

A second presentation focused on the experiences of patients with MS who resumed natalizumab after voluntary discontinuation. While the overall incidence of hypersensitivity reactions or infusion reactions was low, the risks were elevated for patients who had only one or two prior infusions, said Dr. Paul W. O'Connor of St. Michael's Hospital, Toronto.

JCV testing of more than 6,000 plasma samples resulted in less than 1% with detectable JCV DNA.

DR. O'CONNOR

Dr. O'Connor scrutinized the records of 1,089 MS patients who had completed natalizumab pivotal clinical trials but stopped and restarted treatment. Of this group, 384 had formerly received placebo and 705 had been treated with natalizumab. All had been treated for about a year and a half, had received a median of seven infusions, and had MS for about 8 years.

Most (87%) had one or more AEs. About 55 (5%) had a serious AE, most commonly an MS relapse (2%). Overall rates of infusion reactions (5%) and hypersensitivity reactions (less than 1%) were low, and there were no opportunistic infections.

When the group was stratified by the number of prior infusions, the risk of infusion reactions or hypersensitivity reactions jumped to 24.1% and 7.4%, respectively, for those who had only one or two previous treatments.

Testing of over 6,000 plasma samples resulted in less than 1% (6/1,089 samples) with detectable JCV DNA, and these findings were not associated with PML, said Dr. O'Connor. Of the six positive samples, five had become JCV positive while on natalizumab and one was positive at baseline and became negative upon retesting.

Dr. Bozic is an employee of Biogen Idec and holds stock options in the company. Dr. O'Connor has received compensation for activities related to Biogen Idec and research support from them. ■