The most recent big news in neuroprotection broke on January 30, 2008, in the form of a report from Allergan, Inc. (Irvine, CA), to business analysts and investors that included this statement:

“(The company) unmasked the second phase 3 clinical trial examining the safety and efficacy of oral memantine as a treatment for glaucoma. Although the study showed that the progression of disease was significantly lower in patients receiving the higher dose of memantine compared to patients receiving the low dose of memantine, there was no significant benefit compared to patients receiving placebo. Therefore, the study failed to meet its primary endpoint and to sufficiently replicate the results of the first phase 3 trial. While additional analyses are ongoing, the company does not believe that these analyses will support an approval of the drug.”

Many were not surprised by the announcement. Unlike the trials of most glaucoma drugs, the primary endpoint in this study was not lowering IOP. Rather, patients were randomized to placebo or memantine and then followed to assess visual field progression. Given the challenges of achieving reproducible visual fields, multiple tests over a long follow-up period were necessary. Unfortunately, there appeared to be no difference in outcome between the two groups.

The news was deeply disappointing. Memantine represented a new and unique class of medications for patients with glaucoma. It initiated a novel search for a neuroprotective agent for the optic nerve. In effect, oral memantine represented glaucoma therapy that did not depend on controlling IOP, and thus it signaled a promising era for our patients. It was one of the few new compounds that patients would read about on the Web and ask to be placed in the study.

When the FDA approved Namenda (memantine HCL; Forest Laboratories, Inc., New York, NY) in October 2003 for moderate-to-severe Alzheimer’s disease, more than a few of my patients requested a prescription for their glaucoma. Namenda was the first in a class of medications known to work on the glutamate pathway.

It is not unusual for a study to fail to meet its objective, but the memantine trial entailed an exceptional investment of time, effort, and financial support. The limited release of information to the business community is also unfortunate, although Allergan has indicated it will release further data as they are analyzed. I hope to see the trial’s results published in a manner that allows the scientific and clinical community to appreciate how neuroprotective agents should be studied.

Our patients needed a memantine. Is neuroprotection dead? Let’s hope not.

For more on memantine and the future of drug therapy, please read the article by Gary D. Novack, PhD, and the interview with James D. Brandt, MD, in this issue of Glaucoma Today.

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