IVIG Stops Alzheimer's in Its Tracks

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VANCOUVER -- Three years of treatment with intravenous immunoglobulin (IVIG, GammaGard) prevented further cognitive decline in patients with Alzheimer's disease, according to a small study presented here.

As measured by multiple standard instruments -- the Alzheimer's Disease Assessment Scale (ADAS-Cog), the Clinical Global Impression of Change (CGIC) index, the Neuropsychiatric Inventory, and others -- the four patients who received the full 36 months of treatment at 0.4 g/kg every 2 weeks showed no decline in scores, reported Norman Relkin, MD, of Weill Cornell Medical College in New York City.

At a press briefing prior to his formal presentation at the Alzheimer's Association International Conference, Relkin said the treatment was "generally well-tolerated" but did cause some adverse effects. None were unusual and most were relatively mild infusion-related reactions such as rashes.

Some were more serious, though. These included a stroke in one patient, presumably related to the viscosity of IVIG, which is known to increase risk of ischemic events.

A phase III study with 390 patients is already nearing completion, with results expected by mid-2013, he said.

The rationale for IVIG in Alzheimer's disease is that it contains antibodies against beta amyloid proteins and it also modulates immune function to reduce inflammation, Relkin explained.

The current report covered a second open-label extension of an earlier placebo-controlled, double-blind trial that initially lasted 6 months, involving 24 patients with mild to moderate Alzheimer's disease (baseline Mini-Mental State Examination scores of 14 to 26).

As a phase II study, it tested multiple doses and schedules. Besides the four patients assigned to 0.4 g/kg every 2 weeks, four patients each received 0.2 g/kg every 2 weeks, 0.4 g/kg every 4 weeks, and 0.8 g/kg every 4 weeks. Eight patients received placebo.

Results from the randomized phase indicated that, in pooled data for all patients assigned to IVIG, the treatment outperformed placebo in the primary outcome measures of ADAS-Cog and CGIC, as well as in other cognitive assessments.

Participants were allowed to receive an additional year of open-label treatment with IVIG. With continued favorable results -- including inhibition of brain atrophy as well as cognitive protection -- a second 18-month extension was offered, with 21 patients accepting. For this second extension, all patients received 0.4 g/kg every 2 weeks, since that appeared to be the most effective regimen in the previous data.

These included all 16 initially receiving IVIG and five of the placebo group.

The second extension essentially confirmed the earlier findings and showed that the benefits last 3 years, Relkin said.

Patients initially assigned to placebo showed continued decline in cognitive function, but there was "a bend in the curve" when they were switched to IVIG, Relkin said, reflecting a slowing in decline.

Pooled data for the 16 patients in the original IVIG groups showed a significant protective effect relative to the initial placebo group. Mean values for ADAS-Cog and CGIC scores indicated some loss of cognitive ability, but it was relatively small.

But the highlight finding, Relkin said, was that 3-year ADAS-Cog and CGIC scores in the four patients who received 0.4 g/kg every 2 weeks throughout the study were the same as at baseline.

Untreated Alzheimer's disease patients in his clinic nearly always show measurable decline in 3 to 6 months, he said.

"If we have a patient who goes out to 18 or 24 months without changing, usually we begin to doubt that they have Alzheimer's disease. If we have two patients like that in our practice, we begin to doubt our own diagnostic prowess," he said.

"To have four patients... all of whom are effectively unchanged after 3 years, is a remarkable result."

Relkin started his press conference talk with the customary presentation disclaimer that he would be discussing the off-label use of an approved product, but then gave it an unusual emphasis.

He noted that the findings were from very few patients, and therefore very preliminary. "It's a very important point because this agent is in limited supply, and the indications for which it is approved, some of them represent disorders in which patients can only survive by getting this particular product. So we don't want to bankrupt the available supplies."

Action Points

This study was published as an abstract and presented at a conference. These data and conclusions should be considered to be preliminary until published in a peer-reviewed journal.

Note that this very small study reports long term stabilization of Alzheimer's disease symptoms with IVIG treatment over a period of 36 months

Primary source: Alzheimer's Association International Conference

Source reference:

Relkin N, et al "Three-year follow-up on the IVIG for Alzheimer's phase II study" *AAIC* 2012; Abstract P3-381.