PARKINSON DISEASE

Mixed results for rasagiline in PD

Rasagiline is a drug that inhibits monoamine oxidase type B and is already in clinical use as a treatment for Parkinson disease (PD). Animal studies suggest that rasagiline might also have neuroprotective effects. However, a rigorous clinical trial to investigate the drug's disease-modifying potential in patients with early-stage PD has produced mixed results. Positive results were obtained for rasagiline at a dose of 1 mg/day, but not at a dose of 2 mg/day. "The positive results in this delayed-start study are consistent with the possibility that the drug has disease-modifying effects, but we have to interpret the results with caution," comments C. Warren Olanow (Mount Sinai School of Medicine, New York, USA), the lead author of the study.

The delayed-start study included 1,176 patients with early PD and employed three end points. The participants in the trial were split into two main treatment and control groups. Rasagiline was administered to the early-start group at a dose of either 1 mg/day or 2 mg/day for a period of 72 weeks. The delayed-start group received placebo for 36 weeks and were then given either dose of the drug

for a further 36 weeks. "To show a positive result, the treatment groups had to meet each of three hierarchical end points: superiority to placebo between weeks 12 and 36, superiority to delayed-start treatment between baseline and week 72, and noninferiority to delayed-start treatment between weeks 48 and 72," explains Olanow.

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Although the dose of 1 mg/day met all three end points of the trial, with patients showing a marked reduction in the deterioration of their symptoms, the difference in the groups between baseline and week 72 for the 2 mg/day dose was not statistically significant. "That the 2 mg/day dose didn't work casts some uncertainty on the primary conclusion, although subgroup analysis suggests this was because the higher dose had greater symptomatic effects that masked our

ability to detect a positive response. In fact when we did a subgroup analysis of just patients with the mildest PD symptoms the results were positive for 2 mg," comments Olanow.

"Finding a treatment that can slow the progression of Parkinson's is a major goal of PD therapeutics and there are several important issues that we would now like to pursue," explains Olanow. A repetition of the study using the 2 mg dose just in patients with only mild PD symptoms is a priority for the researchers. This could be followed by a long-term investigation to see if early treatment with rasagiline reduces long-term cumulative disability.

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