Cognitive Effects of Safinamide in Early Parkinson’s Disease (PD) Patients

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Objective: This study evaluated the cognitive effects of 100 and 200 mg/day doses of safinamide, a new non-DA-agonist that combines selective, reversible MAO-B and glutamate release inhibition, compared to placebo as an add-on therapy in non-fluctuating, early idiopathic PD patients receiving a stable dose of a single DA-agonist.

Background: PD affects several cognitive domains even in patients with early disease. The most severe areas of impairment are reaction time, working memory and executive functions.

Methods: A subset of 151 PD patients performed the CogTest battery as a part of a phase III 24-week randomised placebo controlled trial. The test included Auditory Number Sequencing (ANS), Simple Reaction Time (SRT), and Spatial Working Memory (SWM), Strategic Target Detection (STDT), Tapping Speed (TS), Simple Reaction Time (SRT) and Visual Target Tracking (VTT).

Results: Data were converted to z-scores based on healthy control data from CogTest database. Changes from baseline to endpoint were assessed with repeated measures analysis of variance. CogTest found impairments across several cognitive domains, and in executive function in these patients. At baseline, no patients were cognitively impaired (z-score <-0.5) for more than 1 of the 10 domains. Using LOCF method, statistically significant effects of safinamide were found (vs placebo) for executive function (measured by the ETC test) and working memory indexed by ANS (p<0.001) where a mean difference was found in SWM (p=0.079). Also, cognitive effects were seen as early as 12 weeks after starting safinamide.

Conclusions: Significant deficits in multiple cognitive measures, most notably in executive function, were found in patients with early idiopathic PD on DA-agonists. Improvements in executive function and working memory were observed with safinamide with a trend for improvements in spatial working memory. These data suggest cognitive deficits are prevalent even in treated PD patients. Cognitive impairments are a clinically relevant, yet understudied aspect of PD, which improved with addition of safinamide to a DA-agonist, suggesting safinamide possesses actions beyond DA enhancement. New trials will investigate safinamide cognitive effects.

INTRODUCTION

Parkinson’s disease (PD) is considered a disorder of motor function with a clinical presentation that includes rigidity, tremor, bradykinesia, akinesia, and postural instability. Cognitive impairments, however, are evident in PD with dementia being present in approximately 30% of the cases. Cognitive impairments are most often associated with motor fluctuations and are evident in the early stages of PD. Cognitively impaired PD patients have poor medication adherence, higher healthcare costs, and decreased quality of life. Dementia in PD has been associated with increased mortality and reduced activity levels.

CONCLUSIONS

In this study of PD patients who were on DA-agonists, improvement in cognition was seen in tests of executive function and working memory. Deficits that are central in PD. It is extremely encouraging that in this sample, cognition was carried on a subsample of patients in an exploratory manner but produced these results. It is also noteworthy that these cognitive improvements were seen without any increase in any adverse events compared to placebo.

REFERENCES


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