[323] Overlap of cognitive deficits in Parkinson's (PD) and Alzheimer's (AD) diseases: Potential use of safinamide

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Objective: We performed a comparison of the cognitive domains affected in AD and in early PD patients and also determined the potential benefits of safinamide in treating the cognitive deficits and the activities of daily living(ADL) of AD based on recent results from a trial in early PD patients.
Background: Cognition is impaired in early AD (perceptual speed, executive functioning, episodic and working memory) and early PD (reaction time, working memory and executive function). Comparisons using the same computerized cognitive battery have not been performed.
Methods: The Cogtest database on 225 early AD patients from 3 prospective studies was compared to data from a Phase III double-blind placebo-controlled randomized 24-week trial evaluating safinamide, a selective reversible MAO-B and glutamate inhibitor, as add-on therapy to a single DA-agonist in 151 early PD patients. Auditory Number Sequencing(ANS), Spatial Working Memory(SWM), Strategic Target Detection(STDT), Tapping Speed, Simple Reaction and Choice Reaction Time were chosen. Data from AD and PD patients were converted to z-scores, based on healthy control data from the Cogtest database and expressed in SD units.
Results: Deficits in AD patients compared to controls showed significant decrements (all p values <0.05) of z scores of processing speed (4.5SD), episodic(5SD) and working memory (4SD) and executive function(1SD). At baseline, all PD patients showed cognitive deficits in at least one domain and 50% had deficits in ≥2 domains. The domains affected were verbal working memory (3.5SD), finger tapping (1.5SD), spatial working memory (6.5SD) and executive function (1SD). Safinamide produced statistically significant benefits in executive function (STDT; p=0.037) and working memory (ANS; p=0.035), as well as in ADL(p=0.024).
Conclusions: Using Cogtest, cognitive deficits noted in early PD and AD overlapped in working memory and executive function. AD patients were impaired, in addition, in episodic memory. Safinamide's cognitive improvement in early PD patients on DA-agonists suggests that the mechanism of benefit may be non-dopaminergic. Based on the similarities in PD and AD, data suggest that safinamide may be of use in treating ADL and cognitive deficits of AD.

Date: Tuesday, June 5, 2007
Session Info: Poster Session 1: Parkinson's disease (12:30 PM-2:30 PM)
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Room: Rumeli Hall-Lower Level

[770] 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 anti-PD agent 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 function.
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), Spatial Working Memory (SWM), Strategic Target Detection (STDT), Tapping Speed, Simple Reaction Time and Choice Reaction Time.
Results: Data were converted to z-scores based on healthy control data from the 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 intact, while >50% were impaired in ≥1 of the domains. Using LOCF method, statistically significant effects of safinamide were found (vs placebo) for executive function as measured by the STDT (p=0.037) and working memory indexed by ANS (p=0.035). A trend level 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.

Date: Thursday, June 7, 2007
Session Info: Poster Session 3: Parkinson's disease (12:30 PM-2:30 PM)
Presentation Time: 12:30 PM
Room: Rumeli Hall-Lower Level

[797] Safinamide potentiates the effects of DA-agonists in early stage Parkinson's disease (PD) patients

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Objective: To evaluate the efficacy and safety of safinamide as add-on to a single DA-agonist, compared with a DA-agonist alone, in early stage PD patients.
Background: The benefits of DA-agonist monotherapy in early PD patients are reduced over 2-3 years. Addition of L-dopa, a common practice, leads to motor fluctuations and potentially, dyskinesias. Safinamide, a new anti-PD agent that combines selective and reversible MAO-B and glutamate release inhibition, has shown potential efficacy in potentiating the effects of DA-agonists.
Methods: In this double-blind, placebo-controlled, multinational, 24-week, Phase III study, 270 non-fluctuating PD patients (<5yr duration) on a stable dose of a single DA-agonist, were randomly assigned to receive safinamide (Low Dose: 50-100mg/day, or High Dose: 150-200mg/day) or placebo. Efficacy and safety evaluations were performed regularly.
Results: The proportion of patients receiving each DA-agonist was: ropinirole 45%, pramipexole 20%, carbergoline 7%, other 28%. In the ITT analysis, the mean changes from baseline to endpoint indicated DA-agonists alone were less effective (p<0.05) than the DA-agonist and safinamide Low Dose group; UPDRS-III: -6.0±7.2 vs. –3.6±7.1 and UPDRS-II: -2.2±3.8 vs. -1.2±3.5. The proportion of "responders" at endpoint was also higher in both safinamide groups, whether based on a ≥ 30% improvement in UPDRS-III (High Dose: 54.3%; Low Dose: 50.6%; Placebo: 36.4%) or a score of 1, 2 or 3 on CGI-Change (High Dose: 65.8%; Low Dose: 67.9%; Placebo: 49.4%). Treatment with safinamide also improved cognitive function, as assessed by the Cogtest battery in a subset of patients. A trend for improvement in quality of life was also noted. In general, safinamide was well tolerated with the incidence of most common adverse events being comparable to that of placebo, and no increase in adverse events, abnormal vital signs, laboratory tests or ECG parameters, compared to DA-agonists alone, despite no restriction on dietary tyramine intake.
Conclusions: Safinamide potentiated the effect of a single DA-agonist in early stage PD patients, improving both motor symptoms and ADL. Beneficial effects of safinamide on cognition were also noted and are being investigated in new trials.

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Session Info: Poster Session 3: Parkinson's disease (12:30 PM-2:30 PM)
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