Cognitive Function of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder in a 2-Year Open-Label Study of Lisdexamfetamine Dimesylate.

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Abstract

BACKGROUND:
SPD489-404 was the first 2-year safety study of lisdexamfetamine dimesylate in the treatment of attention-deficit/hyperactivity disorder in children and adolescents. In accordance with advice from the European Medicines Agency, assessment of cognitive function was a predefined safety outcome in SPD489-404.

OBJECTIVE:
The objective of this study was to assess cognitive function over 2 years in study SPD489-404, using the Cambridge Neuropsychological Test Automated Battery (CANTAB).

METHODS:
Participants aged 6-17 years received dose-optimised open-label lisdexamfetamine dimesylate (30, 50 or 70 mg/day) for 104 weeks. Cognition was assessed using four CANTAB tasks; Delayed Matching to Sample (DMS), Spatial Working Memory (SWM), Stop Signal Task (SST) and Reaction Time (RTI). Key and additional variables were pre-specified for each CANTAB task; groupwise mean percentage changes in key variables from baseline of > 5% were considered potentially clinically significant.

RESULTS:
All 314 enrolled participants received lisdexamfetamine dimesylate and were included in the safety population, and 191 (60.8%) completed the study. No potentially clinically significant deteriorations from baseline were observed in any key CANTAB variable over the 2 years of the study. Based on predefined thresholds, potentially clinically significant improvements from baseline were observed at 6 months (DMS median reaction time, mean per cent change, - 6.6%; SWM total between-search errors, - 22.8%; SST stop signal reaction time, -18.9%), and at the last on-treatment assessment (DMS median reaction time, - 6.5%; SWM total between-search errors, - 32.6%; SST stop signal reaction time, - 25.7%).

CONCLUSIONS:
Lisdexamfetamine dimesylate treatment for 2 years was not associated with deterioration of cognitive function in children and adolescents with attention-deficit/hyperactivity disorder. Although improvements in some cognitive measures were observed, lack of a control group makes interpretation of the findings difficult. Further studies of the impact of stimulants on cognition are required. CLINICALTRIALS.

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