INTRODUCTION

- Lisdexamfetamine dimesylate (LDX) is a long-acting psychostimulant for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children and adolescents.
- A 2-year, open-label study of the safety and efficacy of LDX in children and adolescents with ADHD in Europe.
- The European Medicines Agency recommends CANTAB assessments in long-term studies of ADHD medications.
- The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a battery of computer-based cognitive assessments that is sensitive to the cognitive effects of psychoactive drugs and cognitive dysfunction in people with ADHD.

METHODS

- Participants aged 6–17 years with an ADHD diagnosis received dose-optimized, open-label LDX (30, 50 or 70 mg/day) for up to 104 weeks.
- Cognitive function was assessed using CANTAB at baseline (week 0), at 4, 24, 48, 72 and 104 weeks and at open-label treatment period, and at the final study visit.
- The threshold of clinical significance (> 5% change from baseline) was achieved.
- Changes in CANTAB variables were separated into key variables that potentially influenced clinical significance and additional variables that did not meet the threshold.

RESULTS

Study population

- Of 314 enrolled participants, all received at least one dose of LDX (safety population).
- At baseline, participants had a mean (standard deviation) (SD) age of 11.4 (2.86) years, 53.5% were males, and the mean (SD) ADHD Rating Scale IV total score was 41.1 (7.03).

The Cambridge Neuropsychological Test Automated Battery

Delayed Matching to Sample (DMS)

- The key DMS variable of per cent correct remained close to baseline levels throughout the study (Figure 1a), with no potentially clinically significant changes.
- For mean DMS median reaction time on correct trials (Figure 1b), a potentially clinically significant improvement (indicated by a decrease in reaction time) was seen after 6 months, with a 6.6% reduction from baseline. This improvement was maintained throughout the study.
- Improvements in DMS median reaction time were more consistently demonstrated in the key DMS trials than in more difficult trials with longer delays (Figure 2a).

Spatial Working Memory (SWM)

- In the key SWM variable of total between search errors, improvements (indicated by a decrease in reaction time) were observed (Figures 1e and 1f).
- Reaction time remained close to baseline levels throughout the study. No changes were seen in key SWM variables of between search errors or with 0, 4 or 8 tokens.

Stop Signal Reaction Time (SSRT)

- In the key SSRT variable of reaction time SD on go trials, improvements were also observed in the key SSRT variable of median reaction time on correct trials (Figure 2b).

CONCLUSIONS

- This 2-year study provides evidence that LDX treatment is not associated with cognitive impairment in children and adolescents with ADHD.
- The threshold of clinical significance (≥ 5% change from baseline) was exceeded by mean improvements in the following cognitive domains:
  - recognition memory and short-term visual memory (measured by DMS)
  - retention and manipulation of visuospatial information (measured by SWM)
  - response inhibition and mental processing speed (measured by SSRT).

REFERENCES

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