ADHD

[Abstract:0166] ADHD

Maintenance of effect in Attention Deficit Hyperactivity Disorder: what do placebo-controlled randomized withdrawal studies of atomoxetine and stimulants tell us?

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Objectives: Attention Deficit Hyperactivity Disorder (ADHD) persists into adulthood for approximately two thirds of the patient population. There is a limited amount of information available regarding the appropriate duration of treatment. Treatment rates tend to decline from childhood to adulthood, and many patients with ADHD experience a relapse of their symptoms during treatment as well as upon treatment discontinuation. In addition, stimulant and nonstimulant treatments have differences in their efficacy profiles. Published randomized withdrawal studies have examined the maintenance of symptom control in patients with ADHD who respond when active treatment is continued compared to placebo. This analysis is based on published randomized studies and was conducted to better understand the relapse of ADHD symptoms in children, adolescents, and adults after discontinuation of long-term medication treatment.

Methods: This analysis included published randomized withdrawal studies in children with ADHD treated with methylphenidate, lisdexamphetamine, or atomoxetine. Published randomized withdrawal studies conducted in adults with ADHD and treated with methylphenidate modified release, osmotic-release oral system methylphenidate, lisdexamphetamine, or atomoxetine were also included. Relapse data from the atomoxetine studies were re-analyzed using the relapse criteria most commonly used in studies with stimulants (a 50% increase in Conners' Adult ADHD Rating Scales-Investigator Rated: Screening Version total score and a ≥2-point increase in Clinical Global Impressions for Severity score).

Results: For stimulants and atomoxetine, among patients who were responders (6 weeks to 1 year of active treatment), the proportion of patients relapsing was significantly higher with placebo compared to active treatment. This suggests that there was a clinically significant benefit with continued long-term pharmacotherapy. However, the proportion of patients relapsing after discontinuing stimulants appeared to be higher than that observed when discontinuing atomoxetine. Of atomoxetine-treated children, 37.9% met the study-defined primary relapse criteria during the 9 months after discontinuation of active treatment compared with 61.5% treated with methylphenidate during the 2 weeks after discontinuation and 68% treated with lisdexamphetamine during the 6 weeks after discontinuation. In atomoxetine-treated adults, 7.4% met the primary relapse definition during the 25 weeks after discontinuation of active treatment compared with 49.6% treated with methylphenidate modified release during the 6 months after discontinuation and 75% treated with lisdexamphetamine during the 6 weeks after discontinuation.

Conclusion: In children and adults, the rate of relapse was lower when discontinuing atomoxetine compared with stimulants. This may be a consequence of methodological differences, including study design and response/relapse definitions, or it may reflect differences in mechanisms of action and persistence of the medication effect. Continued investigation is needed regarding factors that affect the risk of symptom relapse on discontinuation of pharmacotherapy. This study was funded by Eli Lilly and Company, Indianapolis, IN, USA. Drs Upadhyaya, Adams, Tanaka, Haynes, and Escobar are full-time employees and stock holders of Eli Lilly and Company. Dr Colla has participated in advisory boards, received speaker’s honoraria or participated in Phase 3 studies within the past 3 years with Shire, Eli Lilly, Janssen-Cilag and Novartis.

Keywords: attention deficit hyperactivity disorder, relapse, atomoxetine