Improvements in Symptoms of Attention-Deficit/Hyperactivity Disorder in School-Aged Children With Lisdexamfetamine (NRP104) and Mixed Amphetamine Salts, Extended-Release versus Placebo

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INTRODUCTION

Although clinical experience has demonstrated the efficacy of stimulant therapies in children with ADHD, concerns remain regarding harm, dose, and dosing. Lisdexamfetamine dimesylate (NRP104) was designed as a pharmacologically active prodrug in which the amphetamine is clinically bound to lysine, a naturally occurring amino acid, to produce a metabolite that the pharmacology and pharmacokinetics are analogous to the pharmacologically active d-amphetamine molecule. Additionally, NRP104 delivery is formulated as a prodrug d-amphetamine molecule is gradually released, which may make drug tampering difficult and impractical. LDX was designed to have comparable efficacy and tolerability to currently marketed once-daily extended-release stimulants with reduced potential for abuse, diversion and overdose.

OBJECTIVES

The objective of this phase 2 trial was to evaluate the efficacy and safety of Lisdexamfetamine (NRP104), a prodrug of amphetamine, and Mixed amphetamine Salts, Extended-Release (MAS XR) in children with ADHD compared with placebo.

METHODS

Study Participants

Study participants were boys and girls aged 6 to 12 years at the time of study consent, with a primary diagnosis of ADHD (DSM-IV-TR), combined or predominantly inattentive type. No subject was taking any concomitant medications at baseline.

Study Design

Phase 2, randomized, multicenter, double-blind, parallel-group study, 3-period, crossover study in an attention classroom environment.

1. 3 treatments: LDX (30 mg, 50 mg, or 70 mg), MAS XR (10 mg, 20 mg, or 30 mg), and placebo

2. 3 periods: 1 week screening; 3-week titration to optimal MAS XR dose; 3-week active treatment

3. Each treatment period lasted 3 weeks, and each period was separated by 2 weeks washout

4. There were 2 treatment groups: Cohort A: 1 week of each of LDX (dose comparable to optimal MAS XR dose, and placebo), as follows:

- Cohort A: 1 week each of MAS XR (20 mg, LDX 50 mg, and placebo)
- Cohort A: 1 week each of MAS XR (30 mg, LDX 70 mg, and placebo)
- Cohort A: 1 week each of placebo (LDX 50 mg, MAS XR 30 mg, and placebo)

5. All treatments were administered 1 hour prior to school in the morning.

RESULTS

Primary Efficacy Outcome Measure

LDX (30 mg) resulted in significant improvements in symptoms of ADHD in school-aged children. LDX was statistically superior to placebo for all measures of ADHD symptoms (P < .05).

Secondary Efficacy Outcome Measures