particular need for treatments for inattentive symptoms, which are the most frequently endorsed ADHD symptoms in adults. AKL-T01 (EndeavorRx®) is an FDA-authorized digital therapeutic, currently approved for attention in children ages 8-12 with inattentive or combined-type ADHD and a demonstrated attention issue. This study evaluated the efficacy and safety of AKL-T01 in adults.

Methods. STARS-ADHD-Adults (NCT05183919) was a multicenter, single-arm trial at 14 US sites. Enrolled patients were 18 or older, had a diagnosis of ADHD (combined or inattentive), and demonstrated attentional impairment with a Test of Variables of Attention (TOVA) Attention Comparison Score (ACS) ≤ -1.8. Treatment involved using AKL-T01 at home 25 minutes/day, 5 days/week, for 6 weeks. The primary endpoint was change in TOVA-ACS. Secondary endpoints were changes in the ADHD Rating Scale-IV (ADHD-RS-IV) inattention subscale and total score, and Adult ADHD Quality of Life (AAQoL) total score. Safety, tolerability, and compliance were assessed.

Results. Of 440 participants screened, 221 were enrolled, and 153 (*M* age = 39.9, 70% female; 39% current stimulant use) had sufficient data for analysis. TOVA-ACS significantly improved from baseline to study day 42, *M* change = 6.46, *SD* = 6.95, $t(152) = 11.49$, $p < .0001$. There was significant improvement across all secondary endpoints (*p*s <.0001). In exploratory responder analyses, 36.6% moved into the normative range on TOVA (ACS>0), and 27.1% had ADHD-RS-IV improvement ≥ 30%. The treatment was well-tolerated (5% reported ADEs; none serious), and compliance was high (*M* = 81.1%).

Conclusions. Results support the efficacy of AKL-T01 in adults, and the magnitude of TOVA change in adults was nearly 7x the change reported in pediatric trials. Given the increasing rates of ADHD in adults, the barriers to accessing evidence-based treatments, and the centrality of inattentive symptoms as ADHD patients develop into adulthood, AKL-T01 holds promise as a scalable, targeted treatment for attention in adult ADHD with impacts to real-world symptoms.

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Evaluation of the Efficacy of Viloxazine ER in Children and Adolescents with ADHD Inattentive and Combined Presentations

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Introduction. Studies show stimulant medications are effective for different ADHD presentations (predominantly inattentive [IA], predominantly hyperactive-impulsive [HI] or combined [C]); however, few studies have evaluated nonstimulant efficacy in different ADHD presentations. Viloxazine ER [VLX ER] is a nonstimulant, FDA-approved medication for pediatric (≥6 yrs) and adult ADHD. This post-hoc analysis of 4 double-blind (DB), Phase 3, clinical trials (2 in adolescents [NCT03247517 and NCT03247556], 2 in children [NCT03247530 and NCT03247543]), evaluates VLX ER efficacy by ADHD presentation as derived from ADHD Rating Scale, 5th Edition (ADHD-RS-5) assessments at Baseline.

Methods. Children and adolescents with ADHD and an ADHD-RS-5 Total score ≥ 28 were eligible for enrollment. ADHD presentation was defined as a rating of ≥2 on at least 6 of 9 ADHD-RS-5 inattention items, or hyperactive-impulsive items or both. For each ADHD presentation, the change from Baseline (CFB) in ADHD-RS-5 Total score (primary outcome in each study) was assessed using mixed models for repeated measures (MMRM). Responder rate (secondary outcome), ≥50% reduction from baseline in ADHD-RS-5 Total score, was analyzed using generalized estimating equations (GEE).

Results. Of 1354 subjects [placebo N = 452, VLX ER N = 902], ADHD presentation was assigned as 288 (21.3%) [IA], 1010 (74.5%) [C], 40 (3.0%) [HI], 16 (1.2%) [none of these]. Due to the small sample size of [HI], only the [IA] and [C] results are presented. At Week 6 (pooled data endpoint), ADHD-RS-5 Total scores were significantly improved for VLX ER relative to placebo for both the [IA] and [C] ADHD presentations. LS mean (SE) treatment differences, p-values were: [IA] -3.1 (1.35), p = 0.0219, and [C] 5.8 (0.97), p < 0.0001. Responder rates were also significantly higher for VLX ER: 43.0% [IA] and 42.7% [C] relative to placebo 29.5% [IA] and 25.5 % [C] (p=.0311 and p<.0001).

Conclusions. Viloxazine ER significantly reduced ADHD symptoms in individuals meeting criteria for ADHD [IA] or [C] presentations at Baseline. Limitations include post-hoc methodology, smaller sample sizes of [IA] and [HI] groups, and the ADHD-RS-5 ≥ 28 eligibility requirement, that may favor enrollment of individuals with ADHD [C] over ADHD [IA] or [HI] presentations. Consistency of response during long-term use should be evaluated.

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Centanafadine Sustained Release Is Efficacious in the Treatment of Adult ADHD Across Disease Severities

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