Poster 109

Serdexmethylphenidate/Dexmethylphenidate for Children With Attention-Deficit Hyperactivity Disorder: Reduction in Disorder Severity From a Laboratory Classroom Study

Ann C. Childress,[1] Scott H. Kollins,[2] Andrew C. Barrett,[3] Rene Braeckman,[3] Sven Guenther,[3] Travis C Mickle,[3] Charles Oh,[4] and Matthew N. Brams[5]

[1]Center for Psychiatry and Behavioral Medicine, Las Vegas, NV, USA; [2]Duke University School of Medicine, Durham, NC, USA; [3]KemPharm, Inc, Celebration, FL, USA; [4]Corium Inc, Grand Rapids, MI, USA; and [5]Bayou City Research, Houston, TX, USA

INTRODUCTION

- Serdexmethylphenidate/dexmethylphenidate (SDX/d-MPH; Azstarys®) is a once-daily treatment approved for patients aged ≥6 years with attention-deficit hyperactivity disorder (ADHD).
- SDX/d-MPH contains 70% SDX, a novel prodrug of d-MPH hydrochloride, and 30% d-MPH.
- Efficacy and safety of SDX/d-MPH were reported from a pivotal double-blind, laboratory classroom study of 6–12-year-old children with ADHD.[1]
  - Swanson, Kotkin, Agler, M-Flynn, and Pelham Rating Scale-Combined (SKAMP-C) score was a primary end point, and Conners 3rd Edition-Parent (Conners 3-P) score was an exploratory end point.
    - SKAMP is a 13-item scale (grouped under the subcategories of attention, deportment, quality of work, and compliance) that measures subjective impairment of classroom behaviors in children with ADHD. SKAMP-C score is obtained by summing the rating values for each of the 13 items.[2]
    - Conners 3-P is a 43-item report by parents and caregivers that measures ADHD severity via the evaluation of inattention, hyperactivity/impulsivity, learning problems, executive functioning, aggression, and peer relationships.[3]

OBJECTIVE

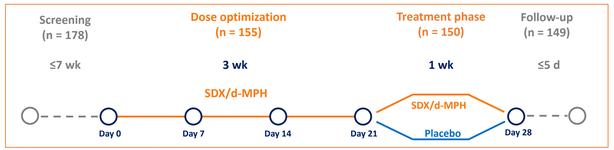
- To evaluate changes in ADHD severity by Conners 3-P in children (aged 6-12 years) with ADHD treated with SDX/d-MPH in a laboratory classroom setting.

METHODS

Study Design

- This was a multicenter, dose-optimized, double-blind, randomized, placebo-controlled, parallel-efficacy laboratory classroom study (NCT03292952).
- During a 3-week open-label, dose-optimization phase, subjects (N = 150) were titrated to a final SDX/d-MPH dose of 26.1/5.2 mg, 39.2/7.8 mg, or 52.3/10.4 mg based on tolerability and best individual response (**Figure 1**).
- During the subsequent 7-day double-blinded treatment period, subjects received once-daily SDX/d-MPH or placebo.

Figure 1. Study design.



SDX/d-MPH, serdexmethylphenidate/dexmethylphenidate.

Assessments

- The primary efficacy end point was mean change from baseline in SKAMP-C scores averaged over the laboratory classroom day (0.5-13 hours after dosing) at the end of the treatment phase.
- The Conners 3-P score, an exploratory end point, assessed weekly changes in ADHD severity during the dose-optimization and treatment phases.

Statistical Analysis

- The differences in SKAMP-C and Conners 3-P score changes from baseline between SDX/d-MPH and placebo at the end of the treatment phase were assessed using a mixed-effect model for repeated measures (significance level of .05).
- The differences in Conners 3-P scores between baseline and each visit of the dose-optimization phase were evaluated using a paired *t*-test.

RESULTS

Subject Demographics

- The subjects' demographics and baseline characteristics are shown in **Table 1**.

Table 1. Subject demographics and baseline characteristics.

Parameter	Subjects (N = 150)
Age, y	9.6 (1.6)
Sex, n (%)	
Male	92 (61.3)
Female	58 (38.7)
Ethnicity, n (%)	
Hispanic or Latino	40 (26.7)
Not Hispanic or Latino	110 (73.3)
Race, n (%)	
White	76 (50.7)
Black/African American	56 (37.3)
Multiracial	10 (6.7)
Asian	7 (4.7)
Other	1 (0.7)
Weight, kg	39.3 (13.8)
Height, cm	140.4 (10.9)
Body mass index, kg/m²	19.5 (4.7)
ADHD-RS-5, overall score	41.8 (7.0)
CGI-S score	4.9 (0.8)

Values shown are mean (SD) unless otherwise noted.
ADHD-RS-5, Attention-Deficit Hyperactivity Disorder Rating Scale-5; CGI-S, Clinical Global Impressions–Severity; SD, standard deviation.

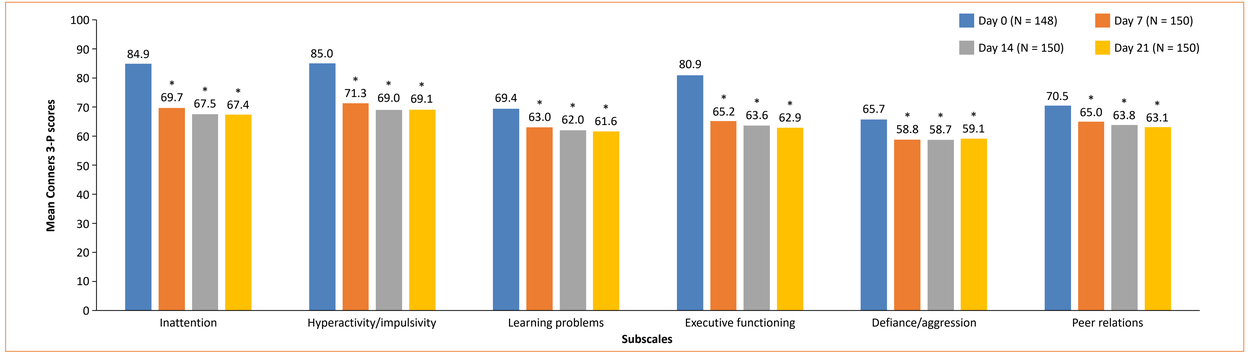
- During the treatment phase, SKAMP-C scores improved significantly with SDX/d-MPH than with placebo (least-squares mean treatment difference [95% CI], −5.4 [−7.1 to −3.7]; *P* < .001), indicating fewer symptoms with SDX/d-MPH treatment than with placebo.
- All mean changes in Conners 3-P scores during the dose-optimization phase as estimated by comparing scores at each visit with baseline scores (day 0) indicated statistically significant improvement in ADHD severity for each subscale at every study visit (*P* < .001; **Figure 2**).
- Least-squares mean changes from baseline (day 0) of Conners 3-P subscale scores for SDX/d-MPH and placebo during the treatment phase are shown in **Figure 3**.
- At the end of the treatment phase (day 28), Conners 3-P scores had significantly improved from baseline to day 28 for SDX/d-MPH versus placebo in the subscales of inattention, hyperactivity/impulsivity, learning problems, and executive functioning (**Table 2**).
  - No statistically significant treatment differences were observed in the subscales of defiance/aggression or peer relations.
- SDX/d-MPH was well tolerated and had no concerning safety signals.[1]

Table 2. LS mean difference between SDX/d-MPH and placebo in Conners 3-P subscale score changes from baseline at day 28 of the treatment phase.

Subscales	SDX/d-MPH vs placebo, LS mean difference (95% CI)	*P* Value
Inattention	−11.2 (−15.7, −6.7)	<.001
Hyperactivity/impulsivity	−9.9 (−14.4, −5.3)	<.001
Learning problems	−5.4 (−8.9, 1.8)	.003
Executive functioning	−9.0 (−13.3, −4.7)	<.001
Defiance/aggression	−4.2 (−8.5, 0.2)	.060
Peer relations	−2.1 (−6.6, 2.5)	.372

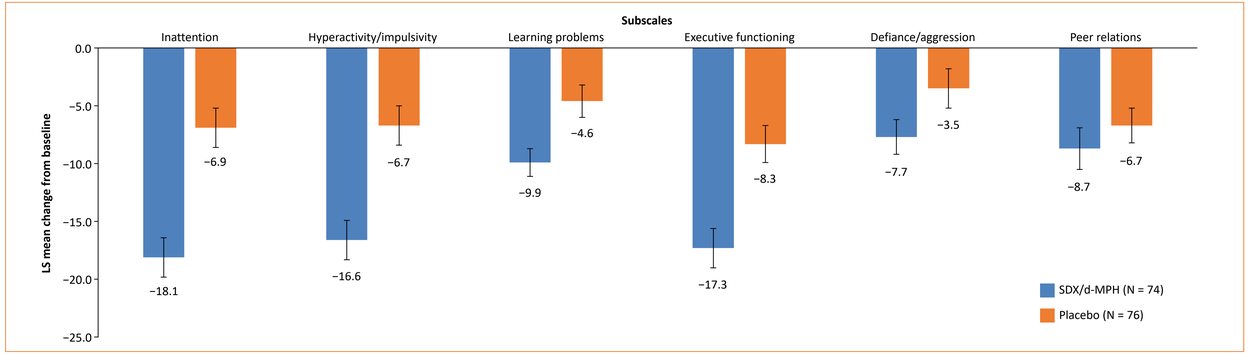
LS, least-squares; Conners 3-P, Conners 3rd Edition-Parent; SDX/d-MPH, serdexmethylphenidate/dexmethylphenidate.

Figure 2. Mean Conners 3-P scores during the open-label dose-optimization phase.



Mean Conners 3-P scores for each subscale were measured at day 0 and at each subsequent visit (days 7, 14, and 21) during the open-label dose-optimization phase with SDX/d-MPH.
Conners 3-P, Conners 3rd Edition-Parent; SDX/d-MPH, serdexmethylphenidate/dexmethylphenidate.
**P <. 001 compared with score at day 0.*

Figure 3. Mean Conners 3-P score changes from baseline during the treatment phase.



Bars are standard errors.
Conners 3-P, Conners 3rd Edition-Parent; LS, least-squares; SDX/d-MPH, serdexmethylphenidate/dexmethylphenidate.

CONCLUSIONS

- SDX/d-MPH demonstrated significant reductions in ADHD severity in 6–12-year-old children, based on the Conners 3-P subscale scores for inattention, hyperactivity/impulsivity, learning problems, and executive functioning.

REFERENCES

1. Kollins SH, et al. *J Child Adolesc Psychopharmacol.* 2021;31(9):597-609.
2. Swanson J, et al. *Psychopharmacol Bull.* 1998;34(1):55-60.
3. Conners CK, et al. Conners 3rd Edition (Conners 3; Conners 2008) In: Encyclopedia of Clinical Neuropsychology. Springer; 2011.

DISCLOSURES

ACC: consultant for Aardvark, Arbor, Attentive, Cingulate, Ironshore, Neos Therapeutics, Otsuka, Purdue, Rhodes, Sunovion, Tris Pharma, KemPharm, Supernus, Jazz, Corium, and Lumos; speaker's bureau for Corium, Takeda (Shire), Arbor, Ironshore, Neos Therapeutics, Tris Pharma, and Supernus; research support from Allergan, Takeda (Shire), Emalex, Pearson, Akili, Arbor, Ironshore, Aevi Genomic Medicine, Neos Therapeutics, Otsuka, Purdue, Sunovion, Tris Pharma, and Supernus; Takeda and its affiliates, Ironshore, and Neos Therapeutics; Takeda (Shire), Neos Therapeutics, Otsuka, Purdue, Rhodes, Sunovion, and Tris Pharma; and advisory boards for Takeda (Shire), Akili, Arbor, Cingulate, Ironshore, Neos Therapeutics, Neuroscience, Otsuka, Purdue, Adlon, Rhodes, Sunovion, Tris Pharma, Supernus, NLS Pharma, and Corium. **SHK:** employee of Holmusk; consultant for and shareholder in Akili Interactive; consulted for Arbor Pharmaceuticals, LLC; Ironshore Pharmaceuticals, Inc; KemPharm, Inc; Otsuka America Pharmaceutical, Inc; Shire; and Tris Pharma, Inc; and research support from Akili Interactive; BehavR; Rose Corporation; KemPharm, Inc; Limbix Health, Inc; Neos Therapeutics; OnDosis AB; Sana Health, Inc; Shire; Tali Health; and Tris Pharma, Inc. **ACB, RB, SG, and TCM:** employees of KemPharm, Inc. **CO:** employee of Corium, Inc. **MNB:** advisor, consultant, or speaker for Allergan; Arbor Pharmaceuticals, LLC; Janssen Global Serves, LLC; H. Lundbeck A/S; OWP Pharmaceuticals, Inc; Neos Therapeutics; Otsuka America Pharmaceuticals, Inc; Shire; Sunovion Pharmaceuticals, Inc; Teva Pharmaceutical Industries Ltd; Tris Pharma, Inc; and Vertical Pharmaceuticals, LLC.

This study was funded by Corium, Grand Rapids, MI, USA.

Medical writing support for the development of this poster, under the direction of the authors, was provided by Gautam Bijur, PhD, with editing support from Mary C. Wiggin, both of Ashfield MedComms, an Inizio company, and funded by Corium, Inc (Grand Rapids, MI, USA).