Marder negative factor (KarXT, -3.8; placebo, -1.8 [LSM difference, -2.0; 95% CI, -2.8 to -1.2; P<0.0001; Cohen's d, 0.42]), and CGI-S scores (KarXT, -1.1; placebo, -0.5 [LSM difference, -0.6; 95% CI, -0.8 to -0.4; P<0.0001; Cohen's d, 0.63]).
Conclusions. In pooled analyses from the EMERGENT trials, KarXT demonstrated statistically significant improvements across efficacy measures with consistent and robust effect sizes. These findings support the potential of KarXT to be first in a new class of medications to treat schizophrenia based on muscarinic receptor agonism and without any direct dopamine D_2 receptor blocking activity.
Funding. Karuna Therapeutics

A Review of the Delivery Technologies used in Attention-Deficit/Hyperactivity Disorder Stimulant Medications

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Introduction. Multiple pharmaceutical technologies have been developed over the years and applied in the Attention-Deficit/Hyperactivity Disorder (ADHD) treatment space. While the base drugs are either the same or similar, these technologies lead to differences in the medications' properties – including mechanism of release, timing of active drug release, and pharmacokinetic profiles. The technology differences also bring up clinical considerations applicable to patients, including delayed- or extended-release properties so that once daily dosing can be achieved.

This review seeks to make side-by-side comparisons of the technical features of the different technologies used in ADHD medications, not an efficacy comparison. The publication will focus on stimulant medications that use methylphenidate or amphetamine formulations. Gaining an understanding of the technologies' properties and their implications will help clinicians to make more informed decisions when developing their patients' treatment plans to fit their individual needs, and potentially improve adherence.
Methods. Sources including published literature, company websites, filed patents, and prescribing information were reviewed to extract data on the technology used for different ADHD medications. The comparison of the technology in ADHD medications included the drug delivery system, mechanism of drug release, and technology components such as use of resins, beads, complexes, coating or layers. Special considerations that come from these properties were elucidated and framed into a broader clinical context.
Results. Although the medications evaluated were all stimulants containing methylphenidate or amphetamine as the active ingredient, they vary significantly in the technology used to deliver medication to patients. Differences in the technologies used to deliver the stimulants are significant and provide the platform to meet individual patient needs. This side-by-side comparison, describing the specific features and benefits of each technology, will better inform prescribers, leading to better treatment of patients' ADHD.
Conclusions. Clarifying the technologies available among ADHD pharmacotherapies and discussing their implications on patient care may help healthcare professionals better understand the treatment landscape and assist them in clinical decision-making for appropriate ADHD treatment. Knowledge of the mechanism of the technology could improve patients' medication adherence. Additionally, understanding the applications of the technology could also benefit research and clinical programs.
Funding. Tris Pharma

Efficacy of Viloxazine ER (Qelbree) for ADHD in Adults Based on Prior Stimulant Exposure

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Introduction. Although many patients respond equally well to both stimulant and nonstimulant medications for ADHD, some patients respond preferentially to one class over another. Currently, most patients receive a stimulant as first-line therapy; however, nonstimulants present fewer obstacles for prescribers and patients and have low abuse/misuse potential. Still, when patients have suboptimal response to stimulants, physicians may be reticent to switch to a nonstimulant medication due to concerns that the nonstimulant response will be less robust or less preferable for patients. Viloxazine ER (viloxazine extended-release capsules; Qelbree®) is a nonstimulant, FDA-approved treatment for ADHD in children (≥6 years) and adults. This post-hoc analysis of adult Phase 3 trial data (NCT04016779) evaluates response to viloxazine ER (200-600 mg/day) based on whether or not patients reported a history of previous stimulant use.
Methods. For patients randomized to viloxazine in this Phase 3, double-blind, placebo-controlled trial, the change from baseline (CFB) in Adult ADHD Investigator Symptom Rating Scale (AISRS) score (primary trial outcome) was analyzed for prior stimulant users vs. nonusers using MMRM. Prior stimulant use was based on patient-reported medication history recorded upon enrollment. Subjects using stimulants at the time of study screening were required to undergo a ≥1-week washout period prior to randomization.
Results. Of 372 patients treated, 189 received viloxazine ER. Of the patients who received viloxazine ER, 40 reported prior stimulant use and 149 did not. Mean (SD) baseline AISRS scores for prior stimulant users and nonusers were 38.5 (7.40) and 38.3

https://doi.org/10.1017/S1092852924001469 Published online by Cambridge University Press

(6.44), respectively. Response appeared similar in both patient groups. At Week 6/End of Study (EOS) the least squares (LS) mean (SE) CFB AISRS scores for prior stimulant users and nonusers were -15.8 (2.51) and -15.6 (1.08)]; treatment difference -0.2 (2.41); P=0.93. Though not significant, prior stimulant users showed a larger magnitude of improvement on the AISRS at early timepoints compared to those without prior stimulant use [Week 1, LS mean (SE) CFB AISRS Total scores: -9.2 (1.40) vs. -6.8 (0.70), respectively; treatment difference: -2.4 (1.56); P=0.12.]
Conclusions. A history of prior stimulant use did not appear to influence the magnitude of ADHD symptom response to viloxazine ER in this preliminary analysis of Phase 3 trial data in adults. Rather, subjects with prior stimulant use showed numerically larger reductions in AISRS scores at early timepoints that were not significantly different from those without prior stimulant use. Additional analysis should be undertaken to evaluate patterns of response in the pediatric population.
Funding. Supernus Pharmaceuticals, Inc.

Do Images in Jackson Pollock's Paintings - Polloglyphs – Arise From His Conscious and Unconscious, Or Are They All in The Viewer's Mind?

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Was Jackson Pollock "Jack the dripper" with paintings "that a dog or cat could have done better," or did Pollock insert Polloglyphs – images that are encrypted that tell a story about Pollock's inner being - into his paintings and then disguise them with drippings? On the one hand, some - especially art critics - have emphasized the formal elements of Pollock's work, arguing that no images are present and the viewer can find whatever they are looking for because such images are artefacts of the "fractal" fuzzy edges to the drippings and are just fooling the eyes. Thus, maybe Pollock's paintings are just a massive set of new Rorschach inkblots to provoke the viewer to project their own emotions onto the painting, whereas there is actually nothing at all in the painting from the artist. On the other hand, from a psychiatric point of view, given that Pollock had bipolar disorder, painted when he was euthymic or manic and not intoxicated nor depressed, had extensive exposure to Rorschach ink blots during his own psychiatric treatment, had visual images and hallucinations of images, clearly incorporated images into his pre-drip paintings (e.g., see Troubled Queen), and used repeatedly the same images in multiple drip paintings (e.g., booze bottles, images of himself, monkeys, clowns, elephants and more), the alternate point of view is that Pollock either consciously or unconsciously encrypted images in his drip paintings. His remarkable ability to do this with Polloglyphs hiding in plain sight may be part of Pollock's creative genius and could have been enhanced by the endowment of extraordinary visual spatial skills that have been described in some bipolar patients. If so, painting could have been Pollock's way to rapidly unspool his images and to do this onto canvas. Pollock himself stated that consciously "I try to stay away from any recognizable image; if it creeps in, I try to do away with it." However, he also admitted "recognizable images are always there in the end." If coming from his deep unconscious creativity and genius, such images may have appeared in spite of himself. Pollock thus may indeed not have been mindful of creating Polloglyphs as he stated "When I am in my painting, I'm not aware of what I am doing." He painted in air, letting gravity make the picture, and dripping became not just another way of obscuring images but as well a new way of creating them. Ultimately, we may never know if there are Polloglyphs present in Jackson Pollock's famous drip paintings, nor can we know for sure whether they are merely in the mind of the beholder or put there consciously or unconsciously by the artist. In the meantime, it can be fun and enlightening to view Pollock's works and decide for yourself.
Funding. No Funding

Viloxazine Extended-Release Capsules in Children and Adolescents with ADHD: Final Results of a Long-Term, Phase 3, Open-Label Extension Study

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Introduction. Viloxazine ER (extended-release capsules; Qelbree®) is a nonstimulant medication, FDA-approved for ADHD in children (≥6 years) and adults. Efficacy and safety for children and adolescents were evaluated in one phase 2 [NCT02633527] and four phase 3 [NCT03247517, NCT03247556, NCT03247530, and NCT03247543], double-blind (DB), placebo-controlled trials that fed into a long-term, open-label extension (OLE) trial [NCT02736656]. Here we report the findings from this OLE trial.
Methods. Participants completing the DB trials were eligible for the OLE. Viloxazine ER was initiated at 100 mg/day (children) or 200 mg/day (adolescents) and adjusted (if needed) over a 12-week Dose-Optimization Period (up to 400 mg/day [children] or 600 mg/day [adolescents]). Maintenance treatment then continued up to 72 months. Safety assessments included adverse events (AEs), clinical laboratory tests, vital signs, ECG (12-lead), and the Columbia Suicide Severity Rating Scale (C-SSRS). Efficacy

https://doi.org/10.1017/S1092852924001469 Published online by Cambridge University Press