Vafidemstat improves aggression scores in Autism: REIMAGINE, third cohort clinical data

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Highlights
- Vafidemstat was safe and well-tolerated in an ASD population
- Vafidemstat produced significant improvements in ASD patients’ agitation and aggression levels

Background
This is the third cohort analyzed in REIMAGINE, a Phase IIa basket trial assessing the effects of vafidemstat, a small, brain penetrant molecule that inhibits histone demethylase LSD1, in aggression as well as other behavioral and psychiatric features in adult population with Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity Disorder (ADHD) and Borderline Personality Disorder (BPD). In previous reports, we have shown that vafidemstat is safe and well tolerated in BPD and ADHD patients, as well as moderate Alzheimer’s patients. Vafidemstat produced significant improvements in aggression and agitation of ADHD and BPD patients, as well as other features of these diseases.

Objectives
REIMAGINE is a Phase IIa open-label study of three psychiatric patient cohorts: ASD, ADHD and BPD (Fig. 1). The aims of this study were to evaluate the safety and tolerability of vafidemstat treatment and assess its efficacy on the treatment of aggression.

Methods
Six patients (age 24 to 44) (Fig. 1) diagnosed with ASD according to DSM-5 criteria have received vafidemstat for eight weeks. REIMAGINE inclusion was based on significant or persistent agitation or aggression that was disruptive to patient’s daily living or put the patient in harm’s way for at least 3 days per week for at least 4 weeks prior to screening visit. Aggression was assessed using the Clinical Global Impression of Severity and Improvement (CGI-S, CGI-I), as well as the Neuropsychiatric Inventory (NPI) 4-item agitation aggression (NPI A/A) subscale. The total NPI score was used to measure global functioning.

Results:
This is the first report of REIMAGINE data from the ASD cohort. Vafidemstat was safe and well-tolerated without significant adverse events (Fig. 2). One ASD patient experienced a transitory event related to hematological alteration, although no clinically relevant modification of the hematological and biochemical parameters tested were observed. No sedation was reported. (Fig. 2). Pharmacokinetic and target engagement results (Fig. 3) are in line with previous data from Phase I and REIMAGINE from the BPD and ADHD cohorts. A significant improvement in CGI-Sverity (CGI-S) and CGI-Improvement (CGI-I) scales was achieved after 2 months treatment with vafidemstat (Fig. 4A). The 4-item agitation/aggression NPI (NPI-A/A) subscale score and the total NPI score evidenced a significant reduction after 2 months of treatment (Fig. 4B). A significant improvement was also observed in the NPI combined score for all other items not related to aggression or agitation.

Conclusions
There are no currently approved treatments that address the core features of ASD, and approved therapies for irritability associated with ASD have unpleasant side-effect profiles. Vafidemstat is a novel therapy that appears to improve aggression and agitation, as well as overall ASD patient functioning, and importantly does not involve sedation or weight gain. Overall, REIMAGINE data support vafidemstat was safe and well tolerated, as well as effective in treating aggression and agitation, as well as non-aggressive features in three distinct psychiatric diseases, with high-unmet medical needs and where current treatments either do not exist or have unfavourable side effect profiles.

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