VAFIDEMSTAT SHOWS EFFICACY IN ALZHEIMER-RELATED AGITATION & AGGRESSION AFTER 12 MONTHS

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OBJECTIVES:

Vafidemstat is a highly brain penetrant LSD1 inhibitor pharmacologically optimized for CNS indications, with demonstrated safety and efficacy in treating agitation and aggression across different psychiatric conditions (REIMAGINE trial). Agitation and aggression are common in Alzheimer's Disease (AD) patients, reducing quality of life for patients and caregivers. Topline 6-month data from the REIMAGINE-AD trial was presented at AAT-ADPD in 2020. The purpose of this poster is to present the 12-month results for those patients consenting to the long-term extension.

METHODS:

REIMAGINE-AD (EudraCT:2019-001436-54) is an open-label, single-centre Phase IIa study which evaluated vafidemstat's efficacy in reducing aggression in moderate/severe AD patients. Inclusion criteria included an MMSE score ≤20 at screening and significant or persistent agitation/aggression. Efficacy was analyzed after 2 and 6 months of treatment, as well as at 12 months for those patients with cognitive improvement at month 6 that consented to the long-term extension (50% of the moderate patients, N=2). The scales used to measure agitation-aggression were CMAI, NPI-A/A subscale and CGI focused on agitation and aggression. Other measures included scales of global patient functioning (NPI), cognition (MMSE) and caregiver burden (ZBI).

HIGHLIGHTS:

- ❖ **Safe and well tolerated**
- ❖ **Significant reduction of agitation/aggression after 6 and 12 months of treatment**
- ❖ **Sustained benefit in cognition after 12 months in a subset of AD patients**

RESULTS:

A total of twelve AD patients were enrolled in REIMAGINE-AD: 4 moderate, 8 severe (see demographics, Table 1). The 6-month data was presented at AAT-AD/PD 2020 highlighting a significant reduction of agitation and aggression, as well as significantly decreased caregiver-burden. This data also showed transient improvement on the MMSE in seven patients by month 2. Although improvement was not maintained in five of these patients, two out of four moderate AD patients' MMSE performance remained improved at month 6 (patients 109 and 111). Therefore, these subjects were offered an opportunity to participate in a long-term 12-month extension.

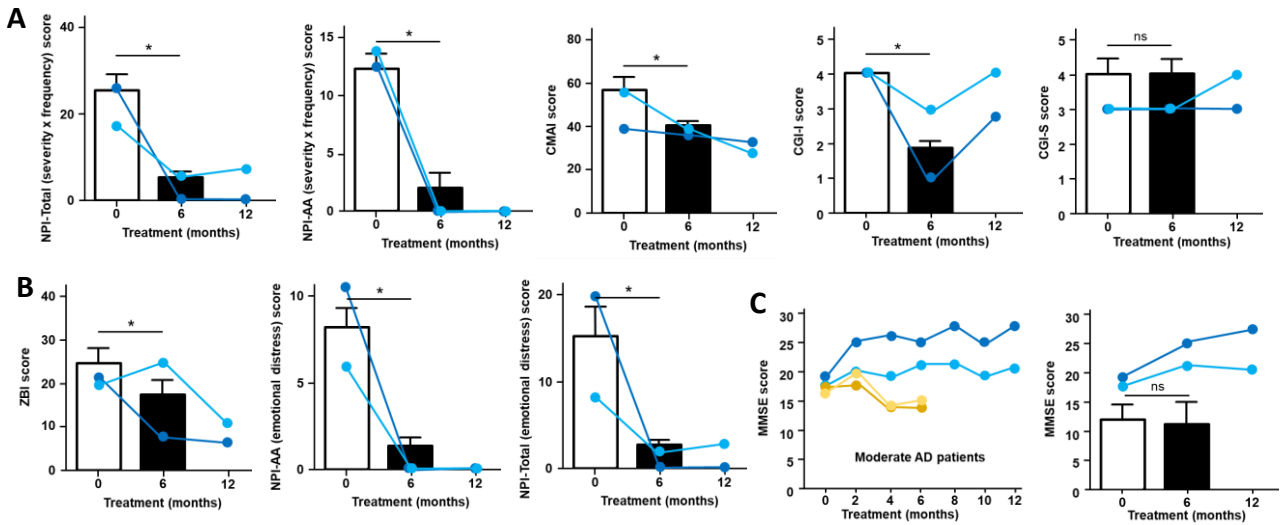

Figure 1. Efficacy evaluation of the effects of vafidemstat on agitation/aggression and global scales (A), caregiver burden (B), and memory/cognition performance (C). Data was analyzed comparing the variation observed after 6 months of vafidemstat treatment versus baseline status using one-tail repeated-measures Wilcoxon signed-rank test. Graphs are represented as mean ± SEM of all patients, plus individual values of patients 109 and 111 are shown in light and dark blue, respectively. Data presented in this poster is preliminary and it will not be final until the clinical study report is issued.

Consistent with the 6-month results, significant improvement in agitation and aggression were maintained at 12 months, measured by NPI-A/A and CMAI (Fig. 1A), and decreased caregiver burden (ZBI and NPI emotional distress scores) (Fig. 1B). As illustrated in Figure 1C Patients 109 and 111 maintained sustained cognitive improvement on the MMSE of 4 to 9 points from baseline by month 12.

No weight gain or other side effects were observed (only transient mild cytopenia in one patient, not requiring any action), and the treatment was safe and very well tolerated through the 12 months.

nº of patients		All patients (N=12)	Patient 109 (light blue)	Patient 111 (dark blue)
Sex	Male Female	5 (41.7%) 7 (58.3%)	0 1	0 1
Age	Median Min / Max	75,00 64/84	80,00	80,00
Race	Caucasian	12 (100%)	1	1
Weight	Median Min / Max	66.0 58.5 / 80.1	58.5	61.5
MMSE	Median Min / Max	9.67 1 / 19	17	19

Table 1. Demographic features of the sample at baseline.

CONCLUSION:

REIMAGINE-AD provided additional support of vafidemstat's safety, as well as efficacy including significant improvement in AD-related agitation and aggression and decreased caregiver burden. The long-term 12-month extension data support vafidemstat's potential as a long-term treatment of AD-related agitation and aggression, as well as provided anecdotal evidence that the drug may improve cognition in a subset of AD patients. Additional investigations are required to confirm this finding.

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