Quantitative analysis of EEG signals in STARS, a Phase 2 safety, tolerability, and exploratory efficacy study of gaboxadol in adolescents and adults with Angelman syndrome

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INTRODUCTION

Angelman syndrome (AS) is a neurodevelopmental disorder with high variable medical and developmental abnormalities. The complex etiology is attributed to deletions, duplications, or rearrangements of chromosome 15q11-13. Gaboxadol (OV101) is a gamma-aminobutyric acid-A receptor agonist that acts extrasynaptically in the brain, which is associated with suppression of tonic inhibition, a presumed pathophysiologic mechanism in AS.

METHODS

The STARS Phase 2 study was a randomized, double-blind, placebo-controlled trial that evaluated safety and tolerability of OV101 at 4 dosage regimens in adolescents and adults with AS. Inclusion criteria were AS diagnosis and severe EEG abnormalities. Gaboxadol was administered for 12 weeks, followed by 1 week of a blinded withdrawal phase. Safety and tolerability, including adverse events and EEG at baseline and week 12, were evaluated.

RESULTS

Demographics

A total of 106 participants (86% completed the study and 73 individuals underwent EEG testing (Table 1)).

Safety and Tolerability

Most adverse effects were mild to moderate. No patients discontinued due to adverse events. Seizures in the treatment group increased by 3.4% from baseline to week 12 (4/34, 11.8%) and in the placebo group increased by 0.2% from baseline to week 12 (1/47, 2.1%).

EEG

Abnormal rhythmicity, as detected by QEEG, improved significantly in the gaboxadol group.

CONCLUSIONS

Gaboxadol was generally safe and well tolerated, particularly in the context of the high prevalence of epilepsy in AS. Additional studies are needed to evaluate clinical efficacy and long-term safety.