Poster
W95

Two Randomized, Double-Blind, Placebo-Controlled Trials of Troriluzole, A Novel Glutamate Modulating Agent, in Obsessive-Compulsive Disorder

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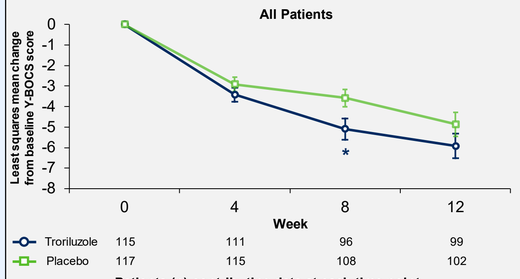
INTRODUCTION

- Few patients with obsessive-compulsive disorder (OCD) experience a complete response to serotonergic and dopaminergic therapies, suggesting other neurochemical systems are involved in OCD pathophysiology.
- Preclinical, clinical, genetic, and neuroimaging studies implicate glutamatergic hyperactivity in the pathogenesis of OCD.[1,2]
- Troriluzole, a novel glutamate modulating agent, may normalize synaptic glutamate levels by increasing expression and function of glutamate transporters and by decreasing presynaptic glutamate release.
- Troriluzole is designed to provide enhanced bioavailability, eliminate the need for fasting, enable once-daily dosing, reduce first-pass metabolism, and minimize hepatotoxicity relative to its active metabolite, riluzole.
- A Phase 2 study of troriluzole in OCD demonstrated consistent treatment benefit at all timepoints. Patients with more severe OCD symptoms at baseline also demonstrated larger treatment effects. These results informed the development of 2 ongoing Phase 3 clinical trials.

Figure 1. Phase 2 Proof-of-Concept Study: Least Squares Mean Change from Baseline in Y-BOCS Score



*The least squares mean change in Y-BOCS score in the primary analysis population was significant at Week 8 ($P = 0.04$) but not significant for the primary endpoint at Week 12 ($P = 0.22$).

OBJECTIVES

- Describe the demographic and baseline characteristics of two Phase 3 clinical trials of troriluzole for OCD

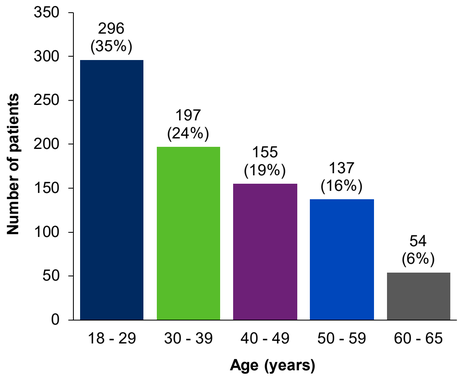
METHODS

- These are two identical Phase 3 randomized, double-blind, placebo-controlled trials (NCT04641143 and NCT04693351) evaluating adjunctive troriluzole 280 mg daily in up to 700 adults for 10 weeks.
- Participants have a history of OCD for ≥1 year with inadequate response to an ongoing standard of care medication, defined as a Yale-Brown Obsessive Compulsive Score (Y-BOCS) ≥ 22 at screening and baseline.
- The primary endpoint is change from baseline in Y-BOCS.
- Preliminary demographics and baseline characteristics were analyzed as of May 2024.

RESULTS

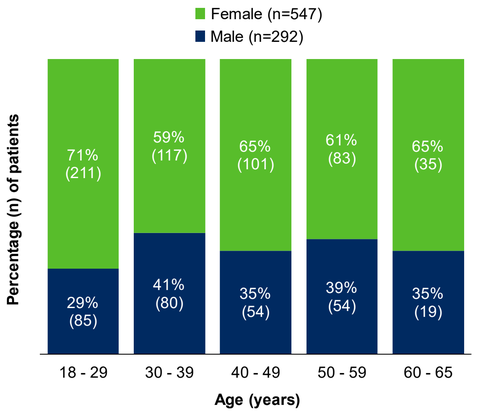
- Demographic data on patients randomized as of May 3, 2024 (N=839) were analyzed
- Patients 18 to 39 years of age comprise 59% of those randomized (Figure 2)

Figure 2. Frequency Distribution by Age Groups



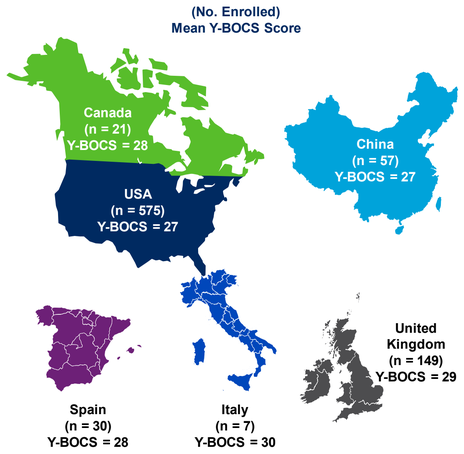
- Most patients (65%) are women (Figure 3)

Figure 3. Age Distribution by Sex



- Most patients (86.3%) are from the USA and the UK (Figure 4)

Figure 4. Geographic Location of Patient Enrollment



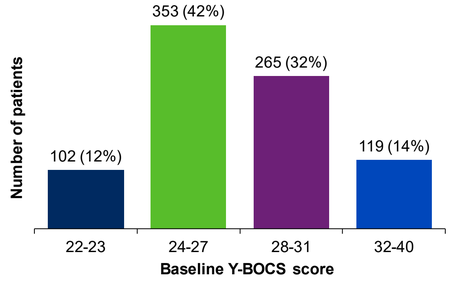
- The most common races in the trial population are White (80.5%), Asian (11.4%) and Black (4.2%) patients (Table 1)

Table 1. Race Distribution Among Patients

Race	n (%)
American Indian or Alaska Native	1 (0.1)
Asian	96 (11.4)
Black or African American	35 (4.2)
Native Hawaiian /Other Pacific Islander	2 (0.2)
Not reported	5 (0.6)
Other	25 (3.0)
White	675 (80.5)

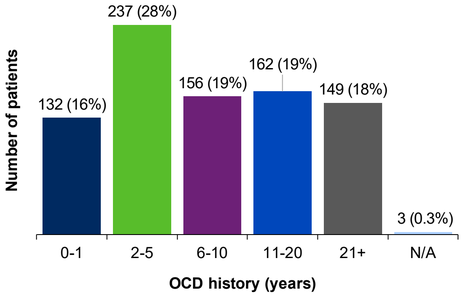
- Distribution of baseline Y-BOCS score is presented in Figure 5. 46% of subjects had a baseline Y-BOCS score ≥28.

Figure 5. Frequency Distribution of Baseline Y-BOCS Scores



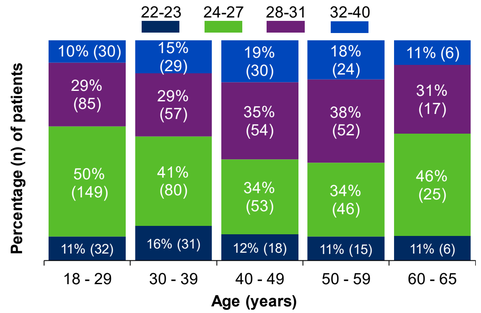
- A majority of patients (63%) reported 10 or fewer years of OCD history (Figure 6); equal percentages (19%) reported 6 to 10 years and 11 to 20 years of OCD history

Figure 6. Frequency Distribution of Reported Years of OCD History



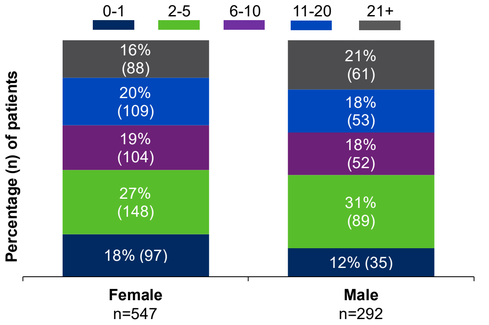
- The most common baseline Y-BOCS score range for patients aged <40 years (YBOCS: 24-27) is lower than for those aged >40 years (YBOCS: 28-31) (Figure 7)

Figure 7. Baseline Y-BOCS Scores by Participant Age



- A greater proportion of females than males reported 6 to 10 years and 11 to 20 years of OCD history (Figure 8)

Figure 8. Reported Years of OCD History by Sex



CONCLUSIONS

- These two Phase 3 clinical trials are evaluating troriluzole in a population with moderate-to-severe OCD symptoms despite standard of care therapy.
- These results underscore the incomplete efficacy of available therapies which are also associated with sexual dysfunction, metabolic syndrome, and extrapyramidal symptoms.
- If troriluzole proves to be safe and efficacious, this will be the first novel mechanism of action in OCD in over 20 years and an important breakthrough for the millions of patients suffering from this disorder.

2024 American Society of Clinical Psychopharmacology Annual Meeting | May 28 – May 31, 2024 | Miami Beach, FL

DISCLOSURES: AM, SK, KG, LD, DS, TM, CJ, IQ, and VC are employed by and hold stock/stock options in Biohaven.

References: 1. Goodman WK et al. *Am J Psychiatry*. 2021;178(1):17-29.
2. Hadi F et al. *BMC Pharmacol Toxicol*. 2021;22(1):69.

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