Group Assignment:
Clinical Study Report Synopsis

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Arizona State University
Edson College of Nursing and Health Innovation

HCR 558: Regulatory Writing
Session A: 14314
Professor Jeanette Ward
February 23, 2025

The Treatment of Children and Adolescent Outpatients with Obsessive-Compulsive Disorder

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Name of Sponsor/Company: **1** **Insert Fictitious Placeholder Name**	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use)*

2	**Name of Finished Product:** NoOCD		
3	**Name of Active Ingredient:** TPAI		
4	**Title of Study:** A 38 Week, Two Phase, Multicenter Study to Investigate the Safety and Effectiveness of NoOCD (10-60 mg/day) in the Treatment of Children and Adolescent Outpatients with Obsessive-Compulsive Disorder		
5	**Study No.:** 29707		
6	**Principal Investigator:** Ethan Caldwell, MD		
7	**Study Centers:** There were 28 study centers planned for this multicenter, two-phase study, however, two centers withdrew prior to enrollment resulting in 26 study centers in the US represented in the analysis.		
8	**Publication (reference):**		
9	**Study period:** ● Study Initiation Date: Jan. 13th, 1997 ● Study Completion Date: Dec. 28th, 1998	**<u>Phase of development:</u>** Phase I: ● A 16 week, open-label phase to evaluate safety and tolerability of NoOCD in both ● children and adolescents diagnosed with OCD. Phase II: ● A 16 week, double-blind, placebo-controlled, randomized phase demonstrating the efficacy of NoOCD in the treatment of OCD in both children and adolescents through the assessment of potential relapse after NoOCD is discontinued in patients and followed by a 5 week NoOCD blinded down titration.	
11	**Objectives:** **Primary:** The primary objective of this study was to evaluate the efficacy of NoOCD in children and adolescent outpatients with OCD who were previously responsive to NoOCD (Phase 1, by assessing the potential for relapse after discontinuation of NoOCD during a 16 week, double-blind, placebo-controlled randomized phase (Phase II).		

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	Secondary: The secondary objective were to establish the clinical effectiveness of NoOCD (10-60 mg/day) in the treatment of children and adolescent outpatients with OCD during a 16 week, open-label phase of the study (Phase I), and to evaluate the safety and tolerability of NoOCD in children and adolescent outpatients with OCD throughout the duration of the study (both open-label and double-blind administration).
12	**Methodology:** **12.1 Study Design:** This multicenter trial assessed the efficacy and safety of an SSRI for OCD in a pediatric population, with a 16-week open-label treatment phase followed by a 16-week double-blind, placebo-controlled phase to determine relapse in patients. **12.2 Study Population and Enrollment:** The study population included children and adolescents aged 8–17 years with a primary diagnosis of OCD, confirmed through structured clinical interviews using the K-SADS-L diagnostic tool. Approximately 375 participants were expected to enroll across 24–26 centers during Phase I, with around 180 participants meeting response criteria to proceed into Phase II. **12.3 Screening Process:** The screening process was conducted one week before the baseline visit. It included obtaining informed consent from parents or legal guardians and assent from participants, verifying the OCD diagnosis, conducting physical examinations, ECG assessments, and laboratory tests, and ensuring compliance with inclusion/exclusion criteria. **12.4 Randomization Structure:** At the end of Phase I, patients demonstrating ≥25% reduction in CY-BOCS total score along with a Clinical Global Impressions-Global Improvement (CGI-I) score of 1 or 2 were randomized (1:1 ratio) into Phase II. Participants were assigned to either continue SSRI treatment or switch to placebo, following a blinded down-titration protocol. **12.5 Visit Schedule:** During Phase I, participants had scheduled evaluations at Weeks 2, 4, 6, 8, 12, and 16. Assessments included the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS), Clinical Global Impressions (CGI), Hamilton Anxiety (HAMA) and Depression (HAMD) Rating Scales, and Yale Global Tic Scale, along with vital signs, laboratory tests, ECGs, and adverse event monitoring. In Phase II, evaluations took place atWeeks 2, 4, 6, 8, 10, 12, and 16, with similar safety and efficacy assessments as in Phase I. **12.6 Medication Administration:** The study drug was administered according to a structured dosing regimen. In Phase I, participants received 10–60 mg/day of the SSRI, beginning at 10 mg/day, with dose increments of 10 mg based on clinical response and tolerability. In Phase II, participants randomized to the SSRI group remained at their final Phase I dose, whereas those assigned to the placebo group underwent a blinded down-titration of 10 mg per week. **12.7 Taper End Visit:** Patients who completed the study or withdrew early followed a gradual tapering schedule of 10 mg per week. At the end-of-taper visit, investigators conducted a physical examination, vital sign assessments, weight measurement, adverse event review, and follow-up laboratory tests or ECGs, if necessary. **12.8 Final Visit Procedures:** At the end of each phase or upon early withdrawal, a final visit was conducted, which included a full physical examination, assessment of vital signs, weight measurement, adverse event evaluation, and laboratory or ECG follow-up if clinically indicated. This ensured the collection of comprehensive safety and efficacy data before study completion.

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Number of Subjects Planned:

Phase	Planned	Enrolled	Analyzed	Case	Controls
Phase I	375	375	300	N/A	N/A
Phase II	194	193	193	98	95

A total of 423 patients were screened, with 88 excluded prior to the open-label phase. In Phase I (open-label), 335 patients participated. For Phase II (double-blind), 194 were eligible, but only 193 were analyzed due to one dropout. The Phase II population included 193 patients, with 95 in the treatment group (NoOCD) and 98 in the placebo group. Patient randomization at each center varied from 0 to 18.

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Ethics:
The study was conducted in line with Good Clinical Practices, relevant regulations, and the Declaration of Helsinki as amended in October 1996 in Somerset West, South Africa. An Institutional Review Board (or Ethics Committee) approved the protocol and informed consent before starting at each center. Written consent was obtained from the patient's parent or legal guardian, along with the patient's agreement to participate, before joining the study. Each patient's data was recorded using specific case report forms.

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Diagnosis and Main Criteria for Inclusion:
This study included children and adolescents aged 8 to 17 who were diagnosed with obsessive-compulsive disorder (OCD) according to the DSM-IV criteria (DSM-IV, 300.30). To participate, written consent from a parent or guardian and agreement from the patient were required. Participants had to be between 8 and 17 years old, meet the DSM-IV criteria for OCD as determined by the K-SADS-L interview, and score 16 or higher on the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) during the screening and baseline phases. Additionally, they needed to have a documented OCD history of at least 3 months and be medically healthy based on a physical exam, medical history, and lab tests.

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Test Product, Dose, and Mode of Administration:
Reference Therapy, Dose, and Mode of Administration:

- **Study Drug:**
  - Supplied/Packaged: Phase I - packed in bottles and Phase II - packed in foil-backed blister.
  - Dispensed at a time: Phase I - 100 tables per pack and Phase II - 60 tablets per pack.
  - Form: White, film coated modified oval tablet
  - Dose: 10 mg, and adjustable dosages of 10–60 mg daily
  - Administration: a single dose daily
  - Batch No: U96157 / (X10-6B10)
- **Reference Therapy (Placebos):**
  - Form: White, film coated modified oval tablet
  - Dose: 10 mg

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	○ Batch No: U96161 / (X9-6B10PL)			
	Drug	**Appearance**	**Dose**	**Batch/(Lot) Numbers**
17	Study Drug	White, film coated modified oval tablet	10 mg	U96157 / (X10-6B10)
	Placebo	White, film coated modified oval tablet	10 mg	U96161 /(X9-6B10PL)
	Duration of Treatment: Each person will participate in the trial for a total of 38 weeks, which includes a screening and taper phase, as well as 16 weeks in Phase I (Open-Label) and 16 weeks in Phase II (Double-Blind, Placebo-Controlled).			
18	**Phase I reference therapy:** N/A **Phase I dose and mode of administration:** 10 - 60 mg/day, oral **Phase I batch number:** U96157 / (X10-6B10)		**Phase II reference therapy:** Placebo **Phase II dose and mode of administration:** 10 - 60 mg/day, oral **Phase II batch number:** U96161 /(X9-6B10PL)	
19	**Criteria for Evaluation:** **Efficacy Criteria:** Efficacy was determined by clinical response and the decrease of OCD symptoms are examined during therapy. ● Primary Endpoints: ○ Patient Who Relapse: Worsening of CGI Global Improvement Score by 1 point for two consecutive visits, by ≥2 points at any visit, or reaching a score of 5 or greater. ○ Dose at Relapse: In both treatment groups, the majority of relapsing patients (19/33 [58%] NoOCD, 25/43 [58%] placebo) were on lower doses (10-30 mg), with NoOCD relapse rates by baseline dose are as follows: 10 mg (1/9), 20 mg (10/20), 30 mg (8/26), 40 mg (5/16), 50 mg (3/10), and 60 mg (6/14), observed in the Per Protocol Population. ○ Patients Who Relapse by Age Subgroup: In the < 12 years age group, the relapse rate was higher in the placebo group (55.3%) compared to the treatment group (36.7%), which showed a meaningful difference of 18.6% that was near statistical significance (p=0.099). ● Secondary Endpoints: ○ Time to Relapse: The analysis showed no significant difference in relapse rates between the treatment and placebo groups, although the placebo group had a higher relapse rate, with most patients withdrawing due to lack of efficacy by Week 4. ○ Percentage of Patients With a CGI Global Improvement Item Score of 1 (Very Much Improved) or 2 (Much Improved) During the Double-Blind Phase (ITT) ○ Average change in CY-BOCS total score from the initial baseline ○ Average change in the obsessive subscale score of CY-BOCS from the initial baseline ○ Average change in the compulsive subscale score of CY-BOCS from the initial baseline ○ Percentage of patients with a 25% or greater reduction in CY-BOCS total score from the initial baseline ○ Change from baseline in the CGI severity of illness rating			

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	○ Initial and changed CGI severity of illness scores during Phase II of the randomized treatment ○ Average change in HAM-A total score from the initial baseline ○ Average change in HAM-D total score from the initial baseline ○ Mean total tic scores on the Yale Global Tic Severity Scale ○ Average change from the baseline in GAF total score
20	**Safety Criteria:** The evaluation of safety was assessed by monitoring examine results, adverse events, and vital signs over the course of the trial. ● Extent of Exposure: Percentage of Patients Exposed by Total Duration of Overall Exposure (Open-Label + Double-Blind) ● Common Adverse Experiences: Number and percentage of patients with adverse experiences (≥ 5%) by body system and treatment. Most common experiences reported (> 10%) by age group (< 12 years, ≥ 12 years) and study phase. ● Adverse Experiences By Age Subgroup: Adverse Experiences Most Frequently Reported (> 10%) by Study Phase and Age Subgroup (<12 years, ≥ 12 years). ● Withdrawal Due to Adverse Events: Summary of patients discontinuing treatment due to adverse experiences. ○ Adverse events that cause treatment to end by age subgroup ● Taper Phase Adverse Experiences: Overview of adverse experiences during the taper phase reported by at least two patients, sorted by body system and treatment. ● Deaths: No deaths were reported during the trial or within 30 days after the last dose. ● Serious Adverse Experiences: Number and percentage of patients with serious adverse experiences. ● ECG Results: Percentage of patients with ECG changes from screening. ● Vital Signs: Percentage of patients with potentially concerning vital sign measurements and mean changes from baseline. ○ Weight and Vital Sign Changes by Treatment Mean (±SD) from Baseline at Each Visit ● Laboratory Tests: Percentage of patients with potentially concerning laboratory values at any time during the study.
21	**Safety and Efficacy Results** **Disposition:** A total of 423 participants were screened, with 84 participants excluded for failing to meet the entrance criteria which left 335 eligible participants for the open-label phase. These patients were enrolled in 26 study centers, with recruitment numbers ranging from one to 32 patients. Among the 335 patients enrolled, 194 (57.9%) advanced to Phase II and were randomized into one of two study arms. One participant was excluded after the randomization phase, resulting in a population of 193 (95 in the drug group, 98 in the placebo group) for the end of Phase II. The number of participants randomized from site to site varied from zero to 18.
22	**Demographics and Baseline Characteristics:** The demographic, baseline characteristics, and efficacy parameters of the study population are summarized in Table 1. The data include key demographic details, baseline clinical scores, and illness severity distributions at both the Open-Label and Double-Blind Baselines.

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	The mean age of participants was approximately 12 years, with a range from 6 to 18 years. The population was evenly divided between children (<12 years: 49.9%) and adolescents (≥12 years: 50.1%). The majority of participants were male (59.1%) and predominantly Caucasian (92%). At Open-Label Baseline, the CY-BOCS mean total score was 26.3, consistent with moderate to severe OCD symptomatology. The GAF score was 54.1, reflective of moderate functional impairment. The HAM-D and HAM-A scores were 6.6 and 8.3, respectively, indicating mild levels of depressive and anxiety symptoms. The CGI Severity of Illness Scores highlighted that 98% of patients at the Open-Label Baseline were rated as at least "Moderately Ill," with 54% classified as "Markedly Ill," "Severely Ill," or "Most Severely Ill." Similar distributions were observed across groups in the Double-Blind Phase, with no significant differences. **Table 1: Demographic, Baseline Characteristics, and Efficacy Parameters**

Characteristic	Open-Label Study Drug (N=335)	Double-Blind Study Drug (N=95)	Double Blinded Placebo (N=98)
Age (years, mean ± SD)	11.8 ± 2.72	11.8 ± 2.56	11.6 ± 2.88
Age Range (years)	6 - 18	7 - 17	6 - 18
Age < 12 years (%)	49.9%	51.6%	48.0%
Age ≥ 12 years (%)	50.1%	48.4%	52.0%
Gender (N, %)			
- Female	137 (40.9%)	48 (50.5%)	40 (40.8%)
- Male	198 (59.1%)	47 (49.5%)	58 (59.2%)
Race (N, %)			
- Black	7 (2.1%)	1 (1.1%)	2 (2.0%)
- Caucasian	308 (91.9%)	87 (91.6%)	89 (90.8%)
- Asian	4 (1.2%)	1 (1.1%)	3 (3.1%)
- Other	16 (4.8%)	6 (6.3%)	4 (4.1%)

23	**Efficacy Results:** This section presents the efficacy outcomes from both the Open-Label Phase (Phase I) and Double-Blind Phase (Phase II) of the study. Results are organized by primary and secondary endpoints, with detailed findings for each pre-specified efficacy criterion.

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Table 1. The Number of Patients comprising the Populations for Analysis of Efficacy in Each Phase

Study Phase	Open-Label (NoOCD) (Phase I)	Double-Blind Phase	
		NoOCD	Placebo
Screening Only	423	---	---
Entered Study Phase	339	96	98
ITT Population	335	95	98
Per Protocol Population	---	81	83

Of 423 screened patients, 335 qualified for the open-label Phase I ITT population, with 193 patients (95 NoOCD, 98 placebo) continuing to the Phase II double-blind ITT population. The Per Protocol population consisted of 164 patients (81 NoOCD, 83 placebo) after excluding 29 patients with major protocol violations.

Open-Label Efficacy Results

Analysis of open-label Phase I efficacy data demonstrated robust treatment response across multiple measures.

CGI Global Improvement: At study endpoint, 73.3% of patients met CGI Global Improvement response criteria (score of 1 or 2), with 87.4% of Week 16 completers being responders and 48.1% rated as "very much improved."

CY-BOCS Response: At study endpoint, 78.4% of patients achieved ≥25% reduction in CY-BOCS total score, with a mean reduction of 13.0 points and 90.8% of Week 16 completers meeting response criteria.

Combined Response Criteria: At study endpoint, 68.7% of patients met both CGI and CY-BOCS response criteria, with 86.2% of Week 16 completers meeting both criteria.

Additional Efficacy Measures: Additional efficacy measures at Week 16 showed improvements from baseline in CGI Severity (71.5% rated mild or better vs 1.8% at baseline), HAM-A (-4.4 points), HAM-D (-3.1 points), GAF (+13.4 points), and Yale Global Tic Score (2.5 to 1.7).

Primary Efficacy Endpoint

The primary objective was to evaluate NoOCD's efficacy in preventing relapse after discontinuation in patients who previously responded to treatment. Relapse was defined as worsening of CGI Global Improvement Score by 1 point for two consecutive visits, by ≥2 points at any visit, or reaching a score of 5 or greater.

1. Proportion of Patients Who Relapse During Phase II

The primary objective of demonstrating superiority of NoOCD over placebo in preventing relapse during Phase II was not met, despite numerical differences favoring NoOCD. The analysis of relapse rates during the double-blind phase showed that in the ITT population, 34.7% (33/95) of NoOCD patients relapsed compared to 43.9% (43/98) of placebo patients (Odds Ratio = 0.62, 95% CI: 0.34-1.16, p=0.136). In the

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Per Protocol population, 32.1% (26/81) of NoOCD patients relapsed compared to 43.4% (36/83) of placebo patients (Odds Ratio = 0.59, 95% CI: 0.30-1.17, p=0.133).

Table 2. Percentage (%) of Relapsers* Based on CGI Global Improvement Item

Double-Blind

Analysis	NoOCD (N= 95)		Placebo (N= 98)		Pairwise Comparisons Odds Ratio /CI/ p-value
	n	%	n	%	
ITT	33	34.7	43	43.9	0.62 0.34-1.16 0.136
Per-Protocol	26	32.1	36	43.4	0.59 0.30-1.17 0.133

Analysis of the primary endpoint showed that while NoOCD had a lower relapse rate (34.7%) compared to placebo (43.9%), this difference did not achieve statistical significance (Odds Ratio=0.62, 95% CI: 0.34-1.16, p=0.136), falling short of the anticipated 60% placebo relapse rate used in study design.

2. Dose at Relapse Analysis of relapse by dose level showed that the majority of relapses (58%) in both NoOCD and placebo groups occurred at lower doses (10-30mg), with the highest relapse rates at 20mg (10/20 patients) and 30mg (8/26 patients) in the NoOCD group.

3. Proportion of Patients Who Relapse by Age Subgroup

Analysis of relapse rates by age subgroup showed that in patients under 12 years, NoOCD had a lower relapse rate (36.7%) compared to placebo (55.3%, p=0.099), while in patients 12 years and older, relapse rates were similar between NoOCD (32.6%) and placebo (33.3%).

Table 3. Percentage (%) of Relapsers* Based on CGI Global Improvement Item by Age Subgroup (ITT)

Double-Blind

Analysis	NoOCD (N= 95)		Placebo (N= 98)		Pairwise Comparisons Odds Ratio /CI/ p-value
	n	%	n	%	
Age < 12 years	18	36.7	27	55.3	0.45 0.18-1.16 0.099

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Age ≥ 12 years	15	32.6	17	33.3	1.07	0.41-2.79	0.883

Analysis of relapse rates by age subgroup showed that in patients under 12 years, NoOCD had a lower relapse rate (36.7%) compared to placebo (55.3%, p=0.099), while in patients 12 years and older, relapse rates were similar between NoOCD (32.6%) and placebo (33.3%, p=0.883).

Secondary Efficacy Endpoints

The secondary efficacy analysis evaluated multiple measures including time to relapse, symptom severity through CY-BOCS scores, global improvement ratings, severity assessments, anxiety and depression measures, tic severity, and functional outcomes during the double-blind phase through 10 key measures.

1. Time to Relapse (CGI Global Improvement Item)

Time to relapse analysis showed a higher relapse rate in the placebo group compared to NoOCD (hazard ratio 1.5, 95% CI: 0.9-2.3, p=0.104), with median time to relapse being longer in the NoOCD group (Q1=35 days) versus placebo (Q1=27 days), and most relapses occurring by Week 4 in both groups.

2. Proportion of Patients Achieving a CGI Global Improvement (Score of 1 or 2)

Analysis of CGI Global Improvement scores showed that a higher proportion of NoOCD patients maintained scores of "Much Improved" or "Very Much Improved" compared to placebo at Week 16 Endpoint (58.7% vs 44.8%) and Week 4 (70% Endpoint) (71.0% vs 59.4%), with the largest differences seen in the "Very Much Improved" category at both timepoints (41.3% vs 22.9% and 45.2% vs 20.8%, respectively).

3. Mean Change From Baseline in CY-BOCS Total Score

Analysis of CY-BOCS scores showed significantly smaller increases from baseline in the NoOCD group compared to placebo at both Week 16 (3.6 vs 6.9, difference -3.38, 95% CI: -5.88,-0.88, p=0.008) and Week 4 (70% endpoint) (2.3 vs 6.3, difference -4.01, 95% CI: -6.30,-1.72, p=0.001).

* Mean Change From Baseline in CY-BOCS Obsessive and Compulsive Subscales

Analysis of CY-BOCS subscales at Week 16 Endpoint showed smaller increases in both obsessive (1.9 vs 4.0) and compulsive (1.7 vs 2.9) symptoms in the NoOCD group compared to placebo, indicating less symptom worsening with active treatment.

***** Proportion of Patients Achieving ≥ 25% Improvement in Baseline CY-BOCS Total Score

Analysis of CY-BOCS Total Score showed significantly higher responder rates in the NoOCD group versus placebo at Week 16 Endpoint (28.9% vs 14.4%, p=0.023, OR=2.41, 95% CI: 1.13-5.13) and Week 4 (70% Endpoint) (26.5% vs 8.9%, p=0.003, OR=3.70, 95% CI: 1.54-8.86).

4. Change From Baseline in CGI Severity of Illness Item

Analysis of CGI Severity scores at Week 16 Endpoint showed that more NoOCD patients had minimal illness severity (No/Borderline illness: 37% vs 25% placebo), while more placebo patients had moderate illness severity (37.5% vs 25% NoOCD), with similar rates of mild and marked/severe illness between groups.

5. Mean Change From Baseline in HAMD Score

Analysis of HAM-D scores showed smaller increases in depression scores in the NoOCD group compared to placebo at both Week 16 Endpoint (1.9 vs 3.1) and Week 4 (70% Endpoint) (1.4 vs 2.3), though differences were not analyzed statistically.

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	6. Mean Change From Baseline in HAMA Score Analysis of HAM-A scores showed smaller increases in anxiety scores in the NoOCD group compared to placebo at both Week 16 Endpoint (1.8 vs 3.1) and Week 4 (70% Endpoint) (1.5 vs 2.4), though differences were not analyzed statistically. **7. The Yale Global Tic Scale - Total Tic Scores** Analysis of Yale Global Tic Scale scores showed consistently lower tic severity in the NoOCD group compared to placebo throughout Phase II, with mean scores at Week 16 Endpoint of 0.8 vs 1.6 and at Week 4 (70% Endpoint) of 0.6 vs 1.5, though differences were not analyzed statistically. **8. Mean Change From Baseline in GAF Score** Analysis of GAF scores showed slightly larger decreases in functional status in the placebo group compared to NoOCD at both Week 16 Endpoint (-8.1 vs -5.8) and Week 4 (70% Endpoint) (-7.2 vs -4.0), though differences were not analyzed statistically.
24	**Safety Results:** This section summarizes the safety findings from both the Open-Label and Double-Blind phases. Most participants used the medication for 12–32 weeks. Headache was the most frequently reported adverse event, with younger patients prone to agitation or hyperkinesia. About 17.6% discontinued due to primarily CNS-related issues, but no deaths were reported, and serious events were rare; often involving emotional or behavioral changes. Lab and ECG findings revealed few concerns, and aside from some weight gain, vital sign changes were minimal. The following sections detail each category of safety outcomes. **1. Extent of Exposure:** The study drug was administered over varying durations, with 43.7% of patients receiving it for 12 to 16 weeks, about 13% for 28 to 32 weeks, and approximately 10% for 4 weeks or less. **2. Adverse Events (AEs):** Adverse events were recorded across study phases. In the Open-Label Phase, headache (24.5%) was the most frequent event, while gastrointestinal issues were more common in the placebo group during the Double-Blind Phase. In the Open-Label Phase, patients under 12 years reported higher rates of agitation (11.4%) and hyperkinesia (14.4%). Conversely, in the Double-Blind Phase, patients aged 12 and older experienced more headache (30–35%) and somnolence, whereas younger patients had increased agitation and neurosis. **3. Adverse Events Leading to Withdrawal:** A total of 59 patients (17.6%) withdrew from the study due to adverse events, primarily CNS-related. In the Open-Label Phase, withdrawals were mainly due to hostility (2.7%), hyperkinesia (2.1%), and agitation (1.8%), while in the Double-Blind Phase, withdrawal rates were higher in the placebo group (10.2%) compared to the treatment group (7.4%). **4. Taper Phase Emergent Adverse Events:** During the taper phase, adverse events were minimal, affecting 20.6% of patients in the Open-Label Phase and 40.9% in the Double-Blind Phase. Headache (9.9%) and nausea (7.0%) were the most common events. No taper-phase adverse events occurred in patients under 12 during the Open-Label Phase, whereas in the Double-Blind Phase, these events were more frequent in patients under 12 (42.1%) compared to those aged 12 and older (26.1%). **5. Deaths:** No deaths were reported during the entire trial, including the 30-day follow-up period after the last dose of the study medication. **6. Serious Adverse Events (SAEs):** Seventeen patients (5.1%) reported serious adverse events, 86.4% of which were CNS-related. Emotional lability (1.5%) was the most frequently reported SAE, with hostility (1.2%) also observed, and one cardiovascular event (extrasystole) recorded during the Open-Label Phase.

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	7. Electrocardiogram (ECG) Results: In the Open-Label Phase, eight patients experienced significant ECG changes—five at Week 8 and three at Week 16—with only one serious event (extrasystoles) reported. No significant ECG changes were observed during the Double-Blind Phase. **8. Vital Signs:** Minimal changes in vital signs were recorded; however, weight gain was notable. In the Open-Label Phase, 8.7% of patients experienced weight gain greater than 7%, while in the Double-Blind Phase, weight gain was observed in 9.6% of the treatment group and 8.2% of the placebo group. Laboratory Tests: Few **9. Laboratory Tests:** Few laboratory abnormalities were of clinical concern. Hematocrit abnormalities were the most common (6.1–8.5%), with low hematocrit reported in 10% of patients in the treatment group during the Double-Blind Phase. Additionally, abnormal alkaline phosphatase levels were observed in 1.9% of patients during the Open-Label Phase.
25	**Conclusions:** According to the results of this two-phase, multicenter, relapse-prevention design study, substantial and supportive evidence show that NoOCD is beneficial in the treatment of children and adolescents with OCD. Although results showed there was no statistically significant difference between NoOCD and the placebo, with respect to the protocol-defined primary measurement of efficacy (the proportion of patients meeting relapse criteria during the double-blind phase), roughly 69%, or three-quarters, of all patients enrolled met the response criteria during the OL phase and the proportion of responders in the double-blind phase (based on CY-BOCS Total Score) was statistically significantly greater in the NoOCD group compared to the placebo group. Safety data generated in both children and adolescents with OCD in this study did not reveal any adverse findings that were unique to this population nor any that would preclude its use in this population.
26	**Date of Report:** February 23, 2025