**Non-Seizure and Seizure Benefits Associated With the Use of Fintepla® (Fenfluramine HCl Oral Solution) in a Subgroup of Dravet Syndrome Patients Participating in a Phase 3 Study: Interim Findings of a Survey of Investigators**

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**INTRODUCTION**

Dravet syndrome (DS) is a rare, treatment-resistant epilepsy syndrome with an age of onset of 1 to 18 months. DS results in developmental delays, behavioral issues, and impairment in cognitive, motor, communication, language, and physical domains. In a recent survey, more than 70% of parents reported substantial concerns and challenges with non-seizure-related outcomes. In a recently completed phase 3 study, clinically meaningful improvement was observed in non-seizure-related outcomes and investigator ratings indicating the fenfluramine (FFA) treatment group relative to placebo (Figure 1). The present study was designed to examine non-seizure outcomes in a subgroup of 34 children and adolescents who were treated with adjunctive FFA for >14 weeks and rated by investigators as “Much Improved” or “Very Much Improved” on the Clinical Global Impression of Improvement (CGI-I) (12% (n=2) to 41% (n=7) of patients showed clinically meaningful improvement in non-seizure-related outcomes; Figure 2).

**OBJECTIVE**

To examine non-seizure outcomes in a subgroup of 34 children and adolescents who were treated with adjunctive FFA for >14 weeks and rated by investigators as “Much Improved” or “Very Much Improved” on the CGI-I during the study.

**METHODS**

Study Design

Patients who received FFA in studies NCT02682927, NCT02826863, and NCT02823145 and were rated by the investigator as being “Much Improved” or “Very Much Improved” on the CGI-I (sensitivity to light, patterns, etc.; learning, speech alertness, motor ability, communication, language, and physical domains) were included in this open-label phase 3 study (n=17). The investigator was contacted via email and asked to complete a short survey for the identified patients (n=12 patients; 71%) (Figure 1). Responses were captured using an electronic data capture system and included an open-ended section for recording clinical observations (Figure 1).

**RESULTS**

Investigators and Patients

- As of November 1, 2017, 17 of 34 surveys had been completed by investigators.
- The 17 patients included in this analysis were from 11 study sites covering 4 countries (Figure 2).
- When asked if their reasoning for rating their patients “Much Improved” or “Very Much Improved” on CGI-I was based on non-seizure improvements only, seizure improvements only, or both, most investigators (82%, n=14) responded “both.” (Figure 3).
- When asked to briefly describe their clinical observations of the patient’s improvements in behavior, speech, cognition, and alertness, variability was noted based on the majority of investigators (91%, n=16) reporting improvements in behavior (Figure 4).

**CONCLUSIONS**

- Both non-seizure- and seizure-related outcomes contributed to the investigators’ ratings of ”Much Improved” or “Very Much Improved” on CGI-I.
- Approximately 25%–40% of the patients in this subset analysis had clinically meaningful improvements in cognition, behavior, speech, and alertness.
- FFA may be an important new treatment option for DS to effectively manage seizure and non-seizure outcomes and improve patient quality of life.

**REFERENCES**


**DISCLOSURES**

All authors enrolled patients in NCT02682927, NCT02826863, and/or NCT02823145. This study was funded by Zogenix, Inc. (Emeryville, CA, USA). Medical writing and editorial assistance were provided by Rachel Anantha, **

**ACKNOWLEDGMENTS**

All authors contributed to the design, execution, and analysis of this study and are responsible for the content of the manuscript. They all have approved the final version of the manuscript. **

**Figure 1. Investigator Survey**

**Figure 2. Distribution of Non-Seizure- and Seizure-Related Outcomes Contributing to Investigator Ratings of “Much Improved” or “Very Much Improved”**

**Figure 3. Primary Drivers for Investigator Ratings of “Much Improved” or “Very Much Improved” on CGI-I**

**Figure 4. Relative Contribution of Non-Seizure- and Seizure-Related Outcomes When Both Were Drivers for Investigator Ratings of “Much Improved” or “Very Much Improved” (n=15)**

**Figure 5. Investigator Global Ratings of Non-Seizure and Seizure Outcomes*”

*No investigator noted “Very Much Worse” for any outcomes.

**Table 1. Clinical Observations of Improvements in Non-Seizure-Related Outcomes After FFA Treatment**

<table>
<thead>
<tr>
<th>Non–Seizure-Related Outcome</th>
<th>% of Patients (N=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure Frequency</td>
<td>50%</td>
</tr>
<tr>
<td>Cognition</td>
<td>60%</td>
</tr>
<tr>
<td>Behavior</td>
<td>100%</td>
</tr>
<tr>
<td>Communication</td>
<td>100%</td>
</tr>
<tr>
<td>Language</td>
<td>41%</td>
</tr>
<tr>
<td>Motor Ability</td>
<td>41%</td>
</tr>
<tr>
<td>Sensitivity to Light, etc.</td>
<td>12%</td>
</tr>
<tr>
<td>Motor Ability</td>
<td>41%</td>
</tr>
<tr>
<td>Communication</td>
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<td>41%</td>
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</tbody>
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**Figure 6. CGI-I After FFA Treatment**

- Between 12% (n=2) and 41% (n=7) of patients showed clinically meaningful improvement in non-seizure-related outcomes except motor ability (Figure 4).
- One patient (6%) showed a rating of “Much Worse” for behavior.

**Presented as part of the Zogenix Scientific Exhibit during the American Epilepsy Society (AES) Annual Meeting, November 30–December 4, 2018, New Orleans, LA**