Fintepla® (Fenfluramine HCl Oral Solution) Reduces Convulsive Seizure Frequency in Dravet Syndrome Patients Receiving an Antiepileptic Drug Treatment Regimen Containing Stiripentol: A Phase 3, Randomized, Placebo-Controlled Clinical Study

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INTRODUCTION

Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy (Incidence: 1:20,000 births) that presents in the first 1-18 months of life with frequent, treatment-refractory convulsive seizures. This study showed that fenfluramine (FFA) significantly reduced mean monthly convulsive seizure frequency ([MCSF]) - Patients receiving stiripentol (STP) were not included in this study.

- The mean percent change from baseline in reduction in MCSF was 34.9% for the FFA 0.5 mg/kg/day treatment group.
- The odds of experiencing a clinically meaningful (≥50%) and profound reduction in MCSF ([≥65%]) vs placebo were 23.7 times higher in the FFA 0.5 mg/kg/day group than in the placebo group.

Efficacy

- Primary efficacy endpoint: Reduction in mean MCSF in FFA treatment group vs placebo.

OBSERVATIONS

Figure 1. Study Design

Figure 2. Primary Efficacy Endpoint: Reduction in Mean MCSF in FFA Treatment Group vs Placebo

Table 1. Patient Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo</th>
<th>FFA 0.5 mg/kg/day</th>
<th>FFA 0.2 mg/kg/day</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>19 (44)</td>
<td>12 (27.9)</td>
<td>7 (16)</td>
<td>16 (35)</td>
</tr>
<tr>
<td>Age, years, mean±SD</td>
<td>43±11</td>
<td>42±11</td>
<td>43±11</td>
<td>42±11</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>19.1±4.9</td>
<td>18±4.9</td>
<td>18±4.9</td>
<td>18±4.9</td>
</tr>
<tr>
<td>Age group &lt;6 years, n (%)</td>
<td>23 (53.5)</td>
<td>27 (63.1)</td>
<td>26 (60.5)</td>
<td>24 (52)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>11 (25.6)</td>
<td>9 (21.4)</td>
<td>8 (19)</td>
<td>8 (17)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>22 (52)</td>
<td>21 (50)</td>
<td>17 (41)</td>
<td>19 (41)</td>
</tr>
</tbody>
</table>

RESULTS

Figure 3. Cumulative Response Curves for Percent Reduction in Mean MCSF from Baseline

Figure 4. Seizure Freedom

Figure 5. Median Percent Reduction from Baseline in Convulsive Seizures

Figure 6. Median Percent Change in MCSF Over Time

Figure 7. Clinical Global Impression (CGI)

Table 2. Mean MCSF at Baseline Across Treatment Groups

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Mean MCSF at Baseline</th>
</tr>
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<tbody>
<tr>
<td>Placebo</td>
<td>5±2</td>
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<tr>
<td>FFA 0.5 mg/kg/day</td>
<td>4.9±2.9</td>
</tr>
<tr>
<td>FFA 0.2 mg/kg/day</td>
<td>5.2±2.8</td>
</tr>
</tbody>
</table>

Efficacy

- Primary efficacy endpoint: FFA versus placebo on the change in MCSF from baseline to combined titration and maintenance periods (T+M).

RESULTS

Figure 8. Reduction in Mean Convulsive Seizures (MCSF)

Figure 9. Convulsive Seizure Frequency per 28 Days

Figure 10. Baseline Comparison of Convulsive Seizures Per 28 Days

Figure 11. Change in Convulsive Seizures per 28 Days

Figure 12. Combined titration and maintenance period; FFA 0.8 mg/kg/day and 0.2 mg/kg/day groups vs placebo group.

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CONCLUSIONS

- Fintepla demonstrated robust efficacy in the phase 3 study in patients with DS optimized on an AED regimen that included STP with or without VPA.
- The odds of experiencing clinically meaningful (≥50%) and profound (≥65%) reduction in MCSF were 24 and 24 times higher, respectively, in patients with FFA vs placebo added to their AED regimen.
- No serious adverse events were observed in any patient at any time during the study.

ACKNOWLEDGMENTS

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REFERENCES

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ADDITIONAL RESOURCES

-A. Zogenix, Inc., Emeryville, CA, USA. 2018. Zogenix thanks all of the patients, their families, and the study sites for their contributions. This study was funded by Zogenix, Inc. (Emeryville, CA, USA).

DISCLOSURES

Zogenix thanks all of the patients, their families, and the study sites for their contributions. This study was funded by Zogenix, Inc. (Emeryville, CA, USA).

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