Fenfluramine HCI Significantly Reduces Frequency of Generalized Tonic–Clonic Seizures in Dravet Syndrome: Pooled Analysis From Two 3 Clinical Trials

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Introduction

• Dravet syndrome is a severe, treatment-refractory developmental epileptic encephalopathy in which generalized tonic-clonic seizures are a common seizure type often refractory to treatment.
• Patients with Dravet syndrome experience elevated disease-specific mortality, most commonly due to sudden unexpected death in epilepsy (SUDEP) or status epilepticus.
• Treatment of Dravet syndrome is challenging. Various disease-modifying treatments are under investigation, with fenfluramine being most widely studied.

Methods

• Patients with Dravet syndrome aged 2-18 years enrolled in 1 of 2 randomized, placebo-controlled clinical trials of fenfluramine.
• Eligible patients were randomized to placebo or fenfluramine at 0.2 or 0.7 mg/kg/day (maximum daily dose of 26 mg/day in patients not currently receiving stiripentol, or fenfluramine at 0.4 mg/kg/day (maximum daily dose of 17 mg/day) in patients also treated with stiripentol.
• Patients enrolled in two Phase 3 clinical trials of fenfluramine added to current antiepileptic drug regimens.

Results

• 105 patients were enrolled and randomized to placebo (n=63), fenfluramine 0.2 mg/kg/day (n=10), 0.4 mg/kg/day (n=13), or 0.7 mg/kg/day (n=19).
• Baseline patient characteristics are shown in Table 1.

Table 1. Demographic and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo</th>
<th>FFA 0.2 mg/kg/day</th>
<th>FFA 0.4 mg/kg/day</th>
<th>FFA 0.7 mg/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean±SD (median)</td>
<td>13.4±3.3</td>
<td>14.4±3.1</td>
<td>14.2±3.0</td>
<td>13.9±3.1</td>
</tr>
<tr>
<td>Number of patients</td>
<td>63</td>
<td>10</td>
<td>13</td>
<td>19</td>
</tr>
<tr>
<td>Sex, n (%): Male</td>
<td>31 / 32%</td>
<td>5 / 50%</td>
<td>6 / 46%</td>
<td>12 / 63%</td>
</tr>
<tr>
<td>Age group, n (%): ≥6 years</td>
<td>31 / 49%</td>
<td>7 / 70%</td>
<td>6 / 46%</td>
<td>10 / 53%</td>
</tr>
</tbody>
</table>
| Baseline patient characteristics are shown in Table 1.

• Treatment-emergent adverse events are presented in Table 2.

Table 2. Treatment-Emergent Adverse Events Occurring in ≥10% of Patients in Any Treatment Group

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Placebo</th>
<th>FFA 0.2 mg/kg/day</th>
<th>FFA 0.4 mg/kg/day</th>
<th>FFA 0.7 mg/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse Event</td>
<td></td>
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</tbody>
</table>

Conclusions

• Fenfluramine provided clinically meaningful (≥50%) and profound (≥75%) reductions in the frequency of generalized tonic-clinic and focal-to-bilateral tonic-clonic seizures in patients with Dravet syndrome.
• Fenfluramine may represent an important, effective new treatment option for patients with Dravet syndrome.

References


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