Cannabinoid (CBD) Significantly Reduces Drop Seizure Frequency in Lennox-Gastaut Syndrome (LGS): Results of a Multi-center, Randomized, Double-blind, Placebo-controlled Trial (GWPCARE4)

**SUMMARY**
- The trial met its primary endpoint, demonstrating that CBD (20 mg/kg/day), as an addition to standard of care, produced significantly greater reductions in drop seizures vs. placebo in patients with Lennox-Gastaut Syndrome (LGS).
- CBD resulted in significantly greater reductions in total seizure and non-drop seizure frequency vs. placebo.
- CBD patients/caregivers were significantly more likely than patients taking placebo to report an improvement in overall condition as measured on the Subject/Caregiver Global Impression of Change (S/C-GIC) scale.
- CBD resulted in more adverse events than placebo, but it was generally well tolerated.

**INTRODUCTION**
- Data from an open-label, expanded access program in the United States have suggested that CBD reduces seizures in patients with LGS (2–55 years old) with LGS.

**DATA FROM AN OPEN-LABEL, EXPANDED ACCESS PROGRAM IN THE UNITED STATES HAVE SUGGESTED THAT CBD REDUCES SEIZURES IN PATIENTS WITH LGS (2–55 YEARS OLD) WITH LGS.**

**EFFECTIVENESS RESULTS**

**Maintenance Period Ambulatory Period Treatment Period**

**A. Drop Seizures**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Drop Seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBD</td>
<td>62 (28%)</td>
</tr>
<tr>
<td>Placebo</td>
<td>90 (41%)</td>
</tr>
</tbody>
</table>

**B. Total Seizures**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total Seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBD</td>
<td>40 (18%)</td>
</tr>
<tr>
<td>Placebo</td>
<td>60 (26%)</td>
</tr>
</tbody>
</table>

**DROP SEIZURE RESPONSE**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBD</td>
<td>72</td>
<td>14</td>
</tr>
<tr>
<td>Placebo</td>
<td>56</td>
<td>29</td>
</tr>
</tbody>
</table>

**SUBJECT/CAREGIVER GLOBAL IMPRESSION OF CHANGE FROM BASELINE AT LAST VISIT**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Improved</th>
<th>Much Improved</th>
<th>Slightly Improved</th>
<th>Much Worse</th>
<th>Much Worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBD</td>
<td>14</td>
<td>17</td>
<td>15</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Placebo</td>
<td>10</td>
<td>14</td>
<td>6</td>
<td>3</td>
<td>1</td>
</tr>
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**SAFETY RESULTS**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>TEAEs reported in &gt;10% of patients by preferred term</th>
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<tr>
<td>CBD</td>
<td>Gastrointestinal problems 17 (19.5%)</td>
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<td>Placebo</td>
<td>No gastrointestinal problems</td>
</tr>
</tbody>
</table>

**EFFICACY RESULTS**

- Significantly greater reductions were reported for CBD than for placebo.
- Reduction in non-drop seizures was statistically different for the subgroup of patients who had non-drop seizures.
- CBD (77-81.5%) vs. placebo (50-60%) (p < 0.05).

**SAFETY RESULTS**

- CBD resulted in more adverse events than placebo, but it was generally well tolerated.
- Global Impression of Change (S/C-GIC) scale.

**SUMMARY**

- CBD significantly reduces drop seizure frequency in patients with LGS.
- CBD is generally well tolerated.
- CBD is more likely to be associated with adverse events compared to placebo.

**METHODS**

- Eligible patients were aged 2–17 years with a diagnosis of LGS inadequately controlled by ≤1 current AED(s).
- Patients had a history of slow wave activity present on at least one EEG recording.
- Patients were randomized to receive CBD (100 mg/mL) in oral solution or matched placebo, administered b.i.d. starting at 2.5 mg/kg/day and titrated up to 20 mg/kg/day over a 2-week period.
- Patients who completed the trial were eligible to continue into an open-label extension study.
- The treatment period consisted of both the titration and maintenance periods.

**TEAEs reported in >10% of patients by preferred term**

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**Variables**

- Age (years)
- Sex
- Screen failures (n=29)
- Treatment (n=72)
- Completed treatment (n=72)
- Treatment period (n=72)
- Maintenance period (n=72)

**CONTACT INFORMATION**

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**REFERENCES**