**Epidiolex (Cannabidiol) in Treatment Resistant Epilepsy**

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**STUDY OVERVIEW**

Cannabidiol (CBD) is the most abundant non-psychoactive cannabinoid in cannabis. Animal studies demonstrate anticonvulsant efficacy in multiple species and models.1 Anecdotal reports suggest CBD to be effective in children with treatment-resistant epilepsies (TRE), especially Dravet syndrome (DS).2 We report results of an open label study in children with TRE in an expanded access treatment program conducted in the US under INDs.

**METHODS**

Children and young adults with severe, childhood onset TRE were enrolled in a prospective interventional study (under expanded access INDs) of CBD. Patients entered a 4 week baseline period when parents/caregivers kept seizure diaries, noting all countable motor seizures. Patients then received a >99% pure, oil-based CBD extract of constant composition (Epidiolex: GW Pharma)

**Inclusion criteria were:**

- **Early onset TRE**
- Up to 4 concomitant AEDs (not including Ketogenic diet or VNS)
- No significant laboratory abnormalities
- Age 1 year or older

- Prior to starting CBD, a 4 week seizure diary was kept, noting all countable motor seizure types with no changes in medication.
- At Week 4, CBD at 2-5 mg/kg/day was added to the baseline AED regimen, then titrated weekly by 2-5 mg/kg increments until intolerance or a maximum dose of 25 mg/kg/day.
- Labs for hemotologic, liver, kidney function, and AED levels were performed at baseline, and after 4, 8 and 12 weeks of CBD therapy.

**RESULTS**

**Patient Profile**

- 137 patients received ≥3 months of CBD (Table 1)
  - Dravet Syndrome – 25 patients
  - Lennox-Gastaut Syndrome (LGS) – 22 patients
  - 48 received ≥ 24 weeks of treatment.
  - Safety data was from 213 patients treated for 58.6 patient-years at 11 sites.
  - Average # of concomitant AEDs was 3

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<th>Table 1</th>
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<td>N = 137</td>
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<td>Age (years)</td>
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<td>Weight (kg)</td>
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<td>Female: Male</td>
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**Diagnoses**

- There was a range of treatment resistant epilepsy subtypes, of which the most common diagnoses were Dravet syndrome in 18% and Lennox Gastaut syndrome in 16%.

**Efficacy**

- After 12 weeks of treatment, overall seizure frequency was reduced by 94% in all patients, and by 63% in DS patients (Figure 1).
- 50% responder analysis for total seizures are summarized on Figure 2.
- At 3 months 9% of all patients and 16% of DS patients were seizure free.
- Among 27 pts with atonic seizures, a 66.7% median reduction was noted over 12 weeks of treatment.
- Co-treatment with clobazam was associated with a higher rate of treatment response (>50% reduction in convulsive seizure frequency at 3 mos): 53% on clobazam versus 29% not on clobazam. This could reflect elevations of the nordsesmethyl-clobazam metabolite.2

![Fig. 1: Median % Reduction in Total Seizures](image)

**Safety**

- AEs in ≥10% patients were somnolence (21%), diarrhea (17%), fatigue (17%), and decreased appetite (16%).
- 10 patients (5%) discontinued treatment due to an AE, 3 of whom subsequently re-started CBD.
- 14 patients withdrew due to lack of efficacy.
- Serious Adverse Events (SAEs) were reported in 52 patients (24%), including 2 deaths, neither were deemed related to Epidiolex. 22 patients had SAEs which were deemed possibly related to treatment, including status epilepticus (10), diarrhea (3), weight loss (2), pneumonia (2), lethargy (1), and hepatotoxicity (1).
- There were no clinically significant changes in WBC, or platelet levels.
- There was a range of treatment resistant epilepsy subtypes, of which the most common diagnoses were Dravet syndrome in 18% and Lennox Gastaut syndrome in 16%.

**CONCLUSIONS**

- Treatment with Epidiolex is associated with a meaningful reduction in seizure frequency in a high proportion of patients with severe TRE. Those who respond early appear to have a prolonged response.
- Seizure freedom occurs in a 9% of all responders, higher in the Dravet cohort.
- There was a substantial reduction in atonic seizures suggesting that Epidiolex may be effective in LGS patients.
- Tolerability seems good, with a low rate of withdrawals from treatment.

**REFERENCES**


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