332 Real-world Insights on the Use of Cannabidiol in Children Aged <2 Years With Probable Lennox-Gastaut Syndrome, Dravet Syndrome, or Tuberous Sclerosis Complex : A Physician Survey

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Introduction

- Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), and tuberous sclerosis complex (TSC)-associated epilepsy are rare, severe developmental epileptic encephalopathies with possible onset in infancy or early childhood.[1–3]
- Although LGS is diagnosed later, it can initiate in children aged <2 years; most children develop DS in infancy, and TSC can be diagnosed from birth.[2–4]
- Clinical trials conducted with plant-derived highly purified cannabidiol (CBD; Epid[iy]olex®; 100 mg/mL oral solution) have recruited patients aged ≥2 years with LGS and DS and ≥1 year with TSC.[5–8]
  - Hence, there is a lack of data on clinical outcomes in the infant and paediatric population aged <2 years, especially for patients with LGS and DS
- As CBD is not approved for use in patients aged <1 year in the USA / <2 years in the UK, EU, and most other countries, real-world data on CBD treatment outcomes also miss the youngest patient population with LGS, DS, and TSC.
- To date, there are limited consensus and practice guidelines on the management of infant patients with probable LGS, DS, and TSC.

Objective

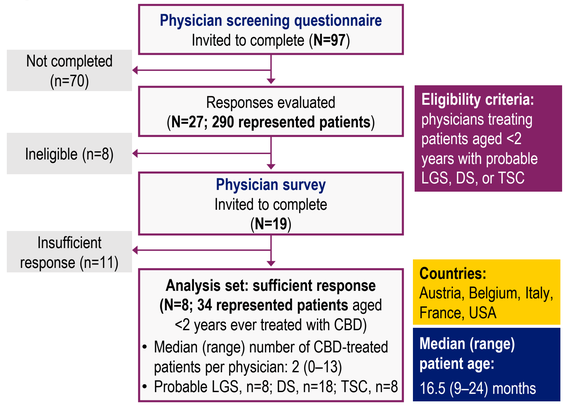
- This exploratory study aimed to better understand the management and treatment outcomes of patients aged <2 years receiving CBD for the treatment of seizures associated with probable LGS, DS, or TSC.

Methods

- A two-step survey requesting aggregate data from physicians treating patients <2 years of age with probable LGS, DS, and/or TSC was conducted.
  - A screening questionnaire (29 Nov 2022–10 Feb 2023) identified eligible participants, who then received the patient management survey (24 Mar–26 Jun 2023)
  - Patients must have been treated with CBD for at least 3 months
  - Each physician provided responses for all eligible patients at their clinic
- Collected survey data were cleaned and analysed; outcomes were quantitative (weighted and unweighted) and qualitative.
  - Quantitative: aggregate counts or proportion of patients estimated to have experienced the outcome, or means/medians of outcomes weighted against the number of eligible patients of each responding physician
  - Qualitative: ranking or aggregate counts of multiple-choice outcomes
- This study was conducted with Epid(iy)olex®, and results do not apply to other CBD-containing products.
- The results of this study are exploratory.

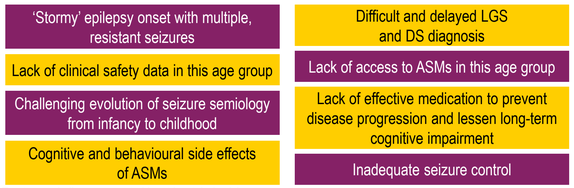
Results

Physician and patient characteristics



CBD, cannabidiol; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; TSC, tuberous sclerosis complex.

Treatment challenges reported by physicians

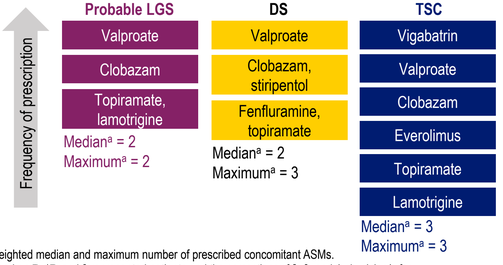


Treatment challenges reported by at least 1 physician.
ASM, antiseizure medication; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

Treatment overview

- The most commonly reported reason for initiation of CBD was inadequate seizure control with the previous treatment; the most commonly reported reason for not initiating CBD was a lack of safety data in this age group.
- Weighted median (range) dosage (n=30) was **5 (2–15) mg/kg/day**.
  - Weighted median (range) dose titration rate was **14 (14–28) days**
- 8/30 (27%) represented patients discontinued CBD; reasons were a lack of treatment efficacy (7/8) and treatment-emergent adverse events (AEs; 1/8).
- On reaching CBD maintenance, concomitant antiseizure medications (ASMs) were withdrawn in 9/30 (30%) patients.

Concomitant ASMs



[a]Weighted median and maximum number of prescribed concomitant ASMs. Based on 7, 17, and 3 represented patients and the perceptions of 2, 3, and 1 physician/s for probable LGS, DS, and TSC, respectively. Patient-level data regarding ASM use were not collected.
ASM, antiseizure medication; DS, Dravet syndrome; LGS Lennox-Gastaut syndrome; TSC, tuberous sclerosis complex.

Safety

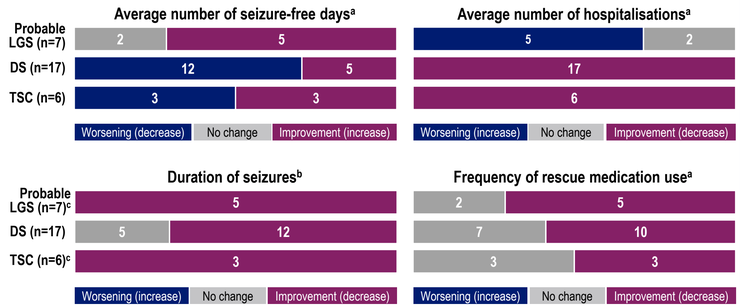
- AEs observed by physicians were somnolence, diarrhoea, change in liver transaminases, fever, and vomiting.
- Physician responses to observed AEs were reducing the dose of CBD / other ASMs or discontinuing other ASMs.

Physician-reported change in seizure frequency

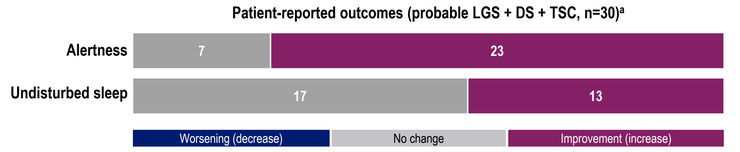
Reduction in seizure frequency (%)[a]	Estimated percentage of represented patients (n=30)[b]
0–25	47.3
26–50	30.0
51–75	13.2
76–100	4.5

[a]After 3 months of CBD treatment, compared with prior to CBD initiation. [b]Based on the perceptions of 6 physicians, with each physician's response representing all patients at their clinic and not individual patient outcomes. The sum of proportions does not equal 100% as not all physicians' responses equalled 100%. CBD, cannabidiol.

Physician-reported change in treatment outcomes following CBD initiation



Physician-reported change in patient outcomes following CBD initiation



[a]After at least 3 months of CBD treatment or [b]after 3 months of CBD treatment, compared with prior to CBD initiation. [c]Responses 'not captured at this clinic' were: probable LGS, n=2; TSC, n=3. Results based on perceptions of 4 physicians for each probable LGS, DS, and TSC, with each physician's response representing all patients at their clinic and not individual patient outcomes.
CBD, cannabidiol, DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; TSC, tuberous sclerosis complex.

Conclusions

- Physicians outlined challenges in the management of patients <2 years of age with probable LGS, DS, and TSC, including delays in diagnosis and a lack of approved ASMs or trial safety data in this age group.
  - The most commonly reported reason for initiation of CBD was inadequate seizure control with a previous treatment, suggesting a need for additional treatment options
  - The most commonly reported reason for not initiating CBD was a lack of safety data in this age group, reflecting a need to address this gap
- Physicians reported a perceived reduction in seizure frequency of >25% in 48% of patients, suggesting potential effectiveness of CBD in this patient cohort.
  - Decreases in seizure duration, rescue medication use, and hospitalisations were also reported
  - These outcomes were reported by physicians despite the low dosages used (<10 mg/kg/day) and the relatively short follow up (3 months)
- AEs observed by physicians were similar to those previously reported in patients >2 years of age.[5–8]
- Study limitations include the exploratory and retrospective nature of the study, the small number of physicians surveyed, and the patient cohort possibly representing those with the most severe symptoms who are using CBD owing to a lack of effectiveness with previous treatments.
- This study reinforces the unmet need for further research and prospective trials in this young patient age group.

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Jazz Pharmaceuticals, Inc.'s formulation of CBD is not approved for any treatment in South Africa. Epidiolex® is approved in the US for the treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex in patients ≥1 years of age. Epidyolex® is approved in the UK and EU for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome, in conjunction with clobazam, in patients ≥2 years of age; it is additionally approved in the UK and EU for the adjunctive treatment of seizures associated with tuberous sclerosis complex in patients ≥2 years of age.

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