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Real-world Insights on the Use of Cannabidiol in Adults With 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 and severe developmental and epileptic encephalopathies with onset in infancy or early childhood.[1–3]
- Seizures and co-occurring non-seizure symptoms persist into adulthood; over a lifetime, new symptoms may appear, and existing symptoms can change.[1,2,4]
- Real-world data on treatment outcomes with plant-derived highly purified cannabidiol (CBD; Epid[iy]olex®; 100 mg/mL oral solution) have been reported from studies including mostly paediatric patients with LGS, DS, or TSC.[5,6]
- Most patients with these conditions recruited in clinical trials conducted with CBD were children and adolescents.[7–10]
  - Hence, there are limited data on clinical outcomes in adult patients
- To date, there are limited consensus and practice guidelines on the management of adult patients with LGS, DS, and TSC.

Objective

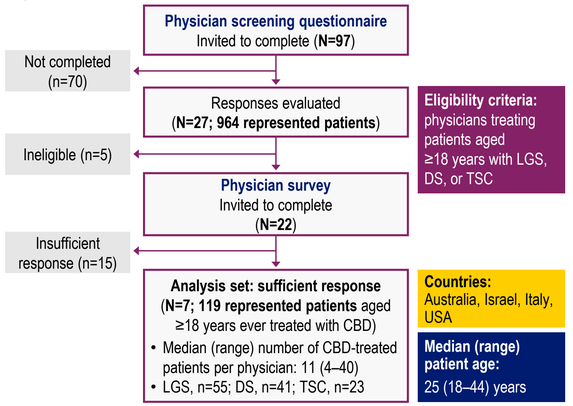
- This real-world study aimed to better understand the management and treatment outcomes of adult patients (aged ≥18 years) receiving CBD for the treatment of seizures associated with LGS, DS, or TSC.

Methods

- A two-step survey requesting aggregate data from physicians treating patients ≥18 years of age with LGS, DS, 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–4 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.

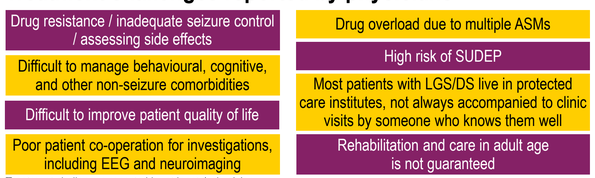
Results

Physician and patient characteristics



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

Treatment challenges reported by physicians

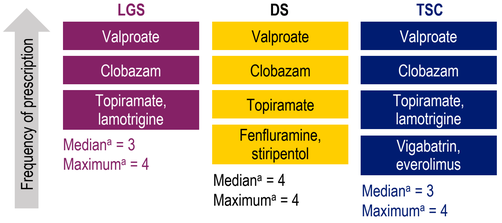


Treatment challenges reported by at least 1 physician.
ASM, antiseizure medication; DS, Dravet syndrome; EEG, electroencephalogram; LGS, Lennox-Gastaut syndrome; SUDEP, sudden unexpected death in epilepsy.

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 potential adverse events (AEs) associated with CBD use.
- Weighted median (range) dosage (n=75) was **12 (3–20) mg/kg/day**.
  - Weighted median (range) dose titration rate was **21 (15–60) days**
- 33/75 (44%) patients discontinued CBD; reasons were a lack of treatment efficacy (23/33), AEs (9/33), and laboratory abnormalities (1/33).
- On reaching CBD maintenance, concomitant antiseizure medications (ASMs) were withdrawn in 12/75 (16%) patients.

Concomitant ASMs



[a]Weighted median and maximum number of prescribed concomitant ASMs.
Based on 53, 40, and 22 represented patients and the perceptions of 6, 5, and 5 physicians for 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

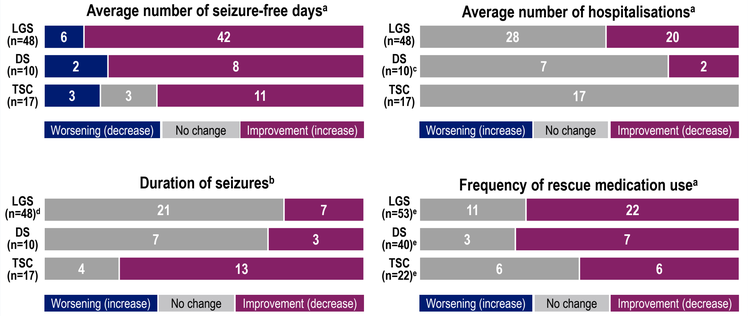
- AEs observed by physicians were somnolence, change in liver transaminases, diarrhoea, fatigue, and decreased appetite.
- Physician responses to observed AEs were reducing the dose of CBD / other ASMs or discontinuing CBD.

Physician-reported change in seizure frequency

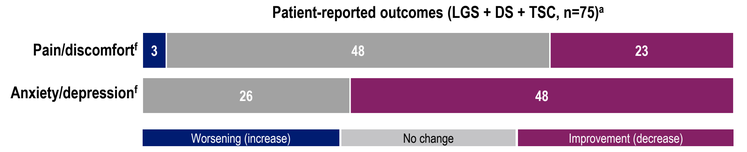
Reduction in seizure frequency (%)[a]	Estimated percentage of represented patients (n=75)[b]
0–25	38.1
26–50	25.9
51–75	19.9
76–100	3.7

[a]After 3 months of CBD treatment, compared with prior to CBD initiation; [b]Based on the perceptions of 5 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. Responses 'not captured at this clinic' were: [c]DS, n=1; [d]LGS, n=20; [e]LGS, n=20; DS, n=30; TSC, n=10; [f]DS, n=1. Results based on perceptions of 5 (seizure-free days, hospitalisations, seizure duration, and patient-reported outcomes) and 6 (rescue medication use) physicians for each 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

- Inadequate seizure control was highlighted by physicians as one of their main challenges in the management of adults with LGS, DS, and TSC, along with the need for multiple ASMs.
  - This suggests a need for more effective treatments used earlier in the treatment pathway
- The most commonly reported reason for initiation of CBD was inadequate seizure control with a previous treatment.
- The physician-reported reduction in seizure frequency of >25% in 50% of patients after 3 months suggests potential benefits of add-on CBD for seizure reduction in this adult patient population.
  - Perceived increases in seizure-free days and decreases in seizure duration and rescue medication use were also reported by physicians, as well as improvements in anxiety/depression
- These outcomes were reported despite some patients taking low dosages (<10 mg/kg/day) and the relatively short follow-up period (3 months).
- AEs observed were consistent with the known safety profile of CBD.[7–10]
- As a limitation, this is a retrospective survey of a small number of physicians and the patient cohort represented may be those with the most severe symptoms for whom treatment options before CBD have not been sufficiently effective.
- This study indicates potential seizure and non-seizure benefits associated with CBD treatment of adult patients with LGS, DS or TSC, and demonstrates that further prospective research is warranted.

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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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