2.406 Clinical Characteristics and Treatment Patterns in Patients With Dravet Syndrome and Lennox-Gastaut Syndrome Who Are Prescribed Cannabidiol (CBD)

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Introduction

- Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) are developmental and epileptic encephalopathies characterized by severe, treatment-resistant seizures, and substantial cognitive and developmental impairments[1]
- Both syndromes are associated with progressive cognitive and behavioral impairment. Patients with DS, in particular, are at an increased risk of sudden unexpected death in epilepsy[1,2]
- Despite increased disease awareness among pediatric neurologists, diagnoses may be delayed for various reasons[1]
- General antiseizure medications (ASMs), commonly referred to as antiepileptic drugs, are typically prescribed to manage symptoms during the initial stages of treatment, including before confirmatory diagnosis of DS or LGS. Once diagnosis is confirmed, treatment may be adjusted to include additional or alternative ASMs tailored to the specific needs of the patient[3,4]
- Epidiolex® is a pharmaceutical formulation of plant-derived highly purified cannabidiol (CBD), approved for the treatment of seizures associated with DS, LGS, and tuberous sclerosis complex in patients ≥1 year of age and has demonstrated effectiveness against a variety of seizure types. A caregiver survey suggests that treatment with Epidiolex® may be associated with both seizure and nonseizure benefits[5–7]
- Real-world evidence on clinical characteristics, treatment patterns, and satisfaction in patients receiving CBD (Epidiolex®) for the treatment of seizures associated with LGS or DS is limited

Objectives

- To understand clinical characteristics of patients with DS or LGS who received CBD treatments
- To understand real-world treatment patterns and outcomes among patients with DS or LGS who received CBD treatments

Methods

- Data were collected as part of the Adelphi DS and LGS Disease Specific Programme™[8,9] by participating adult and pediatric neurologists between July 2022 and August 2023
  - Data were provided by 88 neurologists for 191 patients prescribed CBD at time of survey
- Physician-reported chart data were collected for patients with a confirmed diagnosis of DS or LGS who were prescribed CBD (Epidyolex® [EU]/Epidiolex® [US]; 100 mg/mL oral solution) from France, Germany, Italy, Spain, the UK, and the US
- The forms collected data on patient demographics, clinical characteristics, seizure and nonseizure burden, treatment patterns, treatment satisfaction, and reasons for adding CBD to the treatment regimen
- Descriptive analyses such as median (Q1, Q3) and percentages were summarized

Results

Demographic and clinical characteristics

Table 1. Demographic and clinical patient characteristics

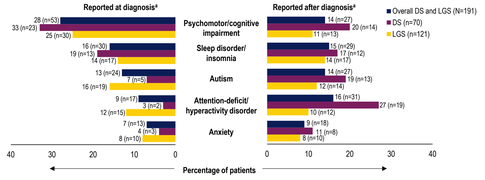
	Overall DS and LGS (N=191)	DS (n=70)	LGS (n=121)
Age			
Median age at time of survey, years (Q1, Q3)	14.0 (6.0, 19.0)	10.0 (4.0, 17.0)	15.0 (8.0, 21.5)
Patients by age, n (%)			
0–12 years	91 (48)	40 (57)	51 (42)
13–17 years	40 (21)	15 (21)	25 (21)
18 years and above	60 (31)	15 (21)	45 (37)
Sex, n (%)			
Male	119 (62)	41 (59)	78 (64)
Female	72 (38)	29 (41)	43 (36)
Age at first seizure[a]	**n=151**	**n=60**	**n=91**
Median, years (Q1, Q3)	2.0 (0.7, 4.0)	0.8 (0.6, 1.7)	3.0 (1.2, 5.0)
Age at diagnosis[a]	**n=145**	**n=56**	**n=89**
Median, years (Q1, Q3)	4.1 (2.0, 6.5)	1.7 (0.8, 4.0)	5.2 (3.4, 8.0)
Time between first seizure and diagnosis[a]	**n=134**	**n=54**	**n=80**
Median, months (Q1, Q3)	12.5 (1.4, 36.4)	7.4 (−1.2, 22.5)	15.4 (2.0, 41.5)
Time between first seizure and diagnosis in patients aged <10 years[b]	**n=63**	**n=31**	**n=32**
Median, months (Q1, Q3)	2.9 (−1.9, 14.6)	2.4 (−2.3, 12.1)	7.8 (−1.4, 8.2)
Time between first seizure and diagnosis in patients aged ≥10 years[b]	**n=71**	**n=23**	**n=48**
Median, months (Q1, Q3)	24.0 (7.8, 64.5)	22.2 (7.4, 64.5)	28.9 (8.2, 68.3)

[a]Some patients may have had incomplete chart records at the time of data collection.
[b]Patients were aged <10 or ≥10 years at the time of data collection to record time between first seizure and diagnosis.
DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; Q1, quartile 1; Q3, quartile 3.

- Median time between first seizure to diagnosis was 7.4 months among patients with DS and 15.4 months in patients with LGS (**Table 1**)
  - Among older patients (aged ≥10 years), the median time between first seizure and diagnosis was longer (22.2 and 28.9 months in patients with DS and LGS, respectively)

Co-occurring conditions

Figure 1. Percentage of patients with the 5 most common co-occurring conditions

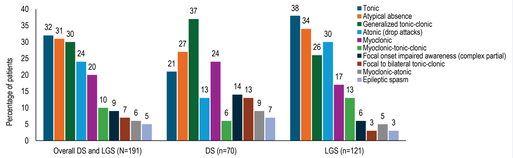


[a]All conditions were present at time of data collection and categorized based on whether they were reported before/at diagnosis or after diagnosis.
DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

- Patients who were taking CBD at data collection had a high prevalence of other comorbid conditions. Some of those conditions were developed/identified after DS/LGS diagnosis (**Figure 1**)

Seizure characteristics

Figure 2. Most common types of seizures experienced in the past 4 weeks[a]

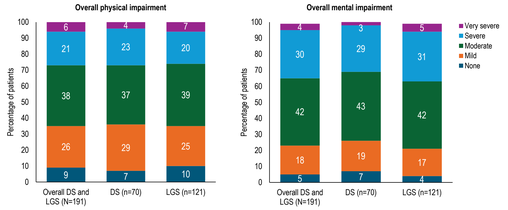


[a]During the time of study (July 2022–August 2023), in the past 4 weeks from the time of data collection.
DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

- Multiple seizure types were reported among patients with DS and LGS, including:
  - Generalized tonic-clonic seizures (37%), myoclonic type (24%), and tonic type (21%) in patients with DS
  - Tonic seizures (38%), atonic type drop attacks (30%), and generalized tonic-clonic types (26%) in patients with LGS (**Figure 2**)

Nonseizure symptoms

Figure 3. Current severity of impairment of nonseizure symptoms



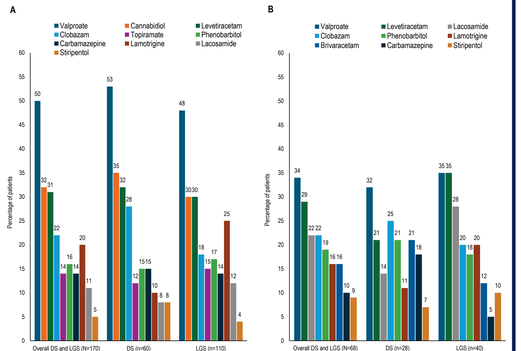
DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

- The majority of patients had moderate to severe physical or mental impairment (**Figure 3**)
  - Moderate to very severe physical impairment was reported in 64% of patients with DS and 65% with LGS
  - Moderate to very severe mental impairment was reported in 74% of patients with DS and 79% with LGS

Treatment patterns and satisfaction

Prior ASM use

Figure 4. ASM treatment (A) before diagnosis among all patients and (B) before diagnosis among a subset of patients who received CBD as first line of treatment after diagnosis with DS or LGS



ASM, antiseizure medication; CBD, cannabidiol; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

- Most patients received treatment with an ASM before diagnosis (overall, 89%; DS, 86%; LGS, 91%), with half of them receiving valproate (overall, 50% [n=85]; DS, 53% [n=32]; LGS, 48% [n=53]) (**Figure 4A**)
- A total of 32% (n=54) of current CBD users were exposed to CBD treatment prior to receiving a diagnosis for DS or LGS (DS, 35% [n=21]; LGS, 30% [n=33])
- Among patients who received CBD as the first line of treatment after diagnosis with DS or LGS, the most common ASM before diagnosis was valproate (34%, n=23) among both patients with DS (32%, n=9) and patients with LGS (35%, n=14), along with levetiracetam (35%, n=14) in patients with LGS (**Figure 4B**)

Treatment satisfaction among CBD users

- Physicians reported being satisfied with the current treatment regimen in 87% (n=61) of patients with DS and 88% (n=106) of patients with LGS

Use of CBD

Table 2. Line of treatment in which CBD was prescribed after diagnosis of DS or LGS

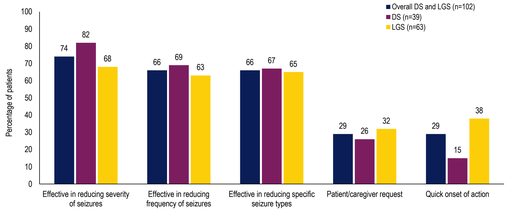
	Overall DS and LGS (n=188)	DS (n=70)	LGS (n=118)
First line, n (%)	74 (39)	28 (40)	46 (39)
Second line, n (%)	34 (18)	17 (24)	17 (14)
Third line, n (%)	41 (22)	11 (16)	30 (25)
Fourth line, n (%)	19 (10)	9 (13)	10 (8)
Fifth line or higher, n (%)	20 (11)	5 (7)	15 (13)

CBD, cannabidiol; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

- Patients with DS currently have a median (Q1, Q3) treatment time of 13.5 months (5.6, 22.1; n=46) on CBD, and patients with LGS have a median treatment time of 14.7 months (7.2, 27.6; n=81)
- Current median (Q1, Q3) dose of CBD was 14.2 mg/kg (10.0, 20.0; n=68) among patients with DS and 15.2 mg/kg (10.0, 20.0; n=106) among patients with LGS
- After receiving a diagnosis for LGS or DS, 40% (n=28) of patients with DS and 39% (n=46) of patients with LGS received CBD as the first ASM treatment (**Table 2**)
- Of patients who received CBD as the first-line treatment after diagnosis, 96% (n=27) with DS and 83% (n=38) with LGS received treatment with another ASM before diagnosis

Reasons for adding CBD to current treatment regimen

Figure 5. Top 5 reasons for adding CBD to treatment regimen



CBD, cannabidiol; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

- The reasons for adding CBD to the current treatment regimen was that it was effective in reducing seizure severity (overall, 74% [n=75]; DS, 82% [n=32]; LGS, 68% [n=43]) and reducing frequency of seizures (overall, 66% [n=67]; DS, 69% [n=27]; LGS, 63% [n=40]) (**Figure 5**)

Conclusions

- In this multicountry study, patients with DS and LGS who received CBD at data collection experienced a median gap of 7 months for DS and 15 months for LGS between their first seizure and diagnosis. Older patients (aged ≥10 years) had substantially longer gaps
- Patients who received CBD at data collection had a high prevalence of other co-occurring conditions such as cognitive impairment, sleep disorder, and anxiety, among others
- Physicians reported a high satisfaction rate among CBD users. The top-rated reasons to add CBD were effectiveness in managing seizure severity and seizure frequency
- Despite co-occurring nonseizure burden, these findings underscore the potential for using CBD earlier in the treatment plan for patients with DS and LGS across the spectrum of severity for physical and mental impairments

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