P1.1-005 Real-World Treatment Patterns of Patients With Dravet Syndrome and Lennox-Gastaut Syndrome in the United States

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Background

- Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) are rare pediatric syndromes characterized by severe, treatment-resistant seizures.[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 (SUDEP).[2]
- Despite increased disease awareness among child neurologists, diagnoses may be delayed for various reasons.
- General antiseizure medications (ASMs) are typically prescribed to manage symptoms during the early stages of treatment, including before confirmatory diagnosis of DS or LGS, followed by more specialized treatment options.[3]
- Data on clinical characteristics, diagnoses, and treatment patterns in patients with LGS or DS are limited.

Objective

- To understand clinical characteristics of patients with DS or LGS.
- To understand real-world treatment patterns for patients with DS or LGS.

Methods

- The data were collected as part of the Adelphi Real World DS and LGS Disease Specific Programme™[4–6] by participating US neurologists between June 2022 and March 2023 based on chart data for patients with DS or LGS.
- The forms collected data on the types of health care professional (HCP), patient demographics, patient's clinical characteristics, seizure and nonseizure burden, treatment patterns, reason for treatment changes, and treatment satisfaction.
- Data are presented for the overall sample and by diagnosis (DS, LGS).
- Treatment patterns are presented starting with the initial treatments (with ASMs) for patients irrespective of whether DS or LGS diagnosis was confirmed and the treatment patterns after confirmatory diagnosis of DS or LGS.
- All analyses are descriptive in nature.

Results

Table 1. Demographic and clinical characteristics

	Overall (N=166)	DS (n=62)	LGS (n=104)
Gender (male), n (%)	95 (57.2)	32 (51.6)	63 (60.6)
Age at the time of data collection (years), median (Q1, Q3)	12.0 (6.0, 17.0)	7.5 (3.8, 13.0)	14.0 (9.0, 18.0)
Age at first seizure (years), median (Q1, Q3)[a]	2.0 (1.0, 4.0)	1.2 (0.6, 2.2)	2.5 (1.2, 5.4)
Age at diagnosis of DS or LGS (years), median (Q1, Q3)[a]	4.4 (2.2, 9.3)	3.0 (1.3, 4.7)	6.0 (2.8, 10.0)
Number of consults before diagnosis of DS or LGS, median (Q1, Q3)	2.0 (2.0, 3.0)	2.0 (1.0, 3.0)	2.0 (2.0, 4.0)
Type of HCP consulted at disease onset, n (%)			
Pediatrician	86 (51.8)	34 (54.8)	52 (50.0)
Neurologist	47 (28.3)	15 (24.2)	32 (30.8)
Pediatric neurologist	15 (9.0)	8 (12.9)	7 (6.7)
Type of HCP consulted at diagnosis of DS or LGS, n (%)			
Pediatrician	5 (3.0)	3 (4.8)	2 (1.9)
Neurologist	54 (32.5)	16 (25.8)	38 (36.5)
Pediatric neurologist	74 (44.6)	34 (54.8)	40 (38.5)
Diagnosed with another seizure disorder prior to confirmed DS or LGS[a], n (%)			
Yes	135 (81.3)	52 (83.9)	83 (79.8)
Epilepsy	72 (43.4)	28 (45.2)	44 (42.3)
General seizure disorder	71 (42.8)	23 (37.1)	48 (46.2)
Rett syndrome	5 (3.0)	2 (3.2)	3 (2.9)

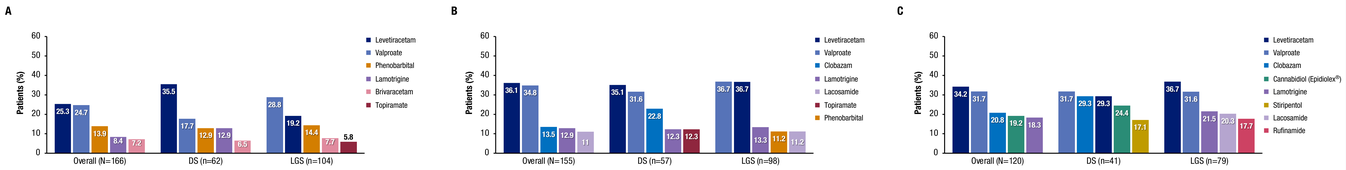
[a]Some patients received multiple diagnoses of another seizure disorder prior to confirmatory DS or LGS diagnosis.
DS, Dravet syndrome; HCP, health care professional; LGS, Lennox-Gastaut syndrome; Q1, first quartile; Q3, third quartile.

- Data was provided by 37 physicians (neurologists, pediatricians) for 166 patients (DS, n=62; LGS, n=104) in the United States.
- At first consultation, developmental delay was the most common nonseizure symptom in both disease groups (DS, 38.7%; LGS, 47.1%). The second most frequent nonseizure symptom was impaired verbal communication (37.1%) in patients with DS and learning and intellectual impairment (40.4%) in patients with LGS.

Figure 1. Mean number of ASMs per treatment regimen (A) irrespective of diagnosis,* (B) since diagnosis of DS or LGS, and (C) at the time of data collection

*ASMs received may be prior to confirmatory diagnosis of DS or LGS. ASM, antiseizure medication; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

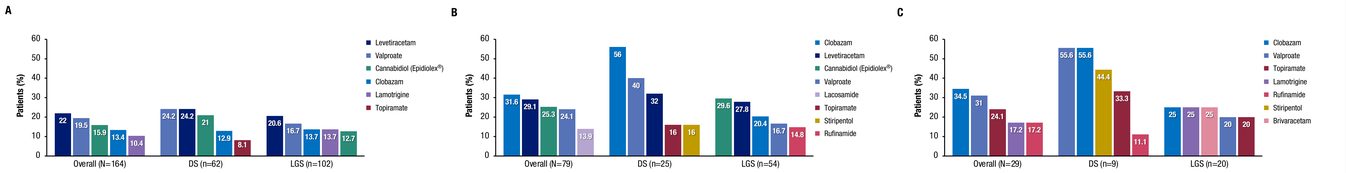
Figure 2. Top 5 ASMs prescribed at (A) first, (B) second, and (C) third regimens irrespective of DS or LGS diagnosis*



*ASMs received may be prior to confirmatory diagnosis of DS or LGS. ASM, antiseizure medication; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

- For patients with DS, levetiracetam was the most frequently prescribed ASM in the first and second regimens irrespective of DS diagnosis. As a third regimen, valproate was the most frequently prescribed ASM **(Figure 2)**.
- For patients with LGS, valproate was the most frequently prescribed ASM in the first regimen irrespective of LGS diagnosis. Levetiracetam and valproate were the most frequently prescribed ASM at second regimen irrespective of diagnosis. Levetiracetam was the most commonly prescribed ASM at third regimen **(Figure 2)**.

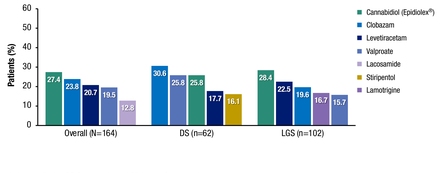
Figure 3. Top 5 ASMs prescribed at (A) first, (B) second, and (C) third regimens since diagnosis of DS or LGS



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

- For patients with DS, valproate and levetiracetam were the most frequently prescribed ASMs in the first and third regimens since confirmatory diagnosis. In the second regimen since diagnosis, clobazam was the most frequently prescribed ASM **(Figure 3)**.
- For patients with LGS, levetiracetam was the most frequently prescribed ASM at first regimen since LGS diagnosis. Cannabidiol (Epidiolex®) was the most frequently prescribed at second regimen, and at third regimen since diagnosis, clobazam and lamotrigine were the most frequently prescribed **(Figure 3)**.

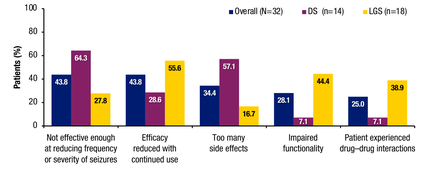
Figure 4. Top 5 ASMs prescribed at the time of data collection



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

- At the time of data collection, clobazam was the most frequently prescribed treatment for patients with DS followed by either cannabidiol (Epidiolex®) or valproate **(Figure 4)**.
- Cannabidiol (Epidiolex®) was the most frequently prescribed treatment at the time of data collection for patients with LGS followed by levetiracetam **(Figure 4)**.

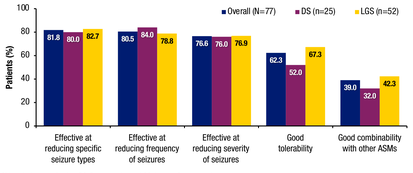
Figure 5. Top 5 reasons for discontinuing an ASM



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

- In the overall population, the most common reasons for discontinuation of a treatment were "not effective enough at reducing frequency or severity of seizures" and "reduced efficacy with continued use". The former was the most common reason for discontinuation in patients with DS, while the latter was the most common reason for discontinuation in patients with LGS (**Figure 5**).
- The most common reason for adding a treatment was "effective at reducing specific seizure types" in both the overall population and in the subgroup of patients with LGS. Among patients with DS, the most common reason for adding a treatment was "effective at reducing the frequency of seizures" (**Figure 6**).

Figure 6. Top 5 reasons for adding an ASM



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

Conclusions

- Patients experienced a delay in disease diagnosis following first seizure (mean: DS, 1.8 years; LGS, 3.5 years), with approximately 80% of patients diagnosed with another seizure disorder prior to DS or LGS.
- Nonseizure burden at first consultation was high, with developmental delay affecting nearly 50% of patients with LGS, and impaired verbal communication affecting approximately 40% of patients with DS.
- Polypharmacy was common prior to and after diagnosis of DS or LGS.
- Levetiracetam and valproate were the most frequently used ASMs, early on (ie, irrespective of diagnosis) and in the first three treatment regimens for patients diagnosed with either DS or LGS.
- Physicians reported inadequate reduction in seizure frequency and side effects as reasons for modifications in ASM use.
- Limitations of this cross-sectional study include selection bias and limited generalizability of the results.
- This study highlights the importance of early diagnosis and effective early treatments, which may reduce the burden of polypharmacy and improve outcomes for US patients with DS or LGS.

References: 1. Marchese F et al. *SN Compr Clin Med.* 2021;3:2167-2179; **2.** Sullivan J et al. *Epilepsia.* 2024 Jan 22. doi: 10.1111/epi.17866. Online ahead of print; **3.** Jacob EC, Jacob SC. *US Pharm.* 2019;44:HS8-HS12; **4.** Anderson P et al. *Curr Med Res Opin.* 2008;24:3063-3072; **5.** Babineaux SM et al. *BMJ Open.* 2016;6:e010352; **6.** Higgins V et al. *Diabetes Metab Syndr Obes.* 2016;9:371-380.

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