Fenfluramine Persistence in Patients With Lennox-Gastaut Syndrome: A Retrospective Analysis Using US Claims Data

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Introduction

- Lennox-Gastaut syndrome (LGS) is a rare, severe, childhood-onset epilepsy that is characterized by various seizure types, abnormal electroencephalogram findings, and cognitive and behavioral impairments[1]
- Fenfluramine has a novel, dual mechanism of action that targets serotonergic and sigma-1 receptor pathways and is associated with minimal risk for CYP450-related drug-drug interactions[2–5]
- Fenfluramine was approved for the management of seizures associated with LGS in patients ≥2 years old in the United States in March 2022[6]
- Despite established clinical efficacy,[7,8] real-world evidence of fenfluramine persistency and use among patients with LGS is limited

Objective

- This study examined fenfluramine persistence in patients with LGS while examining patient characteristics that may be associated with fenfluramine use and persistence using a large US claims database

Methods

- This was a retrospective study of patients with LGS (ICD-10, G40.81) from January 1, 2021–December 31, 2024, using the Komodo US healthcare claims database
- Komodo is a large claims dataset that includes open and closed claims on patients with seizure history that provides comprehensive medical and pharmacy data, mortality information, and demographics such as race, ethnicity, and geography

ANALYSIS

Persistence:

- Patient selection period was from January 1, 2022–June 30, 2024
- Patients were required to have ≥1 fenfluramine prescription claim (earliest claim was used as fenfluramine initiation date), ≥1 LGS claims, ≥3 months of pre-fenfluramine initiation and ≥6 months of post-fenfluramine initiation claims data
- Kaplan–Meier analysis was used to assess the percentage of patients with fenfluramine persistence (continuous fenfluramine claims with no gaps >90 days) in the first 12 months post-fenfluramine initiation

Comparison of demographic and clinical characteristics:

- Patient selection period was from January 1, 2022–December 31, 2023, to allow for 12 months of pre- and post-index data
- Two comparisons of demographic and clinical characteristics were made:
  - Patients who remained fenfluramine persistent for ≥12 months were compared with non-persistent patients (discontinued fenfluramine in <12 months)
  - Patients who received fenfluramine (regardless of persistence) were compared with a population of patients with LGS who did not receive fenfluramine (no fenfluramine claims and ≥1 LGS claim)
- Two sample *t*-tests and chi-square tests were used to assess the group-level comparisons of demographic and baseline characteristics
- For both groupwise comparisons, patients were required to have claims data for 12 months pre- and post-index date
- In each analysis, the fenfluramine initiation date was used for persistent and non-persistent patients and the index date for patients not receiving fenfluramine was January 1, 2023

Overview

QUESTION

- What is the treatment persistence with fenfluramine over 12 months among patients with LGS?
- In patients with LGS, what are the differences in patient demographics and characteristics between patients with fenfluramine treatment persistence and those who are non-persistent?
- Additionally, what are the differences in patient characteristics between patients receiving fenfluramine and those not receiving fenfluramine?

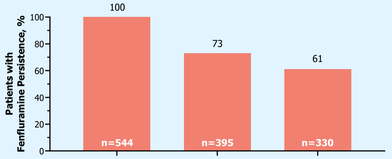
INVESTIGATION

- This was a retrospective study using the Komodo claims database with an analysis period from January 1, 2021, to December 31, 2024
- Patients were required to have ≥1 fenfluramine prescription claim (earliest claim was used as fenfluramine initiation date), ≥1 LGS claim, and ≥3 months of pre-fenfluramine initiation and ≥6 months of post-fenfluramine initiation claims data
- The Komodo claims database was used to analyze:
  - Percentage of patients who were persistent with fenfluramine treatment (continuous fenfluramine claims with no gaps >90 days) in the first 12 months of fenfluramine use
- Differences in demographics and characteristics in:
  - Patients who remained persistent on fenfluramine compared with those who discontinued within 12 months
  - Patients who initiated fenfluramine treatment compared with those who never initiated (no fenfluramine claims and ≥1 LGS claim)

RESULTS

- Of 544 patients with LGS who met treatment persistence criteria, 73% were persistent at 6 months and 61% at 12 months (**Figure**)
- Compared with patients who did not receive fenfluramine, patients receiving fenfluramine were younger and had significantly higher comorbidity burden, HCRU severity score, and mean HCRU claims including status epilepticus claims, ASM claims, rescue medication claims, emergency room visits, and inpatient hospitalizations (**Table**)

Percentage of Patients With Fenfluramine Persistence With 90-Day Claims Gap



Comparison of Demographics and Baseline Clinical Characteristics Between Patients With and Without Fenfluramine Use

	With Fenfluramine Claims (n=373)[a]	Without Fenfluramine Claims (n=2361)[b]	P Value
Mean age at index,[c] years	16	38	<0.01
Comorbidities, frequency, n (%)			
Behavioral disorders	140 (38)	675 (29)	<0.01
Respiratory/CV complications	259 (69)	1207 (51)	<0.01
Developmental impairments	284 (76)	889 (38)	<0.01
GI disorders	197 (53)	973 (41)	<0.01
Mobility dysfunction	134 (36)	522 (22)	<0.01
Sleep disturbances	105 (28)	388 (16)	<0.01
Charlson Comorbidity Index	1.5	2.0	<0.01
Germaine Smith Index	2.3	2.8	<0.01
HCRU severity score[f], mean	128.3	57.1	<0.01
Mean preindex[c] HCRU claims			
Emergency room visits	1.6	1.1	<0.01
Status epilepticus	12.7	4.3	<0.01
Number of unique ASM	5.8	3.7	<0.01
Number of rescue medication	3.3	1.0	<0.01

[a]FFA cohort included patients with 12 months enrollment before and after the first FFA claim.
[b]Non-FFA cohort included patients without any FFA prescription claims, with at least 12 months of data before and after LGS diagnosis during the study period.
[c]Index date for patients with FFA claims was the date of the first FFA prescription claim. Index date for patients without FFA claims was January 1, 2023, which aligns closely with the index date for the FFA group.

CONCLUSIONS

- Fenfluramine treatment persistence in patients with LGS was 73% and 61% at 6 and 12 months
- Significant differences in age, comorbidities, HCRU severity, and HCRU burden (including claims for status epilepticus, ASMs, and rescue medications) indicated greater disease severity in patients receiving fenfluramine compared with those not receiving fenfluramine
- These findings reflect sustained treatment in >60% of patients with LGS who initiated fenfluramine

Abbreviations: ASMs, antiseizure medications; COE, Centers of Excellence; CV, cardiovascular; GI, gastrointestinal; HCRU, healthcare resource utilization; LGS, Lennox-Gastaut syndrome.

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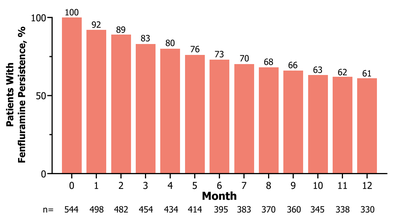
Results

- Data from 544 patients with LGS were included for assessments of 6- and 12-month fenfluramine persistence
- Persistence was 73% at 6 months and 61% at 12 months (**Figure 1**)

Figure 1. Fenfluramine Persistence Across the First Year (N=544)[a]



[a]Persistence analysis cohort included patients with ≥6 months of continuous follow-up after their first FFA prescription claim.
FFA, fenfluramine.

- There were no significant differences in demographics or baseline characteristics between patients with 12-month fenfluramine treatment persistence (n=148) and those who were non-persistent (n=216) (**Table 1**)
- Compared with patients who did not receive fenfluramine (n=2361), patients receiving fenfluramine (n=373) were younger and had significantly higher comorbidity burden, HCRU severity score, and mean HCRU claims including status epilepticus claims, antiseizure medications (ASMs), rescue medications, emergency room visits, and inpatient hospitalizations (**Table 2**)

Table 1. Demographics and Baseline Clinical Characteristics of Patients With Fenfluramine Persistence and Non-persistence

	FFA Persistent Patients (n=148)[a]	FFA Non-persistent Patients (n=216)[b]	*P* value
Mean age at index[c], years	16	16	0.86
Sex, n (%)			
Male	76 (51)	104 (48)	0.62
Female	71 (48)	108 (50)	0.78
Physician specialty, n (%)			
Epileptologists, COE[d]	109 (74)	143 (66)	0.16
Epileptologist	22 (15)	39 (18)	0.51
Pediatric neurologist	14 (9)	27 (13)	0.46
Comorbidities, frequency, n (%)			
Behavioral disorders	53 (36)	84 (39)	0.63
Respiratory/CV complications	104 (70)	149 (69)	0.88
Developmental impairments	118 (80)	160 (74)	0.26
GI disorders	81 (55)	109 (50)	0.49
Mobility dysfunction	52 (35)	81 (38)	0.73
Sleep disturbances	45 (30)	60 (28)	0.67
Payer, n (%)			
Commercial	84 (57)	115 (53)	0.58
Medicaid	41 (28)	65 (30)	0.71
Medicare	10 (7)	22 (10)	0.34
Comorbidity index, mean			
Charlson Comorbidity Index	1.68	1.48	0.26
Germaine Smith Index	2.32	2.33	0.96
Average ADI rank[e]	46.20	48.53	0.29
HCRU severity score[f], mean	133.56	127.27	0.82
Number of concomitant ASMs, mean	5.57	5.88	0.19

[a]Pre-/post-analysis cohort included patients with ≥12 months of data prior to and following their first FFA prescription claim, with continuous or persistent FFA use during the post-treatment period.
[b]Non-persistent FFA cohort included patients with data 12 months before and after their first FFA prescription claim who had <12 months of persistent FFA use during the post-treatment period.
[c]Index date for patients with FFA claims was the date of the first FFA prescription claim.
[d]Epileptologists associated with Level 4 National Association of Epilepsy Centers (NAEC) Centers.
[e]Higher ADI rank is indicative of greater socioeconomic disadvantage, with 100 being the most disadvantaged.
[f]HCRU severity score is an unvalidated weighted composite score of several HCRU elements (number of ER visits, hospitalizations, GTCS claims, SE claims, number of unique ASMs, and number of rescue medications). HRCU weights were assigned as follows: ER Visit, 10 points per ER visit; inpatient admissions, 5 points per day of length of stay; any GTCS claim, 4 points per GTCS claim; any SE claims, 5 points per SE claim; ASM, 2 points for every distinct ASM molecule; rescue medication, 4 points for every claim of rescue medication. (Note: if a patient had an ER visit for SE, the points were counted for both the ER visit and the SE claim).
ADI, area deprivation index; ASMs, antiseizure medications; COE, Centers of Excellence; CV, cardiovascular; ER, emergency room; FFA, fenfluramine; GI, gastrointestinal; GTCS, generalized tonic-clonic seizure; HCRU, healthcare resource utilization; SE, status epilepticus.

Table 2. Demographic and Baseline Clinical Characteristics of Patients With and Without Fenfluramine Claims

	With FFA Claims (n=373)[a]	Without FFA Claims (n=2361)[b]	*P* Value
Mean age at index,[c] years	16	38	<0.01
Sex, n (%)			
Male	184 (49)	1297 (55)	0.05
Female	184 (49)	1034 (44)	0.05
Physician specialty, n (%)			
Epileptologists, COE[d]	256 (69)	1071 (45)	<0.01
Epileptologist	65 (17)	516 (22)	0.06
Neurologist	10 (3)	376 (16)	<0.01
Pediatric neurologist	42 (11)	236 (10)	0.51
Other	0	162 (7)	<0.01
Comorbidities, frequency, n (%)			
Behavioral disorders	140 (38)	675 (29)	<0.01
Respiratory/CV complications	259 (69)	1207 (51)	<0.01
Developmental impairments	284 (76)	889 (38)	<0.01
GI disorders	197 (53)	973 (41)	<0.01
Mobility dysfunction	134 (36)	522 (22)	<0.01
Sleep disturbances	105 (28)	388 (16)	<0.01
Comorbidity index			
Charlson Comorbidity Index	1.5	2.0	<0.01
Germaine Smith Index	2.3	2.8	<0.01
Average ADI rank[e]	47.7	45.2	0.03
HCRU severity score[f], mean	128.3	57.1	<0.01
Mean preindex[c] HCRU claims for			
Emergency room visits	1.6	1.1	<0.01
Length of inpatient stay	3.8	2.3	0.02
GTC seizures	1.2	0.5	0.06
Status epilepticus	12.7	4.3	<0.01
Number of unique ASMs	5.8	3.7	<0.01
Number of rescue medications	3.3	1.0	<0.01

[a]FFA cohort included patients with 12 months enrollment before and after the first FFA claim.
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ADI, area deprivation index; ASMs, antiseizure medications; COE, Centers of Excellence; CV, cardiovascular; ER, emergency room; FFA, fenfluramine; GI, gastrointestinal; GTCS, generalized tonic-clonic seizure; HCRU, healthcare resource utilization; SE, status epilepticus.

Limitations

- The study cohort may have limited generalizability by not fully representing all patients with LGS or those on fenfluramine treatment
- Since the Komodo Healthcare database is comprised of both open and closed claims, we may not be capturing the complete HCRU burden for patients with open claims only

Conclusions

- In this, to our knowledge, first real-world evaluation of patients with LGS who received fenfluramine, persistence was 73% and 61% at 6 and 12 months, respectively
- No significant differences in demographic or clinical characteristics were observed between patients with fenfluramine treatment persistence and those who were non-persistent
- Here, patients who received fenfluramine had a higher incidence of comorbidities, HCRU severity scoring, and HCRU burden including claims for status epilepticus, concomitant ASMs, and rescue medications, indicating greater disease severity
- Additionally, patients who received fenfluramine were younger and resided in more socioeconomically disadvantaged neighborhoods
- While claims data limit the direct, formal measurement of seizure outcomes and outcomes beyond seizures, these findings reflect sustained treatment in >60% of patients with LGS who initiated fenfluramine

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Disclosures

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JK: employee of UCB with stock ownership.
HLH, PO: external contractor of UCB.
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AS: received personal fees and grants from Angelini Pharma, Biocodex, Desitin Arzneimittel, Eisai, Jazz Pharmaceuticals, Takeda, UCB, and UNEEG medical.

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