Analysis of Real-World Characteristics of Patients with CDKL5 Deficiency Disorder Enrolled for Ganaxolone Treatment

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Background

- Cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) is a developmental and epileptic encephalopathy characterized by global developmental impairment and early-onset, refractory seizures
- Ganaxolone, a neuroactive steroid and positive allosteric modulator that targets both synaptic and extrasynaptic $GABA_A$ receptors, is FDA-approved for the treatment of seizures associated with CDD in patients 2 years of age and older

Objective

- To assess the clinical features of patients being prescribed ganaxolone by reviewing the clinical data obtained from ganaxolone patient enrollment forms submitted to a specialty pharmacy for patients with CDD

Methods

- A retrospective analysis was conducted using de-identified patient enrollment form clinical data from a single specialty pharmacy in the United States
- Patients included in the analysis had CDD (ICD-10 G40.42) and were prescribed ganaxolone between July 2022 and February 2023
- Collected clinical data included epilepsy-related ICD-10 codes, age at seizure onset, previously and concomitantly utilized medications, additional seizure interventions, and current seizure burden

Results

- Data from 114 patients were included in the analysis

Seizure Burden and History

- Reported seizure burden demonstrated that 54.4% of patients (n=62) were experiencing daily seizures (>30 seizures/month), 28.9% (n=33) were experiencing weekly seizures (4-29 seizures/month), and 6.1% (n=7) had monthly seizures (1-3 seizures/month) while the remaining 10.5% (n=12) had unknown/unreported seizure burden (**Figure 1**)
- Seizure onset, when known, occurred within the first 3 months of life in 74.5% of patients
  - Analysis of all patients demonstrated a distribution of n=22 at 1 month or younger (19.3%), n=48 at >1 month to ≤3 months (42.1%), n=24 at >3 months or older (21.1%), and n=20 had unknown onset (17.5%) (**Figure 2**)

Figure 1. Seizure Burden at the Time of Ganaxolone Prescription

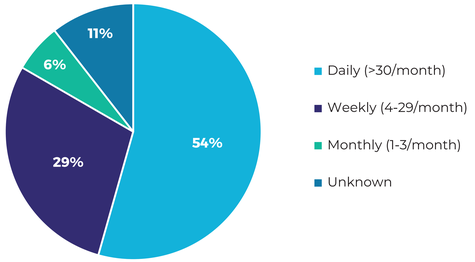
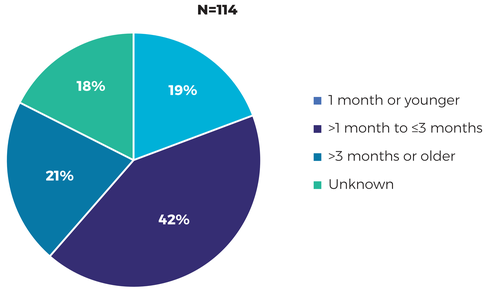


Figure 2. Initial Seizure Onset for Patients Prescribed Ganaxolone

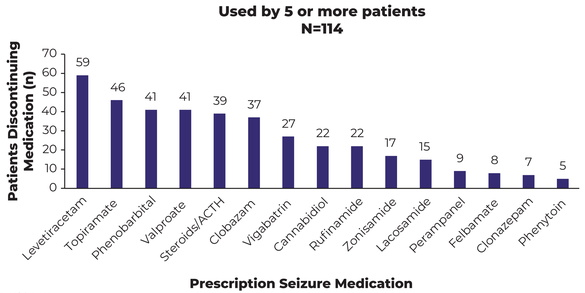


- The three most frequent seizure-related ICD-10 diagnoses beyond CDD (G40.42) were "Lennox-Gastaut Syndrome" (G40.81x), "epilepsy, unspecified" (G40.9xx), and "other generalized epilepsy and epileptic syndromes, intractable" (G40.41x)

Prior and Concomitant Medication Use

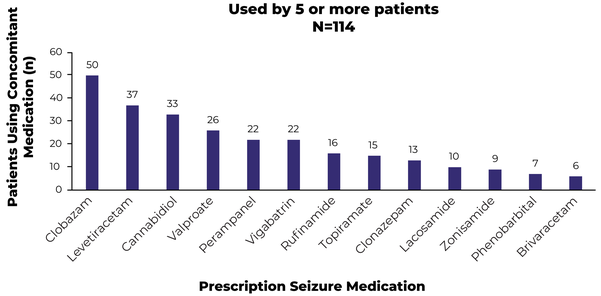
- The most common medications discontinued prior to ganaxolone prescription were levetiracetam (n=59), topiramate (n=46), phenobarbital (n=41), and valproate (n=41), with discontinuation of a mean of 4.46 prior seizure medications (**Figure 3**)

Figure 3. Previously Discontinued Seizure Medications



ACTH, adrenocorticotropic hormone

Figure 4. Concomitant Seizure Medications

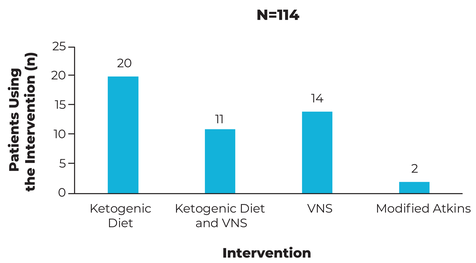


- The most common concomitant medications at the time of ganaxolone prescription were clobazam (n=50), levetiracetam (n=37), cannabidiol (n=33), and valproate (n=26), with concomitant use of a mean of 2.6 seizure medications (**Figure 4**)

Non-pharmacological Interventions

- Additional non-pharmacological interventions included a total of 31 patients on the ketogenic diet and 25 patients with a vagal nerve stimulator; 11 patients were utilizing a combination of the two options (**Figure 5**)
- Two patients reported utilizing a Modified Atkins Diet

Figure 5. Prior or Current Use of Non-pharmacologic Interventions



VNS, vagal nerve stimulator.

Ganaxolone Dosing

- Patient enrollment forms represented the initial 4-week titration of ganaxolone requested by the provider
- Most prescribers utilized the labeled titration schedule whereas approximately a quarter of prescribers elected to titrate either more slowly or to a lower dose

Conclusions

- **These data provide insights into real-world utilization of ganaxolone in the treatment of CDD-associated seizures, including use in patients with highly refractory epilepsy**
- **Dosing information supports both the intention of providers to titrate according to label and to utilize titrations that are slower or achieve a lower initial goal dose compared to label**
- **Such data may inform clinical decision-making in the treatment of CDD**

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