# An Online Survey of Caregivers of Patients With *KCNQ2* Developmental and Epileptic Encephalopathy

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## RATIONALE

- *KCNQ2* developmental and epileptic encephalopathy (*KCNQ2*-DEE) is a rare, severe neurodevelopmental disorder caused by variants in the *KCNQ2* gene encoding the $K_V7.2$ potassium channel[1,2]
- It is characterized by frequent daily refractory tonic seizures in the first days of life, severe developmental delays, cognitive impairment, and motor disabilities
- Seizure activity typically decreases with age, with some patients becoming seizure free or experiencing a reduced seizure burden by 3–5 years of age[3,4]
- KCNQ2 Cure Alliance (https://www.kcnq2cure.org/) is an advocacy group with a mission to improve the lives of patients with *KCNQ2*-DEE
- This online caregiver survey was conducted in collaboration with the KCNQ2 Cure Alliance to better understand the seizure burden and treatment response in this patient population

## METHODS

- A 28-question online survey was developed to obtain deidentified data from caregivers of children with *KCNQ2*-DEE located in the USA, Canada, Australia, and the UK
- The survey investigated demographics, seizure onset and frequency, prior and current use of antiseizure medications (ASMs), and caregiver perception of ASMs
- Families were recruited by targeted email outreach, a social media campaign, and an educational webinar
- All results were based on available responses and analyzed descriptively

**ACKNOWLEDGMENTS** We thank the patients and their families for their participation in this survey. Medical writing support was provided by Robin Smith, PhD, of The Curry Rockefeller Group, LLC (Tarrytown, NY), and was funded by Xenon Pharmaceuticals Inc.

**FUNDING** This study was funded by Xenon Pharmaceuticals Inc.

**DISCLOSURES** Cynthia Harden, Celene Grayson, Alix Helper, Constanza Luzon Rosenblut, and Noam Butterfield are employees of and own stock or stock options in Xenon Pharmaceuticals Inc. Jim Johnson, Caroline Loewy, and Scotty Sims serve on the KCNQ2 Cure Alliance Board of Directors. The KCNQ2 Cure Alliance receives funds from Xenon for projects and events, but not directly for this caregiver survey. John J. Millichap reports royalties from Up-To-Date; consulting fees from Eisai, Xenon, Biomarin, Greenwich, Praxis, Neurelis, Neurocrine, and Biohaven; and grants from NIH.

**REFERENCES** **1.** Miceli F, et al, eds. KCNQ2-*Related Disorders*. GeneReviews; 2010 [Updated 2022]. **2.** Morrison-Levy N, et al. *Pediatr Neurol*. 2021;116:85-94. **3.** Millichap JJ, et al. *Neurol Genet*. 2016;2(5):e96. **4.** Olson HE, et al. *Ann Neurol*. 2017;81(3):419-429.

## RESULTS

### Demographics

- 72 caregivers completed the survey and 55 were included in this analysis (**Table 1**)

**Table 1. Demographics of Survey Population**

| | |
|---|---|
| **Data Available** | • 72 complete responses, 55 included in analysis<br>• Exclusions as follows:<br>– 7 non–English-speaking origin<br>– 6 known gain-of-function variants<br>– 4 atypical clinical presentation |
| **Locations, n (%)** | • USA, 35 (64%)<br>• Australia, 7 (13%)<br>• United Kingdom, 7 (13%)<br>• Canada, 6 (11%) |
| **Patient Age, n (%)** | • 20 (36%) <4 years<br>• 35 (64%) ≥4 years |
| ***KCNQ2* Gene Variants, n (%)** | • Patients with a variant reported 1×, 30 (55%)<br>• Patients with variant reported >1×, 14 (25%)<br>• No variant reported, 11 (20%) |

- The majority of patients (64%) were ≥4 years of age
- A total of 35 *KCNQ2* gene variants were reported
  - 30 variants were reported in 1 patient each and 5 were reported in >1 patient

### Seizure Onset

- Seizure onset was reported within the first 2 days of life for 91% of patients (50/55) and within the first 5 days of life for the remaining 9% of patients (5/55; **Figure 1**)
- There was a high seizure burden at onset, with 58% (32/55) of patients experiencing >10 seizures per day, and 98% (54/55) experiencing at least daily seizures (**Figure 2**)

**Figure 1. Age at Seizure Onset**

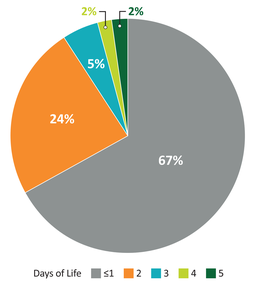
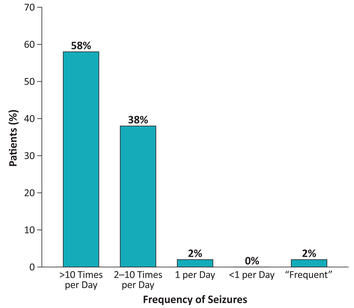


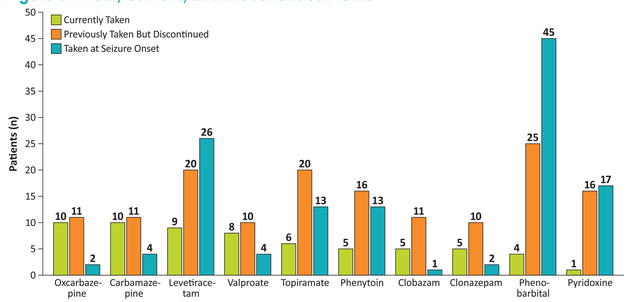

**Figure 2. Frequency of Seizures at Onset**




### ASMs

- Most patients were initially treated with phenobarbital or levetiracetam (**Figure 3**)
- Phenobarbital and levetiracetam were also the ASMs most discontinued, along with topiramate

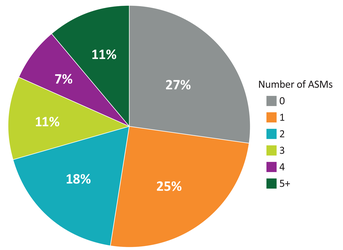
**Figure 3. Initial, Current, and Discontinued ASMs**




*ASM, antiseizure medication. Note: A single patient could report multiple ASMs.*

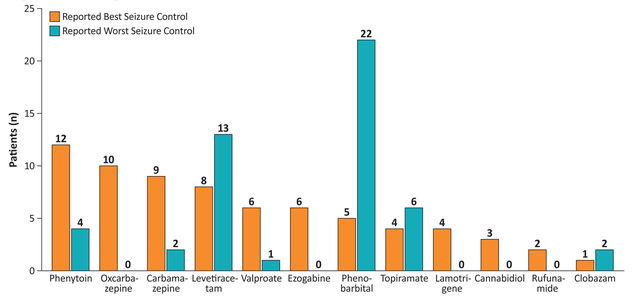
- The currently taken ASMs used most frequently were oxcarbazepine and carbamazepine
- 47% of patients (26/55) were currently taking ≥2 ASMs, 25% (14/55) were taking monotherapy, and 27% (15/55) were not currently taking an ASM (**Figure 4**)
- Caregivers (n=31) reported that the sodium channel blockers phenytoin, oxcarbazepine and carbamazepine were the best ASMs for seizure control (**Figure 5**)

**Figure 4. Number of Currently Taken ASMs**




*ASM, antiseizure medication.*

**Figure 5. Caregiver Perceptions of Best and Worst ASMs**



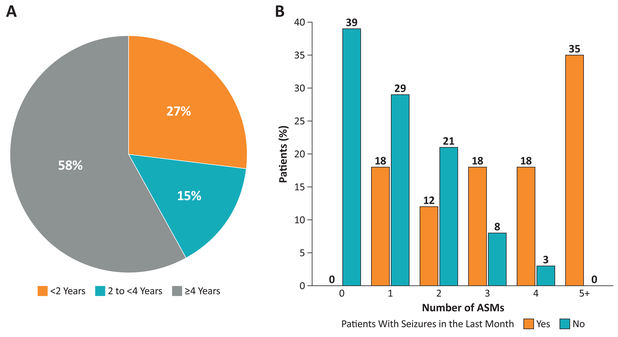

*Note: A single patient could report >1 best and worst ASM. ASM, antiseizure medication.*

- The 2 medications that most patients received as initial treatment, phenobarbital and levetiracetam, were also reported by the caregivers as the worst ASMs for seizure control

### Current Seizure Burden and Treatment Regimens

- At the time of the survey, the current seizure frequency ranged from no seizures to several seizures per day
- 47% (26/55) of patients had experienced seizures within the past 6 months; the majority (58%, 15/26) of these patients were ≥4 years of age (**Figure 6A**)

**Figure 6. A, Age of Patients With Seizures Reported in Past 6 Months; B, Current Seizure Burden and Number of ASMs**




*ASM, antiseizure medication.*

- In patients reporting seizures in the past month, more than half (53%) were taking ≥4 ASMs (**Figure 6B**)

## CONCLUSIONS

- The significance of these caregiver survey results is that *KCNQ2*-DEE imposes a considerable seizure burden at disease onset, and that seizures persist in almost half of the patients, including in patients ≥4 years of age
- Caregivers described dissatisfaction with current treatment options, with the medications frequently used at disease onset rated by caregivers as the worst for seizure control and the most often discontinued
- A substantial portion of patients still experience seizures requiring 5 ASMs
- There is a significant unmet medical need for better treatments for seizures in patients with *KCNQ2*-DEE

Poster No. 1.372 | American Epilepsy Society Annual Meeting | Nashville, TN | December 2–6, 2022

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