Genetic Mutations and Related Epileptic Encephalopathies

- Caused by single gene de novo mutations in voltage gated ion channels
- Severe phenotypes characterized by frequent refractory seizures, severe developmental delays, autistic features, motor disabilities, and increased SUDEP risk
- Selective ion channel modulators may directly target disease causal gene, with potential to treat epileptogenesis and improve long term outcomes
- Mutations in KCNQ2 are amongst the most common resulting in pediatric epilepsies

RESULTS

Preliminary Demographics and Seizure Burden of Survey Patients

Demographics

- Data available: 68 complete survey responses received
- 17 exclusions from preliminary analysis as follows:
  - 7 from non-IRB approved jurisdictions
  - 6 with known gene-of-function variants
  - 4 with atypical phenotype

Locations (n)

- USA (32); Canada (5); UK (7); Australia (7)

Presents during first week of life

- 6 with known gain
- 4 with atypical phenotype

- 61% had more than 10 seizures per day

EIEE was reported to be well tolerated by survey respondents

ELEF

- Caregivers reported children took ezogabine for both seizure control and other potential benefits (behavioural and developmental), and reported benefits for both

Caregiver Narratives: Ezogabine-specific Effects

- “Cognitive improvements documented weekly by therapists who did not know the child was on Potiga and [by] parent observation”
- “Child was not having seizures, but starting Potiga coincided with improvements in EEG and attention/awareness.”
- “Started at 3 months old, achieved seizure freedom around 5 months old for approximately 6 months when infants started to walk. With seizure freedom, my child began to respond and get stronger”
- “We thought Potiga was the best medication for cognitive improvements. Potiga was never taken for seizure control as seizures had stopped and EEG was normal.”
- “Ezogabine used to treat epilepsy for his longer seizures which stopped after 2 months which also stopped Potiga. We’ve also noticed good improvements with Trileptal and Depakene which he is currently taking.”

Caregiver Narratives: Seizure Control and Quality of Life

- Which medication or combination of medications or treatments (current or previous) do you consider to be the best for your child’s overall quality of life and why?
- Which medication or combination of medications or treatments (current or previous) do you consider to be the best for your child’s seizures and why?

METHODS

- We performed an on-line survey of caregivers to better understand the symptoms and their experiences with KCNQ2-DEE and perceived gaps in pharmacologic treatment
- The 28-question survey, was conducted by Xenon in collaboration with The KCNQ2 Cure Alliance
- Survey included items such as demographics, comorbidities, seizure onset and frequency, prior and current antiepileptic medication (ASM) use, and history of ezogabine use
- Families were recruited by targeted email outreach, social media campaign and an educational webinar
- Survey responses collected over a three-week period in 2019

CONCLUSIONS

- Survey was informative regarding clinical trial design and improved knowledge of disease course and pharmacologic treatment from a caregivers’ perspective
- Survey highlighted significant seizure burden at disease onset, with a significant proportion of patients continuing to experience seizures over the age 4 years
- Caregivers reported children took ezogabine for both seizure control and other potential benefits (behavioural and developmental), and reported benefits for both
- Ezogabine was reported to be well tolerated by survey respondents
- Study limitations include retrospective reporting with possible memory bias as well as possible data overlap with published cases

Next Steps:

- Phase 3 clinical trial in KCNQ2-DEE expected to initiate by the end of 2020

An Online Survey of Caregivers of Patients with KCNQ2 Developmental and Epileptic Encephalopathy (KCNQ2-DEE)

Celine Grayson1, Noam Butterfield1, Cynthia Harden1, Constanza Luzon1, Alix Helper1, Caroline Loewy3, Jim Johnson2, Scotty Sims2, John J. Millichap3, Dennis J. Dubog4, Simon N. Pimstone3, Ernesto Ayacdi1

1Xenon Pharmaceuticals Inc., 2KCNQ2 Cure Alliance, 3Ann and Robert H. Lurie Children’s Hospital of Chicago; 4Children’s Hospital of Philadelphia