SURVEY METHODS AND RESULTS

• We performed a caregiver survey to obtain additional phenotypic information regarding history of KCNQ2-DEE disease as well as Anti-Seizure Medication (ASM) use, with a focus on ezogabine

• Demographics, comorbidities, seizure onset and frequency, ASM use, and history of ezogabine use

• 30 question survey, conducted by Xenon in collaboration with the KCNQ2 Cure Alliance for KCNQ2 syndrome

• Implemented by M3 Global research and reviewed and approved by Vertex Independent Review Board

• Families recruited by targeted email outreach, social media and an educational webinar

• Survey responses collected over a three-week period for each syndrome in late 2019

Preliminary Demographics and Seizure Burden of Survey Patients

Demographics

Data available
67 complete responses for analysis; Exclusions as follows:
• 8 non-English speaking
• 6 known GOF
• 1 suspected phenotype

Locations (n)
USA (31); Canada (5); UK (7); Australia (7)

Patient Age, n (%) 18 (36%) younger than 4 years 32 (64%) older than 4 years

Age of seizure onset

Birth = 4.6% of seizures; Most common associated with severe developmental delay

Present with language/social impairment, outbursts, repetitive and self-injurious behaviours

Motor disabilities

Seizures were of 4 years of age, can occur in clusters thereafter

Inherited autonomic dysfunction/autonomic \n
Inherited autonomic dysfunction/autonomic

drugs, mutations cause Benign Familial Neonatal/Seizures

Frequently present with multiple seizures without overt developmental delay

KCNQ2 Epilepsy Panel Screening

Scottish national cohort study (Symonds et al., Brain 2019)

Birth rate of pathogenic KCNQ2 variants 1/17,000

Dravet Syndrome 1/2,200 births

9411 Inplex epilepsy panel tests (Trutty et al., Epilepsia 2019)

219 subjects with KCNQ2 genotype (116 VUS; 103 LP/P)

Further characterization of VUS likely to identify many more variants as LP/P

Approaching Dravet Syndrome birth rate?

Approximately half of KCNQ2 variants cause DEE

40% of BNFS families reported with delayed psychomotor development (Steinlein et al., Epilepsy Research 2007)

Separate screen identified 159/8565 tests as pathogenic (Lindy et al., Epilepsia, 2018)

Dravet Syndrome 322/8565 tests

Caregiver Narratives: Ezogabine and Potiga

• Our hope is that KCN466 could represent a genetically targeted treatment that improves the lives of children living with this debilitating disease.

Caregiver Narratives: Ezogabine-Specific Effects

Did you see any improvements in your child’s seizures, behaviour or development while they were taking ezogabine? All RESPONDENTS ANSWERED “YES”

• Cognitive improvements documented (by) therapists who did not know the child was on Potiga and (by) parent

• Seizure control and developmental gains - smiling, eating by mouth.

• Seizure control coincided with improvements in EEG and attention/awareness.

Conclusions

Survey was informative regarding clinical trial design and improved knowledge of disease course from a patient/family experience

Survey identified significant proportion of patients seizing over the age of 4 years

Caregivers who have taken ezogabine for both seizure control and other reasons and reported benefits for both

Ezogabine was reported to be well tolerated by survey respondents

Study limitations include retrospective report with possible memory bias as well as possible overlap with published cases

Next Steps

• Phase 3 protocol being finalized with input from KOLs

• To initiate Phase 3 pivotal trial in 2020

Background

Seeking Novel Disease Modifying Medications for Developmental and Epileptic Encephalopathies

• Caused by single gene de novo mutations in voltage-gated ion channels

• Severe phenotypes characterized by frequent refractory seizures, severe developmental delays, autistics 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

An Online Survey of Caregivers of Patients with KCNQ2 Developmental & Epileptic Encephalopathy (KCNQ2-DEE): Focus on Ezogabine

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Informational Poster Presented at Xenon Pharmaceuticals Inc. 1

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