An Online Survey of Caregivers of Patients with SCN8A-Related Epilepsy

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Informational Poster Prepared by Xenon Pharmaceuticals Inc.

BACKGROUND

XEN901: A novel selective sodium channel inhibitor

• XEN901 developed as a precision medicine to selectively address the etiology of SCN8A-DEE
• Selective inhibition of Na\textsubscript{1.6} channel
• Does not inhibit other sodium channels
• FDA feedback supports near-term pediatric program
• On Dec. 2, 2019, Neurocrine Biosciences obtained an exclusive license to XEN901.

SURVEY OBJECTIVES AND METHODS

• A caregiver survey was performed to obtain additional phenotypic information regarding the history of SCN8A-DEE as well as Anti-Status Epilepticus Medication (ASM)
• Demographics, comorbidities, seizure onset and frequency, ASM use
• 36 question survey, conducted by Xenon in collaboration with The Cute Syndrome Foundation
• Implemented by M3 Global research and reviewed and approved by Veritas Independent Review Board
• Families recruited by targeted email outreach, social media campaign and an educational webinar
• Survey responses collected over a three-week period in late 2019

RESULTS

Spectrum of Clinical Presentation

Preliminary Demographics and Seizure Burden of Survey Patients

![Graph showing demographics and seizure burden](image)

- **Data available**: 125 complete responses for analysis; Exclusions as follows:
  - 2 non-English speaking origin
- **Locations (n=125)**: USA (93), Canada (12), UK (12), Australia (8)
- **Patient Age, n (%)**: 30 (24%) younger than 4 years, 95 (76%) older than 4 years
- **Seizure History, n (%)**: 8 (7%) report no seizure history, 13 (55%) report seizure history of more than one, generalized tonic-clonic seizure were most common initial seizure (89%), followed by focal seizures (9%)
- **Spectrum of Seizure Onset**:
  - Average age of seizure onset was 4 months, range was 1 day to 24 months
  - Initial seizure frequency (n=115): 25% had more than 10 seizures per day, 50% had between 2-10 seizures per day, 25% had 1 seizure per day
  - Current seizure frequency (n=109): 65% had seizures occur past 30 days, 75% had seizures occur past 90 days, 75% had seizures occur past 120 days

• Access to genetic testing allows identifying cause of seizures and implementation of specific treatments in many cases
• Supports patient ID for clinical studies
• Builds physician database

Response to Anti-Status Epilepticus Medications (Data From Other Studies)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Response</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levetiracetam (Keppra)</td>
<td>40% successful</td>
<td>25% seizures decreased</td>
</tr>
<tr>
<td>Sodium Valproate</td>
<td>30% successful</td>
<td>20% seizures decreased</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>25% successful</td>
<td>15% seizures decreased</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• Survey helps to improve the knowledge of disease course and phenotypic heterogeneity
• Time to genetic diagnosis from first seizure is decreasing over time
• Broad use of ASMs is apparent in this population and survey confirmed observations from previous studies that Levetiracetam (Keppra), although commonly used as a first line treatment, may not be recommended for use in SCN8A-DEE patients
• Study limitations include retrospective report with possible memory bias

Phase 2 Clinical Planning:

• Survey was informative regarding clinical trial design
• Completed development of a pediatric-specific granule formulation of XEN901
• Completed juvenile toxicology studies to support pediatric development activities
• PK study in healthy adult volunteers with the new pediatric formulation ongoing
• Neurocrine Biosciences anticipates filing an IND application with the FDA in the middle of 2020 in order to start a proposed clinical trial for XEN901 in SCN8A-DEE patients.