1. Background

- SCN2A consists of a sodium voltage-gated sodium channel, NaV1.2 that is primarily found in excitatory neurons throughout the brain.
- SCN2A is one of the genes most commonly associated with early-onset epilepsy, and has been linked to autism spectrum disorder, and developmental delays.
- SCN2A associated developmental and epileptic encephalopathy (DEE) is a condition with highly variable phenotype and extremely low prevalence (1/10,000 predicted in the United States).
- Outcomes targeting patient-important, core, common features of SCN2A-DEE are needed for future precision medicine trials (e.g., gene-targeted) to ensure eligibility of a maximum number of patients (FDA guidance 2009, 2013, 2022).

2. Study Design

- The SCN2A Clinical Trials Readiness Study (CTRS) is a longitudinal study designed with parents to assess outcomes in their children that are life-changing, life-threatening, and ultimately important to parents.
- The primary goal of the study is to prepare the SCN2A community with necessary outcomes measures for precision medicine clinical trials.
- As part of the Inception pilot study, 10 of the families also participated in a Goal Attainment Scaling (GAS) process in which parents identified 3 critically important goals of their choice for their child. Communication was overwhelmingly chosen as a domain of importance by parents and caregivers.

3. Patient Demographics

- 65 families from Ontario, Canada, 32 recruited within 30 days of diagnosis, 33 recruited within 1 month of diagnosis.
- 12% children with epilepsy.
- 34% children with autism spectrum disorder.
- 27% children with intellectual disability.
- 63% children with behavior problems.
- 24% of children with anxiety or depression.
- 38% of children with language or communication delays.

4. Choosing the Right VABS-3 Scoring for SCN2A GSV and SS

- Standard Scores (SS), which compare an individual to same-aged individuals in the population, are the common approach using instruments such as the Vineland. GSV and VABS-3 are standardized to a mean of 50 and standard deviation of 1.5. They are sensitive for detecting with age in severely affected groups such as SCN2A-DEE.

5. Vineland – 3

- GSV Show Better Range and Few Floor Effects Relative to SS

6. Initial Proof of Concept

- VABS-3 GSV More Sensitive than SS in SCN2A

- GSV show better discrimination across distinct levels of impairment. Cross-sectionally, they discriminate better across levels of important epilepsy-related factors. These findings suggest the GSV may be more sensitive than SS to changes related to these and perhaps other key factors.

7. CTRS Conclusions

- Comparison of subdomains within the two scales (VABS-3 and GSV).

References

3. AED Poster # 3-452 The Feasibility of Goal Attainment Scaling in SCN2A-associated Neurodevelopmental Disorders. Chapman C. et al. 2022