**PL31. Number needed to treat (NNT) with fenfluramine to achieve a clinically meaningful reduction in convulsive seizure frequency in patients with Dravet syndrome**

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**Introduction**
- Assessments of group responses to placebo and active treatment in clinical antiepileptic drug (AED) trials are regulatory requirements, but decisions in clinical practice are made on individual-patient basis.
- Use of number needed to treat (NNT) can assist in translating clinical trial data to clinical practice.
- Selecting the right endpoints from which to calculate NNT is critical for them to be useful in informing individual decision-making.

**Objectives**
- The post hoc analysis used data from phase 3 and long-term extension studies of fenfluramine for the treatment of Dravet syndrome in pediatric patients (NCT02682272, NCT02082863, NCT02528988, NCT02625143).
- To determine clinically meaningful changes in monthly convulsive seizure frequency (MCSF) by evaluating the association between seizure reduction and improvement ratings on the Clinical Global Impression of Improvement ( CGI-I) scale as a metric determining clinically meaningful changes in MCSF.
- To determine the NNT with fenfluramine to achieve “clinically meaningful” MCSF reductions in a pediatric Dravet syndrome population by CGI-I ratings and performance on the Behavior Rating Inventory of Executive Function (BRIEF).
- Reliable Change Index (RCI) was used to determine the magnitude of the change in BRIEF score that would be outside “normal,” defined as a change in 1.5 SDs.

**Methods**
- Both the CGI-I and BRIEF scores were analyzed using the RCI to determine if the change was a reliable change or a chance occurrence.
- Statistical approaches were used to determine which degree of change in MCSF was correlated with those definitions of clinically meaningful improvement.

**Results**
- Of 119 total patients in Study 1 with MCSF data at Visits 12–14 weeks, 68% responded to fenfluramine, and 62% had a RCI-defined improvement.
- Patients at Times of Analysis (Table 1): NNT calculations using ROC-a
derived MCSF cut points at Week 14 (Table 2: Figure 1).

**Conclusions**
- NNTs based on clinically meaningful endpoints provide complementary information to group mean changes often reported in clinical trials in understanding the efficiency of treatment to achieve this level of results.
- For every 2 to 3 patients with Dravet syndrome treated with fenfluramine, 1 patient achieved ≥50% or ≥75% MCSF reduction compared with placebo (large treatment effect, Cohen’s d=0.8).
- FFA’s NNT results compare favorably to similar studies of other therapies in Dravet syndrome NNT at 4 and for ≥30% response [12] and other forms of refractory epilepsy [13-17].
- Lower NNTs for a given treatment translate to fewer non-responders and lower associated burden on patients and their families.

**References**
- Perucca E. JAMA Neurol. 2017;83:90-100.
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**Disclosures**
- None.

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**Figure 1. NNT by Level of Improvement on Caregiver CGI-I (ROC Analysis)**

- **Figure 2. Proportion of Patients With Significant, Clinically Meaningful Improvement (≥10 Point Change in Scores) in BRIEF/2 Index/Composite Scores (Post-randomization Baseline to Year 1)**

**Figure 3. Fenfluramine NNT for ≥75% (Profound) Reduction in Convulsive Seizure Frequency**

- **Table 1. NNT Interpretation**

- **Table 2. NNT Analysis Using ROC-Derived MCSF Cut Points at Week 14**

- **Table 3. ROC-Derived Thresholds for Clinically Meaningful Change in Seizure Frequency at Week 14**