**BACKGROUND**

- Developmental and epileptic encephalopathies (DEEs) are a severe group of neurodevelopmental disorders characterized by seizures and abnormal electroencephalogram patterns that negatively impact development.
- DEEs include, but are not limited to, West syndrome, Lennox-Gastaut syndrome (LGs), and Dravet syndrome. DEEs onset before 18 months have an incidence of 1 in 2000 live births.
- Seizures are generally refractory to antiseizure medications (ASMs) and oral administration of ASMs can be difficult due to behavioral and cognitive impairments.
- Children with DEEs are medically fragile and have multiple comorbidities including intellectual disabilities and cognitive impairment, attention deficit spectrum disorder (ASD), and sleep disturbance, which further increase disability.2-4
- Cannabidiol (CBD) is the main noneuphoric cannabinoid of the Cannabis plant, and an oral formulation is approved to reduce seizures in DEE syndrome of LGs and Dravet syndrome.5
- Zynerba is a pharmaceutical manufacturer transdermal CBD gel currently in clinical development for reduction of seizures in DEEs, and improvement in behavioral symptoms in patients with ASD and Fragile X Syndrome (FXS).

**OBJECTIVES**

- To evaluate the efficacy of ZYN002 in children and adolescent patients with DEEs.
- To evaluate the tolerability of ZYN002 in children and adolescent patients with DEEs.
- An exploratory analysis to evaluate efficacy of ZYN002 in DEE patients with ASD.

**METHODS**

**TRIAL DESIGN AND TREATMENT**

- ZYN002-CL-025 (BELIEVE) was an open-label, two-center, multiple-group, randomized, controlled study.
- An exploratory analysis to evaluate efficacy of ZYN002 in DEE patients.
- To evaluate the efficacy of ZYN002 in children and adolescent patients with DEEs.
- To evaluate the tolerability of ZYN002 in children and adolescent patients with DEEs.
- An exploratory analysis to evaluate efficacy of ZYN002 in DEE patients with ASD.

**PATIENTS**

- **Key inclusion criteria**
  - Male and female patients aged 3 to <18 years
  - Diagnosis of DEE as defined by International League Against Epilepsy classification
  - Stable regimen of 1 to 4 ASMs that was maintained throughout the entire study
  - History of regression, slowing, or plateau in at least one seizure type
  - Male and female patients aged 3 to <18 years
  - Diagnosis of DEE as defined by International League Against Epilepsy classification

- **Key exclusion criteria**
  - Use of any topically applied or - CBD-containing product ≤12 weeks before screening

- **Study groups**
  - Treatment with a strong inhibitor/inducer of CYP3A4
  - Treatment with a strong inhibitor/inducer of CYP3A4

- **Screening**
  - FIAS, FBTCS) + AT, ES, FAM

- **Baseline**
  - Recorded FIAS and or TCS in Baseline

- **Weeks 4 to 26**
  - ≤25 kg: 125-250 mg
  - ≥25 kg: 250-375 mg

- **Period A**
  - Completed 12 months

- **Period B**
  - Withdraw consent at Week 42

- **Completed 12 months**
  - 28 completed Period A and 28 completed through Month 12 of Period B

**RESULTS**

- Of 48 patients who enrolled in ZYN002-CL-025, 40 patients completed Period A and 28 completed through Month 12 of Period A (Table 1).

**Efficacy**

- Over the 12-month treatment period, the median percentage reduction from baseline in monthly frequency of FIAS and TCS ranged from 44% to 74% (Figure 1).
- When analyzed by seizure type, median reductions from baseline in monthly frequency of FIAS and TCS were 100%, 83% and 59%, respectively. At Month 12, the median reductions for FIAS, GTCS and TCS were 100%, 83% and 59%, respectively.

**Safety**

- Zynerba was well tolerated in BELIEVE.4
- Most treatment-emergent adverse events (TEAEs) (any event, whether unrelated or related to study drug) were mild or moderate.
- There were no serious adverse events reported by 14 patients over the 72-week treatment period, of which two (lower respiratory tract infection and status epilepticus) were considered possibly drug-related.
- One patient, with a history of ketosis prone, discontinued study medication due to an increase in ketonemia, 4.5 mmol/L (3.0-12.0 mmol/L).

**Conclusions**

- ZYN002 was well tolerated in BELIEVE.
- Most treatment-emergent adverse events (TEAEs) (any event, whether unrelated or related to study drug) were mild or moderate.
- There were no serious adverse events reported by 14 patients over the 72-week treatment period, of which two (lower respiratory tract infection and status epilepticus) were considered possibly drug-related.
- One patient, with a history of ketosis prone, discontinued study medication due to an increase in ketonemia, 4.5 mmol/L (3.0-12.0 mmol/L).

**REFERENCES**

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