INTRODUCTION

Dravet syndrome (DS) is a rare, severe, and often drug-resistant epilepsy syndrome—

- Incidence is 1 in 20,000 to 1 in 40,000 live births
- Typically presents as a developmental epileptic encephalopathy in infancy
- SCN1A mutation found in approximately 85% of DS patients

Fenfluramine has been reported to have long-term beneficial activity in a cohort of DS patients in Belgium.

Here we describe the continuing observations from a prospective, open-label study of low-dose fenfluramine in a new cohort of DS patients with initiation of a standardized protocol of assessments.

METHODS

Patients from 6 months to 50 years of age with a diagnosis of DS were eligible to enroll

Patients with cardiovascular disease, including drug-treatment hypertension and cardiac valvulopathy, were excluded.

Following a 3-month run-in period, fenfluramine was added to each patient’s current anti-epileptic drug regimen at a dose of 0.1 to 0.5 mg/kg/day (maximum 30 mg/day).

The incidence of major motor seizures (tonic, clonic, tonic-clonic, atonic, and myoclonic seizures lasting >30 sec) in both the run-in and treatment periods was assessed via a seizure diary.

Periodic echocardiographic examinations during the treatment period were used to assess cardiovascular safety.

RESULTS

Fifteen patients (ages 1.2 to 29.8 years) enrolled in the study (Table 1) and were treated with fenfluramine for a median duration of 3.0 years (range, 0.1 to 7.2 years) (Table 2).

Median frequency of major motor seizures was 2.4 per month in the run-in period with a median reduction of 87% with a range of 5% to 100% (Table 2 and Figure 1).

The most common adverse events were anorexia (n=11), sleepiness (n=9), fatigue (n=8), mood changes (n=8), sleep problems (n=3), headache (n=2), and thrombocytopenia (n=1).

Most patients demonstrated a reduction in seizure frequency during the treatment period with a median reduction of 87% with a range of 5% to 100% (Table 2 and Figure 1).

CONCLUSIONS

The effectiveness of low-dose fenfluramine as an add-on therapy for DS in this new cohort supports previous findings.

Fenfluramine exhibited a favorable tolerability profile in this patient population with no echocardiographic or clinical evidence of cardiac valvulopathy or pulmonary hypertension.

The efficacy and safety of fenfluramine in this DS cohort were recently replicated in 2 randomized controlled trials demonstrating a superior reduction in convulsive seizure frequency vs placebo.

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REFERENCES


DISCLOSURES

AS Consultant/advisor: Brabant, Zogenix.
AGS Employee: Zogenix; Stock ownership: Zogenix.
LL Consultant/advisor and Speaker: LivaNova, Novartis, Ovid, Shire, UCB, Zogenix.
BC Consultant/advisor and Investigator: Brabant, Novartis, UCB, Zogenix.

Dr. Lieven Logae and Beren Caeulemans and the KU Leuven University/Antwerp University Hospital may financially benefit from a royalty arrangement if Zogenix is successful in marketing its product fenfluramine, that is related to this research. The terms of this arrangement have been reviewed and approved by the KU Leuven University/ Antwerp University Hospital.