Effect of ZX008 (Fenfluramine HCl Oral Solution) on Total Seizures in Dravet Syndrome in a Phase 3 Clinical Trial

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INTRODUCTION

Dravet syndrome is a rare, severe, pediatric-onset, treatment-resistant epileptic encephalopathy

– Characterized by different types of seizures, and neurodevelopmental and psychomotor disabilities
– Current treatment most commonly involves polypharmacy with multiple antiepileptic drugs (AEDs)
– 45% of patients continue to experience ≥4 seizures per month despite multiple AED regimens (1)

ZX008 (fenfluramine hydrochloride oral solution) has recently been shown to substantially reduce the frequency of convulsive seizures (defined as tonic-clonic, tonic, clonic, hemiconic, tonic-clonic, and tonic motor seizures) in patients with Dravet syndrome compared with placebo in a phase 3 clinical trial (Study 1) (2)

– Here we present a post hoc analysis of the effect of ZX008 in enrolled subjects
– In addition to the convulsive seizures listed above, the following seizure types were also reported in some subjects (n=48): absence or atypical absence, myoclonic, atonic, and focal without clear observable motor signs

METHODS

Study 1: (Figure 1) It is a prospective merged analysis of two identical double-blind, placebo-controlled, fixed-dose clinical trials

Figure 1. Schematic representation of Study 1.

RESULTS

Baseline demographics and seizure frequencies are presented in Table 1

Table 1. Demographics and Baseline Seizure Frequency

Table 2 presents the median percentage reductions for seizure subtypes during treatment in Study 1

Table 2. Median Percentage Reduction from Baseline in Seizure Subtypes during Treatment in Study 1

Figure 2. Median percentage reduction from baseline in (A) other seizure subtypes and (B) total seizure frequency per 28 days during the combined titration and maintenance periods.

ZX008 significantly reduced total seizure frequency in a dose-related manner (Figure 2)

CONCLUSIONS

– ZX008 significantly improved both total and convulsive seizure frequency in this phase 3 trial for adjunctive treatment of seizures in subjects with Dravet syndrome
– Despite large observed reductions in the placebo group, highlighting the difficulty in enrolling these other seizure subtypes, subjects treated with ZX008 during titration (30 mg/d) demonstrated a greater median reduction in seizure frequency compared with placebo-treated subjects
– ZX008 was generally well tolerated, and no echocardiographic signs of cardiac valvulopathy or pulmonary hypertension were observed in any subject during the study
– ZX008 may represent an important and effective new treatment option for patients with Dravet syndrome

REFERENCES

4. Zogenix, Inc., Emeryville, CA, USA.

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