Safety and Effectiveness of Adjunctive Fenfluramine in an Open-Label Extension Study of Children (Under 6 Years Old) With Dravet Syndrome

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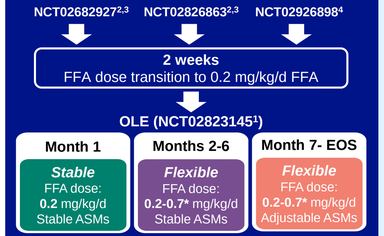
QUESTION

- What is the safety and effectiveness profile of long-term treatment with fenfluramine (FFA) for seizures associated with Dravet syndrome (DS) in patients 2 to <6 years old?

METHODS

- Detailed methods have been reported previously[1]
- Final analysis of add-on FFA in patients with DS aged 2 to <6 in the open-label extension (OLE)
- Effectiveness: change in monthly convulsive seizure frequency (MCSF) vs baseline
- Clinical Global Impression – Improvement (CGI-I) ratings used as measure of global functioning

Study Design



*Maximum daily dose, 26 mg/d without stiripentol; 17 mg/d with stiripentol.
ASM, antiseizure medication; FFA, fenfluramine; OLE, open-label extension.

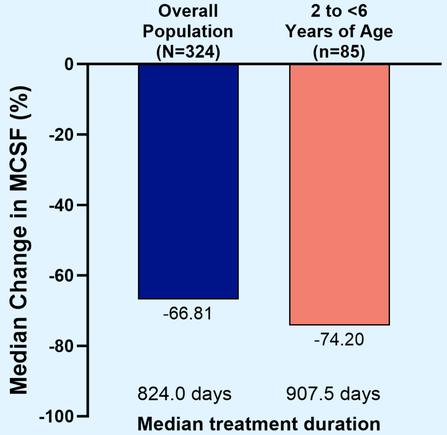
RESULTS

Patient Demographics and Safety in Patients 2 to <6 Years of Age

Patients Enrolled	N=92
Age, years	
Mean ± SD	3.5 ± 1.1
Sex, n (%)	
Male	51 (55.4)
Female	41 (44.6)
Patient disposition, n (%)	
Completed all study visits	12 (13.0)
Reasons for discontinuation	
Transition to other study / commercial product	61 (66.3)
Lack of effectiveness	10 (10.9)
Withdrawal by subject	5 (5.4)
Death (SUDEP)[a]	2 (2.2)
Physician decision	1 (1.1)
Other	1 (1.1)
Duration of treatment with FFA in OLE, days	
Mean ± SD	831.4 ± 307.0
Median (min, max)	907.5 (81, 1280)
Patients reporting ≥1 TEAE, n (%)[b]	
Pyrexia	42 (45.7)
Nasopharyngitis	38 (41.3)
Upper respiratory tract infection	24 (26.1)
Ear infection	20 (21.7)
Vomiting	17 (18.5)
Gastroenteritis	17 (18.5)
Viral infection	14 (15.2)

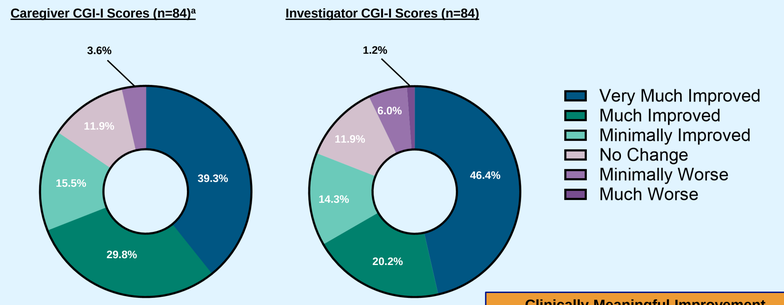
Demographic and safety data were collected from the safety population (patients between 2 to <6 years old receiving ≥1 dose FFA).
[a]Deaths were not treatment related.
[b]TEAEs that were observed in ≥15% of enrolled patients in the safety population.
FFA, fenfluramine; OLE, open-label extension; SD, standard deviation; SUDEP, sudden unexpected death in epilepsy.

Median MCSF Percentage Change During OLE, Overall vs Patients 2 to <6 Years of Age (mITT, n=85)



mITT population: patients 2 to <6 years old with RCT baseline data who received ≥1 dose FFA with ≥30 days of valid seizure data during the OLE.
FFA, fenfluramine; MCSF, median convulsive seizure frequency; mITT, modified intent-to-treat; OLE, open-label extension; RCT, randomized controlled trial.

Caregiver and Investigator CGI-I Scores at Final Visit (mITT, n=84)



Clinically Meaningful Improvement
Scores of "Very Much Improved" or "Much Improved" on CGI-I

mITT population: patients 2 to <6 years old with RCT baseline data who received ≥1 dose FFA with ≥30 days of valid seizure data during the OLE.
There were no responses of "very much worse" by caregivers or investigators.
[a]There were no responses of "much worse" (0%) on CGI-I by caregivers.
CGI-I, Clinical Global Impression—Improvement; FFA, fenfluramine; mITT, modified intent-to-treat; OLE, open-label extension; RCT, randomized controlled trial.

CONCLUSIONS

- FFA treatment in patients with DS aged 2 to <6 was well tolerated with no new safety signals or observations of valvular heart disease or pulmonary arterial hypertension up to 3 years
- FFA treatment was also associated with meaningful reductions in MCSF and improvements in caregiver and investigator reports of global functioning that may reflect seizure and non-seizure benefits

References

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This is a summary of the main findings.

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