Safety and Effectiveness of Adjunctive Fenfluramine in an Open-Label Extension Study of Patients With Dravet Syndrome

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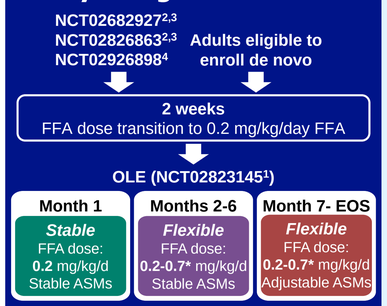
QUESTION

- Does long-term treatment with fenfluramine (FFA) for seizures associated with Dravet syndrome (DS) support an acceptable safety and tolerability profile and long-term effectiveness?

METHODS

- Detailed methods have been reported previously[1]
- Long-term safety was monitored in patients receiving ≥1 dose FFA
- FFA effectiveness was measured by the change in MCSF versus baseline in the modified intention-to-treat population
- CGI-I scores were used as a measure of global functioning

Study Design



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

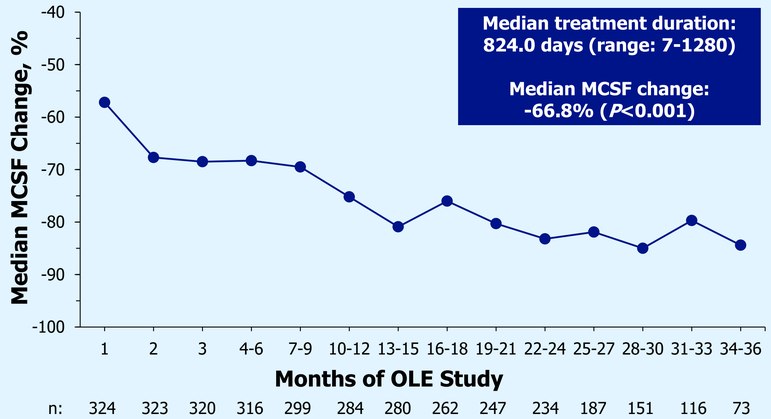
RESULTS

Safety Data Summary

Safety population, n (%)	N=374[a]
Patients experiencing ≥1 TEAE	367 (98.1)
Non-cardiovascular TEAEs occurring in ≥15% of patients	
Pyrexia	112 (29.9)
Nasopharyngitis	104 (27.8)
Decreased appetite	100 (26.7)
Blood glucose decreased	89 (23.8)
Diarrhea	73 (19.5)
Upper respiratory tract infection	66 (17.6)
Seizure	58 (15.5)
Patients experiencing ≥1 SAE	99 (26.5)
Patients experiencing ≥1 SAE related to treatment	9 (2.4)
Any TEAE that led to discontinuation of treatment	13 (3.5)
Any TEAE resulting in death[b]	3 (0.8)
Any TEAE resulting in death related to treatment	0

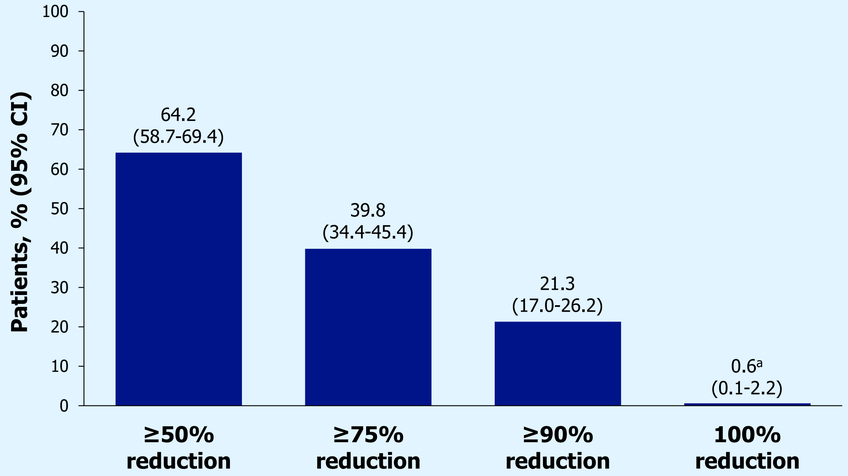
[a]One enrolled patient did not receive treatment and was excluded from the safety population.
[b]All deaths were sudden unexpected death in epilepsy, not related to FFA treatment.
OLE, open-label extension; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Median Percent MCSF Change Throughout OLE



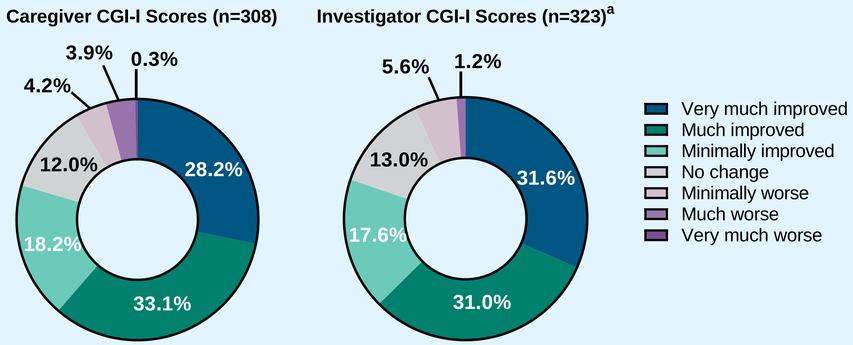
MCSF, monthly convulsive seizure frequency; OLE, open-label extension.

Patients Meeting MCSF Reduction Thresholds of Interest Throughout OLE



[a]Two patients were seizure free for 81 days and 456 days, respectively.
MCSF, monthly convulsive seizure frequency.

Caregiver and Investigator CGI-I Scores at Final Visit



[a]There were no responses of "very much worse" by investigators.
CGI-I, Clinical Global Impression of Improvement.

CONCLUSIONS

- FFA treatment for up to 3 years in patients with DS was well tolerated, with no new or unexpected safety signals identified, and showed clinically significant, durable reductions in MCSF
- Global functioning scores by caregivers and investigators showed a majority of patients were "much improved" or "very much improved" from FFA treatment

References

1. Sullivan J, et al. *Epilepsia.* 2020;61(11):2396-404.
2. Lagae L, et al. *Lancet.* 2019;394(10216):2243-54.
3. Sullivan J, et al. *Epilepsia.* 2023;64(10):2653-66.
4. Nabbout R, et al. *JAMA Neurol.* 2020;77(3):300-8.

Acknowledgements

UCB Pharma-sponsored. The authors acknowledge Tom Grant, PhD (UCB Pharma, Slough, UK), for managing the development of the poster, and Eric Scocchera, PhD, and Scott Bergfeld, PhD (PharmaWrite, LLC, Princeton, NJ, USA), for writing assistance, which was funded by UCB Pharma.

Disclosures (for author-specific disclosures, please see full poster):

Acadia, ActioBiosciences, Advicenne, Amicus, Anavex Life Sciences, Aquestive, Arvelle, Ascenseuron, Atheneum Partners, Australian Academy of Health and Medical Sciences, Australian Council of Learned Academies Ltd., Bellberry Ltd., Biocodex, Biogen, BioMarin, Biopharm, BridgeBio, California Cannabis Enterprises (CCE), Care Beyond Diagnosis, Centers for Disease Control and Prevention (CDC), Cerebral Therapeutics, Cerecin Inc., Cereval Therapeutics, Chiesi, Dravet Syndrome Foundation, Elsai, Empatica, Encoded Therapeutics, Epihunter, EpiMinder Inc, Epilepsy.com, Epilepsy Study Consortium, Epygenyx, ES-Therapeutics, GeneMedicine, GlaxoSmithKline, GW Pharma (now Jazz Pharmaceuticals), Hitch Biosciences, Knopp Biosciences, Liva Nova, Longboard Pharmaceuticals, Marinus, Multidisciplinary University Research Initiative (MURI), MHLW Research program on rare and intractable diseases, National Institute of Mental Health (NIMH), National Institute of Neurological Disorders and Stroke (NINDS), National Science Foundation (NSF), NEL, Neurocrine BioSciences, Nutricia, Novartis, PhiFundVentures, Ovid Therapeutics, QstateBiosciences, Receptor Life Sciences, Regel Biosciences, Roche, Rogcon, Sanofi, SilverSpike, Script Biosciences, Shire, Stoke, Takeda Pharmaceuticals, TevardBiosciences, Tilray, UCB Pharma, Ultragenyx, Upsher Smith, Xenon Pharmaceuticals, Zogenix (now a part of UCB) and Zynerba Pharmaceuticals.

This is a summary of the main findings.

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