Fenfluramine Increases Seizure-Free Days in Patients With Lennox-Gastaut Syndrome

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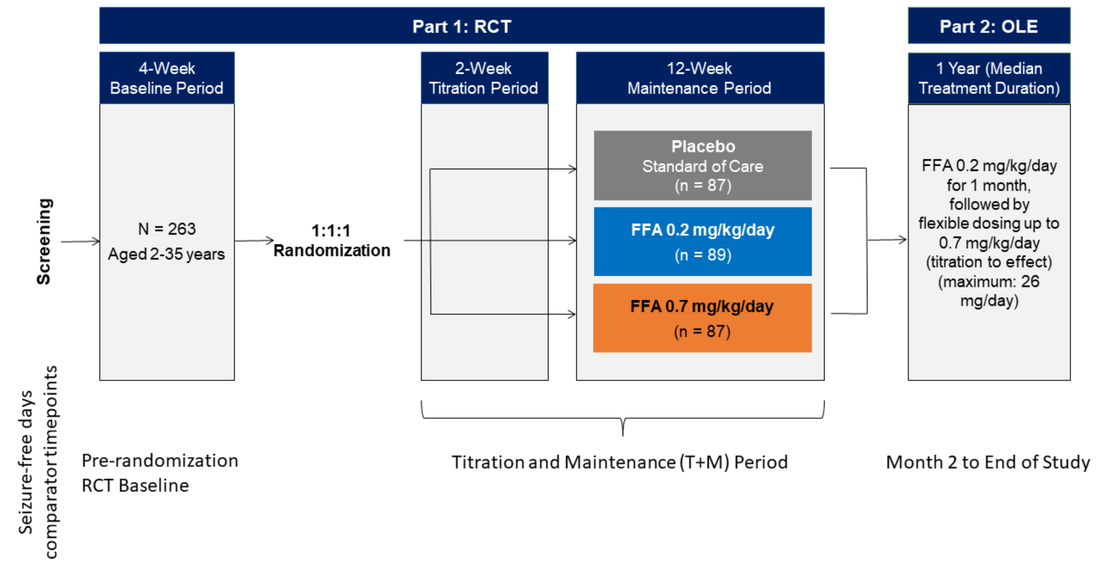
Question

How does the percentage of seizure-free days differ between patients with Lennox-Gastaut syndrome treated with standard of care (placebo arm) compared to escalating doses of fenfluramine (FFA)?

Investigation

Figure 1. Study design



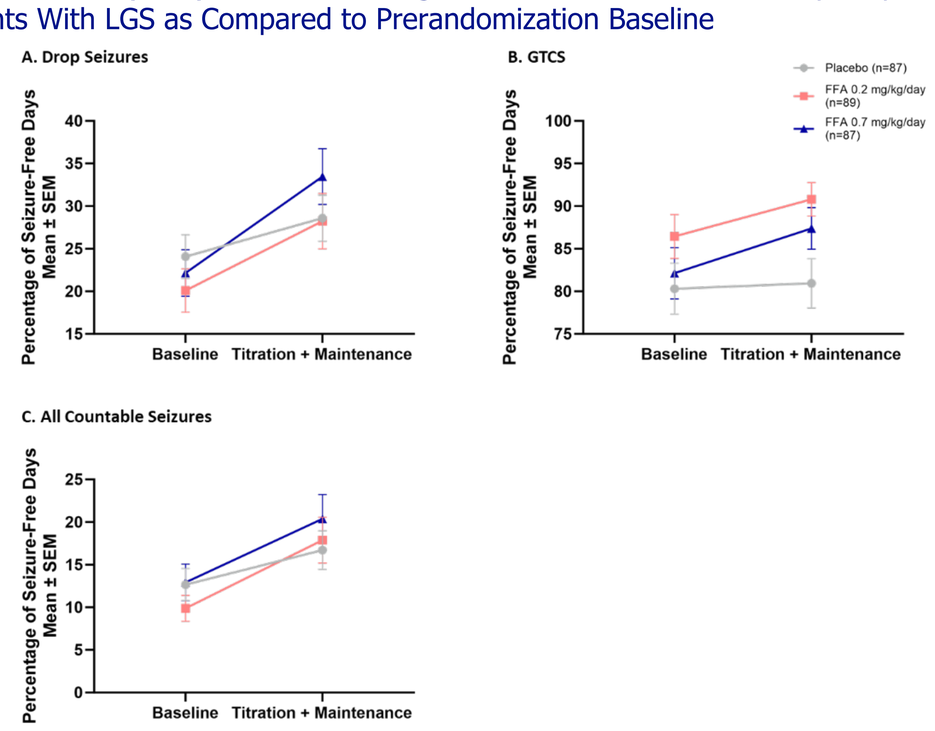
FFA, fenfluramine; OLE, open-label extension; RCT, randomized clinical trial.

- The change in percentage of seizure-free days from pre-randomization in the randomized clinical trial (RCT) for each dosing group (FFA: 0.2 mg/kg/d, 0.7 mg/kg/d) and the open-label extension (OLE) for each mean daily dosing group (FFA: <0.3 mg/kg/d, 0.3-0.5 mg/kg/d, >0.5 mg/kg/d) were calculated
- Percentage of seizure-free days was calculated for drop seizures, generalized tonic-clonic seizures (GTCS), and all countable (motor) seizures
  - Drop seizures were defined as seizures associated with a drop or fall including GTCS, secondary GTCS (SGTC; focal to bilateral tonic–clonic), tonic seizures, atonic seizures, and tonic–atonic seizures

Results

- Patients in all FFA dose groups experienced a significant increase in percentage of seizure-free days across all analyzed seizure types in the RCT (**Figure 2**) and OLE compared to the pre-randomization RCT baseline (**Figure 3**)
- In the RCT (**Table 1**) and the OLE (**Table 2**), the percentage of seizure-free days from pre-randomization baseline increased with dose across all analyzed seizure types

Figure 2. RCT (T+M): Mean Percentage Increase of Seizure-Free Days Experienced by Patients With LGS as Compared to Prerandomization Baseline



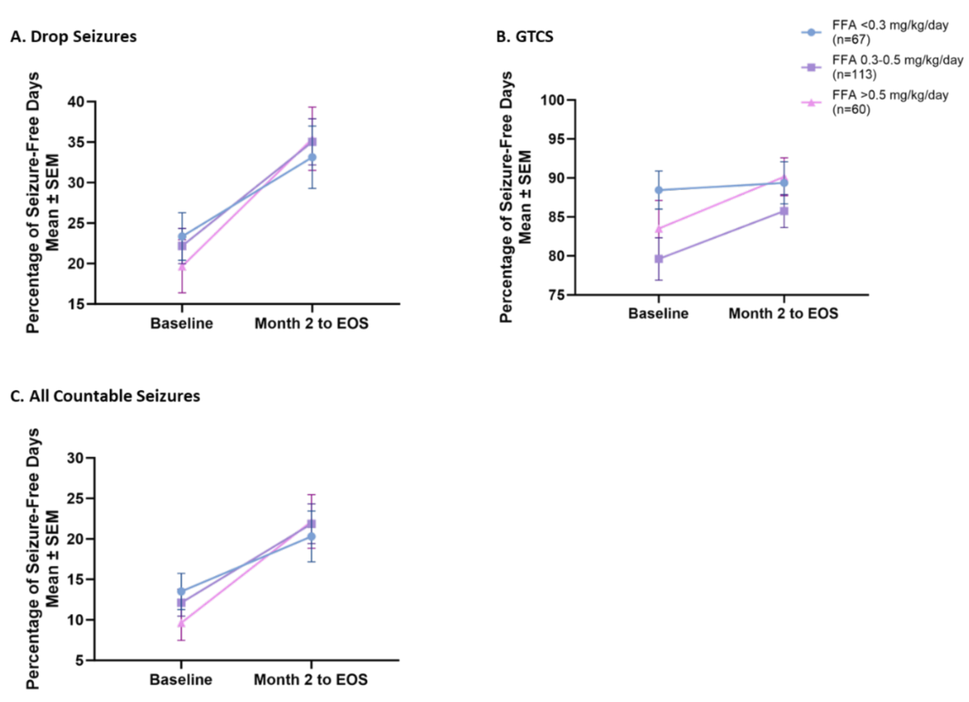
FFA, fenfluramine; GTCS, generalized tonic-clonic seizures; LGS, Lennox-Gastaut syndrome; SEM, standard error of the mean; RCT, randomized clinical trial.

Table 1. Change in Mean Percentage of Seizure-Free Days Relative to Placebo in Patients During the RCT From Baseline

	Placebo n = 87	FFA 0.2 mg/kg/d n = 89	FFA 0.7 mg/kg/d n = 87
Drop Seizures	4.5% increase	8.2% increase P<0.0001	11.3% increase P<0.0001
GTCS	0.6% increase	4.4% increase P<0.0001	5.3% increase P<0.0001
All Countable Seizures	4.1% increase	8.0% increase P<0.0001	7.5% increase P<0.0001

Results are based on a logistic regression model with treatment group (3 levels) and baseline percentage of seizure-free days as covariates, and percentage of seizure-free days at Titration + Maintenance as the outcome variable. A different model was fitted for each seizure type. P-value is vs placebo.
FFA, fenfluramine; GTCS, generalized tonic-clonic seizures; RCT, randomized clinical trial.

Figure 3. OLE (Month 2 to EOS): Mean Percentage Increase of Seizure-Free Days Experienced by Patients With LGS as Compared to Pre-randomization Baseline



Baseline value is pre-randomization RCT baseline.
EOS, end of study; FFA, fenfluramine; GTCS, generalized tonic-clonic seizure; LGS, Lennox-Gastaut syndrome; OLE, open-label extension; SEM, standard error of the mean.

Table 2. Change in Mean Percentage of Seizure-Free Days in Patients During the OLE From Pre-Randomization RCT Baseline

	FFA <0.3 mg/kg/d n = 67	FFA 0.3-0.5 mg/kg/d n = 113	FFA >0.5 mg/kg/d n = 60
Drop Seizures	9.7% increase	12.3% increase	15.0% increase
GTCS	1.1% increase	6.1% increase	6.7% increase
All Countable Seizures	7.7% increase	9.8% increase	12.5% increase

FFA, fenfluramine; GTCS, generalized tonic-clonic seizures; OLE, open-label extension; RCT, randomized clinical trial.

Conclusions

- FFA treatment resulted in an increase in the percentage of seizure-free days for drop seizures, GTCS, and all countable seizures
- An increase in seizure-free days with FFA treatment may improve patient and caregiver quality of life

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This is a summary of the main findings. Please use the QR code to download the full poster.

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