INPLASY PROTOCOL

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Support: **None.**

Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

Conflicts of interest:
None declared.

Efficacy and safety of fenfluramine for developmental and epileptic encephalopathy: Findings from Randomized Controlled Trials

Wang JH[1].

Review question / Objective: **Population: Patients with developmental and epileptic encephalopathy; ntervention: Fenfluramine; Comparison: Placebo; Outcome: Efficacy and safety; Study design: RCTs.**
Eligibility criteria: **(a) Study type: only randomized controlled trials; (b) Restriction on language: no restriction; (c) Population: patients with developmental and epileptic encephalopathy; (d) Intervention: fenfluramine.**
Main outcome(s): **Efficacy: Proportion of reduction in monthly convulsive seizure frequency (MCSF) compared to baseline, ≥25/50/75/100% reduction in MCSF, near seizure freedom, change from baseline in clinical global impression ratings by both parents or caregivers and investigators, days of rescue medication use per 28 days, and total seizure frequency (including nonconvulsive seizure types) per 28 days. Safety: The proportion of any treatment-emergent adverse events (TEAEs) and serious TEAEs.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 May 2022 and was last updated on 14 May 2022 (registration number INPLASY202250089).

INTRODUCTION

Review question / Objective: **Population: Patients with developmental and epileptic encephalopathy; ntervention: Fenfluramine; Comparison: Placebo; Outcome: Efficacy and safety; Study design: RCTs.**

Condition being studied: **Efficacy and safety of fenfluramine for developmental and epileptic encephalopathy.**

METHODS

Participant or population: **Patients with developmental and epileptic encephalopathy.**

Intervention: Fenfluramine.

Comparator: Efficacy and safety.

Study designs to be included: Randomized controlled trials of fenfluramine for Patients with developmental and epileptic encephalopathy.

Eligibility criteria: (a) Study type: only randomized controlled trials; (b) Restriction on language: no restriction; (c) Population: patients with developmental and epileptic encephalopathy; (d) Intervention: fenfluramine.

Information sources: PubMed, Embase, Cochrane library.

Main outcome(s): Efficacy: Proportion of reduction in monthly convulsive seizure frequency (MCSF) compared to baseline, ≥25/50/75/100% reduction in MCSF, near seizure freedom, change from baseline in clinical global impression ratings by both parents or caregivers and investigators, days of rescue medication use per 28 days, and total seizure frequency (including nonconvulsive seizure types) per 28 days. Safety: The proportion of any treatment-emergent adverse events (TEAEs) and serious TEAEs.

Strategy of data synthesis: Data were assessed by Review manager 5.4 software. Continuous or dichotomous outcomes were analyzed separately as mean difference (MD), odds ratio (OR), or the risk ratio (RR) using 95% confidence interval (CI) by fixed effects model. Statistical heterogeneity was evaluated by the I2 statistic, defined as follows: I2 < 30% means "low heterogeneity", 30% < I2 < 50% represents "moderate heterogeneity", and I2 > 50% denotes "substantial heterogeneity". Subgroup analysis was performed to investigate the stability of the consolidated results. Furthermore, P-value <0.05 was considered as significant and two-tailed tests were used for all analyses.

Subgroup analysis: Subgroup analysis based on different symptoms and doses.

Sensitivity analysis: Review Manager 5.4 software was used to do the sensitivity analysis.

Country(ies) involved: China.

Keywords: fenfluramine; developmental and epileptic encephalopathy; Dravet Syndrome; Lennox-Gastaut Syndrome; meta-analysis.

Contributions of each author:
Author 1 - Jiahe Wang drafted the manuscript.