Intravenous Ganaxolone for the Treatment of Refractory Status Epilepticus: Results From an Open-Label, Dose-Finding, Phase 2 Study

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Introduction

Ganaxolone (GNX) is a medium-chain fatty acid ester with activity and mechanisms of action complementary to established anti-epileptic drugs (AEDs). The purpose of the study was to determine the safety and pharmacokinetics of a novel intravenous (IV) formulation of GNX in RSE patients (NCT03350035).

Methods

This was a Phase 2, open-label, dose-finding study of Phases 1 and 2. Patients were randomized to one of three cohorts: Low Dose (500 mg/d), Medium Dose (650 mg/d), or High Dose (713 mg/d). The primary endpoint was seizure cessation within 24 hours of IV GNX initiation. Secondary endpoints included safety and tolerability.

Results

Baseline Characteristics:

- Total number of patients: 15
- Patient demographics:
  - Mean age: 57 years old (range, 23-88)
  - Gender: 7 male, 8 female

Clinical Endpoints:

- Primary endpoint: seizure cessation occurred within 5 minutes (median) (Figure 2).
- Secondary endpoints: additional efficacy, safety, and tolerability.

No escalation to IV anesthetics within the first 24 hours after GNX discontinuation (primary endpoint).

Conclusions

IV GNX showed an acceptable safety profile in patients with RSE.

Figure 1. Current Status Epilepticus Standard of Care Treatment Progression and Clinical Definitions

Figure 2. Predicted GNX Plasma Concentrations

Figure 3. Investigator-Determined Time of Status Epilepticus Cessation in 15 Evaluable Patients

Figure 4. Percentage Change In EEG Suture Burden In Each Dose Cohort

Figure 5. Safety Summary

Table 1. Dosing Cohorts

Table 2. Summary Efficacy Results

Table 3. Summary Safety Results

Potential role for Neuropeptide Steroids in RSE

- Neuroactive steroids (NAS) are endogenous hormones produced by the brain.
- They are potent positive allosteric modulators of GABAa receptors.
- They exhibit rapid brain penetration, leading to early onset pharmacodynamic effects.

Figure 3. Predicted GNX Plasma Concentrations

Figure 4. Percentage Change In EEG Suture Burden In Each Dose Cohort

Figure 5. Safety Summary

Table 1. Dosing Cohorts

Table 2. Summary Efficacy Results

Reference


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