Adjunctive rufinamide reduces refractory partial-onset seizures

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Researchers from the Arkansas Epilepsy Program found treatment with rufinamide results in a significant reduction in seizure frequency compared with placebo, for patients with uncontrolled partial-onset seizures (POS). Details of this study are now available online in *Epilepsia*, a journal published by Wiley-Blackwell on behalf of the International League Against Epilepsy.

Epilepsy affects up to 2% of the worldwide population according to the Centers for Disease Control and Prevention. More than half of these patients experience POS, or focal seizures, which are initiated in one part of the brain. Despite an expanding number of antiepileptic drugs (AEDs) available to treat partial-onset epilepsy, about one-third of epilepsy patients remain resistant to available treatments and many more experience intolerable side effects, driving the search for therapeutic alternatives. The current study evaluated rufinamide, an AED with a novel triazole-derivative structure, to confirm its efficacy and safety at a dose of 1,600 mg twice daily as adjunctive treatment for refractory POS.

Eligible patients were male or female, aged 12-80 years, with POS with or without secondarily generalized seizures. Patients' seizures were inadequately controlled on stable doses of up to three concomitantly administered AEDs, with no evidence of AED treatment noncompliance. All medication taken regularly by patients, including AEDs, remained unchanged for at least 1 month prior to study start and throughout the study. Patients were enrolled at 61 centers in the U.S. and at four centers in Canada between February 2006 and March 2009. In total, 357 patients

were randomly assigned to receive rufinamide (n = 176) or placebo (n = 181) and entered the titration phase, and 139 and 156 patients, respectively, completed the study. This study comprised a 56-day baseline phase (BP), 12-day titration phase, and 84-day maintenance phase (MP).

The researchers found that treatment with rufinamide resulted in a statistically significant reduction in total partial seizure frequency compared with placebo. Results also showed a 50% reduction in responder rate and total partial seizure frequency rate in patients treated with rufinamide. Several exploratory efficacy variables, including at least 75% responder rate and increase in the number of seizure-free days, were also associated with notably better results for rufinamide.

With respect to efficacy by seizure type, rufinamide was significantly superior to placebo for complex partial seizures, the most common seizure type, and numerically superior to placebo for simple partial seizures and secondarily generalized partial seizures. The median reduction in secondarily generalized partial seizures of 40% in this study is consistent with that previously observed at identical rufinamide dosage.

Study leader Victor Biton, M.D., comments, "Overall, there were no significant pharmacokinetic (PK) effects on either rufinamide or any second-generation AED when given with other medications." The research team confirmed PK results found in previous studies—showing lower oral bioavailability of rufinamide at higher doses, increased clearance of rufinamide with increasing body weight, and no effect of prolonged rufinamide dosing on the PK of rufinamide."

"Our study demonstrates that rufinamide is effective as adjunctive therapy in reducing total partial seizure frequency in treatment-refractory adolescent and adult patients, and confirms the known safety

and tolerability profile of rufinamide in this patient population," concludes Dr. Biton.

More information: "A Randomized, Double-blind, Placebo-controlled, Parallel-group Study of Rufinamide as Adjunctive Therapy for Refractory Partial-onset Seizures." Victor Biton, Gregory Krauss, Blanca Vasquez-Santana, Francesco Bibbiani, Allison Mann, Carlos Perdomo, and Milind Narurkar. Epilepsia; Published Online: October 1, 2010 DOI:10.1111/j.1528-1167.2009.02729.x

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