Lacosamide validated as promising therapy for uncontrolled partial-onset seizures

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A recent multi-center study has confirmed earlier study results that 400 mg/day of lacosamide provides a good balance of efficacy and tolerability for patients with uncontrolled partial-onset seizures (POS), and doses of 600mg/day may provide additional benefit for some patients. Researchers from the Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Thomas Jefferson University Medical School, Arkansas Epilepsy Program, Schwarz Biosciences and Johns Hopkins University Hospital conducted this study which is available early online in *Epilepsia*, a journal published by Wiley-Blackwell on behalf of the International League Against Epilepsy.

Epilepsy is one of the most common neurologic disorders, affecting up to 2% of the worldwide population according to the Centers for Disease Control and Prevention (CDC). More than half of the total epilepsy population experience POS, or focal seizures, which occur in one part of the brain. While several anti-epileptic drugs have entered the market in the past decade, approximately 30% of patients with epilepsy experience recurrent seizures and undesirable side effects from their medication. There remains a significant unmet need for well-tolerated medications able to provide adequate seizure control. Lacosamide is emerging as a promising candidate to reduce seizure frequency and severity with few adverse effects.

The efficacy and safety of adjunctive lacosamide for POS was established in three multicenter, randomized, double-blind, placebo-controlled trials. Results of the first trial indicated that study participants

taking 400 and 600 mg/day of lacosamide experienced significantly larger reductions in seizure frequency and significantly greater responder rates compared with placebo. Two additional phase III trials were conducted in parallel to confirm these results.

Steve Chung, M.D., and colleagues report the results of the second phase III trial, which was conducted in an expanded patient population of 405 men and women, aged 16-70 in the U.S. The primary objective of the trial was to evaluate the efficacy of lacosamide 400 and 600 mg/day as adjunctive treatment for POS; the secondary objective was to further assess the safety, potential dose-response relationships, and steady-state plasma concentrations of lacosamide and concomitant antiepileptic drugs (AEDs). This trial randomized patients 1:2:1 to placebo, lacosamide 400 mg, or lacosamide 600 mg/day. After an 8-week baseline period, patients began treatment with placebo or lacosamide 100 mg/day, were force-titrated weekly (100 mg/day increments) to the target dose, and entered a 12-week maintenance period. Study participants had at least a 2-year history of POS despite treatment with at least two AEDs (concurrently or sequentially) and were experiencing at least four partial-onset seizures per 28 days, with no seizure-free period longer than 21 days during the 8 weeks prior to baseline and during the 8-week baseline period.

Adjunctive treatment with lacosamide 400 and 600 mg/day was found to be effective in reducing the frequency of POS (with or without secondary generalization) in patients with uncontrolled seizures while taking one to three concomitant AEDs. Of the 338 patients completing titration, 274 (81.1%) achieved their target dose of trial medication without the need for dose reduction prior to entry into maintenance.

"The efficacy results observed in this trial are notable given the epilepsy treatment history and the frequency of the seizures experienced by enrolled patients," said Dr. Michael Sperling one of the study authors.

"Despite this difficult-to-treat study population, treatment with lacosamide 400 and 600 mg/day resulted in significant reductions from baseline in seizures, as well as significantly higher responder rates and a higher rate of seizure freedom compared with placebo—results that are comparable to established and second-generation AEDs."

More information: "Lacosamide as adjunctive therapy for partial-onset seizures: A randomized controlled trial." Steve Chung, Michael R. Sperling, Victor Biton, Gregory Krauss, David Hebert, G. David Rudd, and Pamela Doty on behalf of the SP754 Study Group. Epilepsia; Published Online: January 27, 2010. DOI:10.1111/j.1528-1167.2009.02496.x

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