BREEZE 2: Gabapentin-ER Tames Hot Flashes

BY RICHARD HYER
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CHICAGO – An extended-release formulation of gabapentin for hot flashes showed the potential both to minimize peak adverse events and to allow for less frequent dosing in a randomized, controlled trial of 565 women, said Dr. Wulf Utian.

“The results of the BREEZE 2 study suggest that gabapentin-extended release 1,800 mg/day may be effective and well tolerated for the treatment of moderate to severe hot flashes in postmenopausal women,” Dr. Utian, the Arthur H. Bill Professor Emeritus of Reproductive Biology and Obstetrics and Gynecology at Case Western Reserve University in Cleveland. Gabapentin is an anticonvulsant that is also used to relieve nerve-related pain.

BREEZE 2 is a prospective, multicenter, randomized, double-blind, placebo-controlled study in postmenopausal women ages 18-70 years at 45 sites across the United States. The study had two active arms: gabapentin ER 1,200 mg given once daily, and 1,800 mg given as 600 mg in the morning and 1,200 in the evening. Efficacy was assessed at 4 and 12 weeks, and the treatment duration was 3 months. The primary efficacy end points were reductions in the mean frequency of moderate to severe hot flashes and the average severity of hot flashes.

The trial’s secondary end points were the proportion of patients who were categorized as “much improved” or “very much improved” at 12 weeks in the self-reported Patient Global Impression of Change scale. Investigators also recorded their impression of the results of the therapy using the Clinician Global Impression of Change scale.

Postmenopausal women who had been experiencing seven or more moderate to severe hot flashes per day (or at least 50 per week), accompanied by sweating during at least the previous 30 days, were the trial population.

Baseline characteristics were similar across the three groups. In the 1,800-mg group, for example, the average age was 54 years, the women were 71% white, and the average body mass index was less than 30 kg/m².

Data were subjected to both parametric and nonparametric analysis, said Dr. Utian, because parametric analyses can be influenced by outliers.

At 4 weeks and 12 weeks, changes in the mean severity of moderate and severe hot flashes were -0.6 and -0.8 for the 1,800-mg group, compared with the placebo group; both were significant differences.

More than 60% of patients in both active treatment groups and more than 40% in the placebo group self-reported and were clinician reported as “very much improved” at 12 weeks. “This was a particularly high placebo response,” said Dr. Utian.

Nonparametric analysis revealed a statistically significant change and median frequency of moderate to severe hot flashes at 4 weeks and 12 weeks in both active groups, compared with the placebo group.

Dizziness was the most commonly reported adverse event in both the 1,800-mg and 1,200-mg groups, whereas headache was most commonly reported in the placebo group. Somnolence was the second most common complaint in the active treatment groups. A total of 48 patients across both active treatment groups discontinued because of adverse events.

“Essentially, this long-release product was well tolerated, adverse events were mild, the difference was a slight difference in dizziness and somnolence during the titration, and [there was] no real difference in the adverse events between the 1,800-mg and the 1,200-mg dosing regimens, said Dr. Utian. ‘The incidence of the adverse events declined markedly after 2-4 weeks of study.’

References:

Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately.

PRECAUTIONS: PRENATE ESSENTIAL is a multivitamin/mineral/essential fatty acid supplement indicated for use in improving the nutritional status of women throughout pregnancy and in the postnatal period for both lactating and non-lactating mothers. PRENATE ESSENTIAL can also be beneficial in improving the nutritional status of women prior to conception.

CONTRAINDICATIONS: PRENATE ESSENTIAL is contraindicated in patients with a known hypersensitivity to any of the ingredients.

WARNINGS: Ingestion of more than 3 grams of omega-3 fatty acids (such as DHA) per day has been shown to have potential antithrombotic effects, including an increased bleeding time and International Normalized Ratio (INR). Administration of omega-3 fatty acids should be avoided in patients taking anticoagulants and in those known to have an inherited or acquired predisposition to bleeding.

The trial was sponsored by Depomed, Inc., maker of gabapentin-ER. Dr. Utian is a consultant to Depomed. Some of the study investigators are Depomed employees.

BREEZE 2 trial database of 565 postmenopausal women with moderate to severe hot flashes who were randomized to gabapentin-ER in two active arms (1,800 mg or 1,200 mg) or placebo for 13 weeks in this phase III, double-blind, placebo-controlled, randomized trial.

Disclosures: The trial was sponsored by Depomed Inc., maker of gabapentin-ER. Dr. Utian is a consultant to Depomed. Some of the study investigators are Depomed employees.