BREEZE 2: Gabapentin-ER Tames Hot Flashes

BY RICHARD HYER

FROM THE ANNUAL MEETING OF THE NORTH AMERICAN MENOPAUSE SOCIETY

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," he noted at the meeting.

Gabapentin-ER releases over 8 hours, potentially minimizing peak adverse events and allowing once daily or twice daily dosing, said 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 aged 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/m^2.

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 in 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 therapy." ■

VITALS

Major Finding: Gabapentin-ER 1,800 mg/day may be effective and well tolerated for the treatment of moderate to severe hot flashes in postmenopausal women.

Data Source: 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.

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Vitamin B_6	25 mg	1250%	1000%
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Vitamin B_{12}	12 mcg	200%	150%
Biotin	250 mcg	83%	83%
Calcium (calcium carbonate)	140 mg	14%	11%
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