(S150) DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTINATIONAL STUDY OF AVP-923 FOR PSEUDOBULBAR AFFECT IN MULTIPLE SCLEROSIS

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Background: Pseudobulbar affect (PBA) is characterized by uncontrollable outbursts of laughter or crying incongruent with the patient’s emotional state. Although it results in considerable distress for patients and caregivers, it is often underrecognized and undertreated. DMq is a combination of dextromethorphan (an NMDA receptor antagonist/sigma receptor agonist) and quinidine (a CYP2D6 inhibitor) that has demonstrated efficacy in PBA. Methods: Adults with PBA in conjunction with multiple sclerosis (MS) or amyotrophic lateral sclerosis (ALS) were recruited in the United States and Latin America. Center for Neurologic Studies–Lability Scale (CNS-LS) score \( \geq 13 \) was required. Eligible patients were randomized (1:1:1) to receive 1 of 2 doses of DMq (dextromethorphan 20 mg/quinidine 10 mg or dextromethorphan 30 mg/quinidine 10 mg) or placebo twice a day for 12 weeks. The primary outcome was change in number of laughing or crying episodes per day, analyzed using longitudinal negative binomial regression. Secondary outcomes included change in CNS-LS score and on a Pain Rating Scale (PRS). Safety/tolerability assessments included adverse event reports. Results: Of 326 subjects, 129 had underlying MS. At baseline, they suffered, on average, >3 PBA episodes per day and had an average CNS-LS score of approximately 20. In the longitudinal analysis of PBA rate, the therapeutic effect relative to placebo was significant in the higher-dose group (\( P = .0280 \)). A generalized estimating equation analysis showed a trend for superiority in both DMq groups (\( P = .0647 \) and \( P = .0527 \)). Reductions in mean CNS-LS score were demonstrated for both DMq groups (vs. placebo) but did not reach statistical significance. In the higher-dose group, mean pain scores across time and means at days 15 and 29 showed trends for superiority over placebo (\( P = .0512 \) and \( P = .0859 \)). The most common adverse events more frequent in the DMq groups than in the placebo group were dizziness, diarrhea, and somnolence. One patient in the higher-dose group and two in the placebo group reported nonfatal serious adverse events. Conclusions: At both doses, efficacy results resembled those in previous studies of DMq containing quinidine at a higher dose, and safety and tolerability were improved.

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