Dextromethorphan/Quinidine for Pseudobulbar Affect Secondary to Alzheimer's Disease/Dementia: Effect on Mood Symptoms

Introduction

- Pseudobulbar affect (PBA) occurs secondary to a variety of otherwise unrelated neurologic conditions, and is characterized by sudden, uncontrollable laughing or crying spells that are exaggerated in response to minor stimuli or social contact.
- PBA episodes are disruptive and often disabling, and are associated with impaired social function and quality of life (QOL).
- Although the US prevalence of PBA is estimated at approximately 2 million, the condition remains under-recognized and may be mistaken for depression.
- Dextromethorphan hydrobromide and quinidine sulfinate (DM/Q) is a new FDA-approved treatment for PBA, with trials in patients with ALS and MS.

Objectives

- The PRISM II study was conducted to provide additional DM/Q safety, tolerability, and effectiveness evidence in PBA secondary to stroke, traumatic brain injury (TBI), or dementia.
- The primary objective was to evaluate the effectiveness of DM/Q for the treatment of PBA episodes in adults with a clinical diagnosis of PBA.
- The secondary objectives were to evaluate the safety, tolerability, and effectiveness of DM/Q in patients with PBA.

Methods

Study Design

- Placebo-controlled, multicenter (~120 US sites), 12-week trial (NCT01066414).

Eligibility

- Adults with a clinical diagnosis of PBA and baseline Center for Neurologic Study–Lability Scale (CNS-LS) score ≥ 13, a scale ranging from 0 to 21, with higher scores indicating severity of depression.
- Stable neuromuscular condition.

Randomization and Blinding

- Randomized to receive DM/Q 20/10 mg twice daily (once daily during Week 1).
- The study was double-blind with blinded assessments of clinical and functional outcome measures.
- Safety and tolerability were assessed prospectively.

Assessments

- Study site and mean scores are shown in Table 3, where DM/Q showed significant improvement compared to placebo.
- The primary endpoint was Change from baseline in CNS-LS score at Day 90/Final Visit vs. baseline.
- Secondary end-point: PBA episode count change from baseline measured using PBA episode diary.

Results

Patient Disposition and Baseline Characteristics

- Of 110 patients randomized, 106 (79.1%) completed the trial (Visit 2).
- Median PBA episode count was 12 (7) episodes/week at baseline.
- CPG defined efficacy population included 102 patients, of which 95 (93.3%) completed the study.
- No serious AEs occurred; no deaths attributed to treatment were reported.
- No clinically meaningful changes were observed in vital signs, ECG, or laboratory tests.

Primary and Secondary Effectiveness Outcomes

- CNS-LS: A 21-point reduction from baseline was observed at Day 30 and a 23-point reduction at Day 90/Final Visit vs. baseline.
- PBA episode count: showed a 67.7% reduction at Day 90/Final Visit vs. baseline.
- Global QOL-VAS: A significant 30.6-point improvement at Day 30 and a 21.0-point improvement at Day 90/Final Visit vs. baseline.

Conclusions

- DM/Q was associated with a significant reduction in depressive symptoms in patients with PBA.
- The lack of strong correlation between PHQ-9 and PBA episode count may reflect the presence of depression in patients with PBA.

References

9. Stephen D’Amico has received honoraria as a consultant and speaker for Avanir Pharmaceuticals, Inc.