Dextromethorphan/Quinidine for Treatment of Pseudobulbar Affect in Patients With Dementia: Examination of CNS-LS Outcomes in a 12-Week Open-Label Trial (PRISM II)

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Introduction
Pseudobulbar affect (PBA) is characterized by frequent, unprovoked episodes of crying or laughing that are inappropriate for the situation and may be associated with other neurovegetative symptoms such as autonomic dysregulation.

• PBA occurs when frontal lesions or tumors cause neuronal pathology and neurotransmitter dysfunction over time.

• PBA episodes are discrete, often followed by embarrassment and may be precipitated by stress or emotional events.

• PBA may be so severe as to cause patients to seek medical evaluation.

• CNS reduction in PBA is an established PBA rating instrument.

• Dextromethorphan/Quinidine for Treatment of Pseudobulbar Affect (PRISM II) was a pivotal trial conducted by Avanir Pharmaceuticals, Inc., Aliso Viejo, CA.

• This study (PRISM II) was conducted to provide additional (PRISM II) effectiveness, safety, and tolerance data in patient cohorts with PBA secondary to ALS and MS.

• The results of this study demonstrated that dextromethorphan/quinidine is effective in reducing symptoms of PBA in patients with dementia.

Methods
Study Design
Open-label, multicenter (n=134), 12-week trial.

• Adults with a clinical diagnosis of PBA and baseline CNS-LS score ≥31.

• Clinical symptoms duration of at least 1 month.

• Stable disease (within 8 weeks of enrollment) and no new psychiatric diagnosis or changes in psychotropic medications.

• No history of psychotropic or antidepressant CNS medication, alcohol, or other neurovegetative symptoms.

• No history of pneumonia or other life-threatening conditions.

• Randomization to dextromethorphan/quinidine or placebo for 10 weeks.

• Open-label study.

• PBA= pseudobulbar affect; CNS-LS = Center for Neurologic Study - Lability Scale.

Results
Patient Characteristics
131 patients with PBA and dementia were evaluated for safety; 130 (93%) were included in effectiveness analyses; 108 (83%) for the primary analysis.

• Patient characteristics are shown in Table 1.

• Safety

• AE Category, n (%)

- N=134

- N=108

- N=102

Safety

- N=134

- N=108

- N=102

AE=adverse event; CNS-LS=Center for Neurologic Study-Lability Scale; LBD=late-stage dementia.

Table 2: AEs Occurring in ≥20% Patients

AE Category, n (%)

- Safety

- N=134

- N=108

- N=102

Safety

- N=134

- N=108

- N=102

Table 2: AEs Occurring in ≥20% Patients

Safety

- AEs 5 Risk of treatment-related AEs, comparator

- AEs were monitored weekly for all patients in the pivotal trial from study Day 0 through Week 8.

- The safety data from this study were consistent with DM/Q prescribing information.

- All treatment-emergent AEs (TEAEs) are presented regardless of causality.

- SAEs were monitored weekly and all patients in the pivotal trial from study Day 0 through Week 8.

- The incidence of TEAEs for all patients was presented in Table 2.

- AE=adverse event; CNS-LS=Center for Neurologic Study-Lability Scale; LBD=late-stage dementia.

Table 2: AEs Occurring in ≥20% Patients

Safety

- N=134

- N=108

- N=102

Safety

- N=134

- N=108

- N=102

Conclusion
PBA is the first FDA-approved treatment for PBA in patients with dementia.

• Patients with dementia who were taking DM/Q experienced significantly reduced PBA symptoms of both unprovoked laughing and crying over the 12-week open-label treatment period.

• Improvement in the CNS-LS including overall score, laughing and crying sub-scores, and individual CNS-LS item scores was associated with reductions in the number of PBA occurrence and global impact scores (PBA-ICO).

• DM/Q appeared well tolerated in the large, elderly population with dementia, with low rates of treatment-related AEs.

• Absence of treatment-emergent AEs was observed in this open-label study.

• This trial was conducted in patients with PBA secondary to ALS or MS, and represents improvement over the 7.4 [6.1] placebo increase (P<.001) in the 12-week pivotal trial in patients with PBA secondary to ALS or MS, supporting the CNS-LS as a valid measure for assessing PBA symptoms and the effectiveness of treatments in these patient populations.

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References
The references are listed at the end of the report.