Dexmedetomidine Sublingual Film for Acute Agitation Associated With Schizophrenia or Bipolar Disorder: Pooled Trial Data

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INTRODUCTION

Acute agitation is frequently managed in US emergency departments. Dexmedetomidine sublingual film is a self-administered treatment for acute agitation associated with schizophrenia or bipolar disorder. Dexmedetomidine is a selective alpha-2 adrenergic receptors agonist.

OBJECTIVE

To determine the efficacy of sublingual dexmedetomidine for treatment of acute agitation associated with schizophrenia or bipolar disorder assessed by the Positive and Negative Syndrome Scale (PANSS) – Excited Component (PEC) change from baseline after drug treatment.

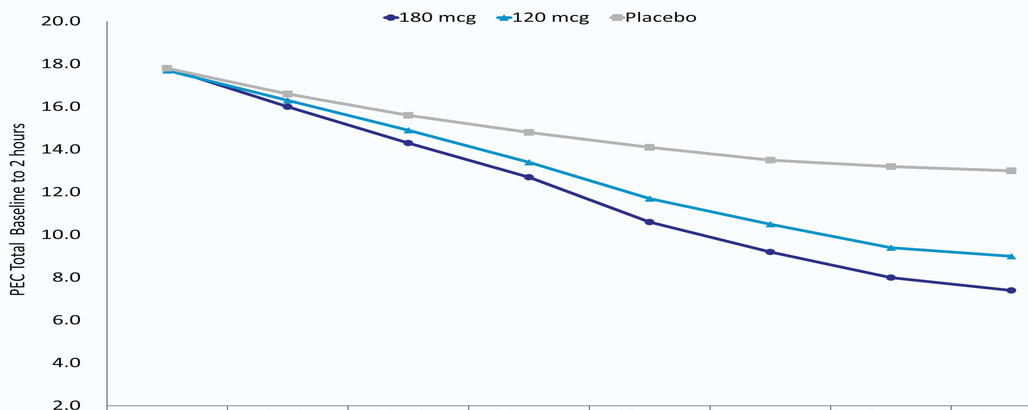
METHODS

- A post hoc analysis of pooled data from 2 similarly-designed US multicenter, randomized, double-blind, placebo-controlled phase 3 trials of dexmedetomidine sublingual film (180 mcg or 120 mcg). The trials were conducted in participants aged 18-75 with acute agitation and either SCZ or BPD.
- Acute agitation was defined as a total score ≥14 on the PEC scale and ≥4 on at least 1 of the 5 PEC items (poor impulse control, tension, hostility, uncooperativeness, excitement). The primary endpoint was change from baseline in PEC total at 2 hours. The secondary endpoint was earliest time of a statistically significant separation of active drug from placebo on the. PEC total score.

ADVERSE EVENTS

- There were no drug-related serious or severe AEs in either trial. No participant was unarousable either by AE reporting or by the Agitation and Calmness Evaluation Scale (ACES).
- The most common treatment emergent adverse events (TEAEs) were somnolence (21.5%), dry mouth (5.9%), hypotension (5.3%), dizziness (4.9%), orthostatic hypotension (4.0%), oral hypoesthesia (3.8%), and headache (3.6%). Of 110 somnolence reports, 86% were mild and 14% moderate. **Table 1**

Figure 1: Pooled PEC Total Scores Baseline to 2 hours



	Baseline	10 mins Postdose	20 mins Postdose	30 mins Postdose	45 mins Postdose	1 hour Postdose	1.5 hours Postdose	2 hours Postdose
180 mcg	17.8	16.0	14.3	12.7	10.6	9.2	8.0	7.4
120 mcg	17.7	16.3	14.9	13.4	11.7	10.5	9.4	9.0
Placebo	17.8	16.6	15.6	14.8	14.1	13.5	13.2	13.0

Table 1: Pooled Adverse Events

	180 mcg (N=252)	120 mcg (N=255)	Placebo (N=252)
Somnolence	**56 (22.2)**	**54 (21.2)**	**16 (6.3)**
Mild	40 (15.9)	43 (16.9)	15 (6.0)
Moderate	16 (6.3)	11 (4.3)	1 (0.4)
Dry mouth	**11 (4.4)**	**19 (7.5)**	**3 (1.2)**
Hypotension	**13 (5.2)**	**14 (5.5)**	**0**
Mild	10 (4.0)	10 (3.9)	0
Moderate	3 (1.2)	4 (1.6)	0
Dizziness	**15 (6.0)**	**10 (3.9)**	**2 (0.8)**
Orthostatic hypotension	**13 (5.2)**	**7 (2.7)**	**1 (0.4)**
Mild	9 (3.6)	7 (2.7)	1 (0.4)
Moderate	4 (1.6)	0	0
Oral Hypoesthesia	**12 (4.8)**	**7 (2.7)**	**1 (0.04)**
Headache	**6 (2.4)**	**12 (4.7)**	**12 (4.8)**
Nausea	**7 (2.8)**	**6 (2.4)**	**4 (1.6)**
Paresthesia oral	**6 (2.4)**	**7 (2.7)**	**1 (0.4)**

Treatment Emergent Adverse Events (TEAEs) with >2% incidence rate in one or more treatment groups are included, sorted by decreasing frequency in the order of 180 ug BXCL501, 120 ug BXCL501, Placebo. Subjects counted once at highest severity within each term based on MedDRA (Medical Dictionary for Regulatory Activities) version 23.0

RESULTS

- 760 patients enrolled in the 2 trials. All doses of dexmedetomidine SF met the primary endpoint of statistically significant change from baseline in PEC total at 2h vs placebo (P<.001).
- Mean (SD) reductions in PEC total at 2 hours were -10.4 (4.4), -8.7 (5.0), and -4.8 (4.7) for 180 mcg, 120 mcg, and placebo, respectively.
- Statistically significant separation from placebo occurred as early as 10 minutes at 180 mcg (*P*=.004) and 20 minutes at 120 mcg (*P*=.015). **Figure 1**

KEY FINDINGS

- Dexmedetomidine sublingual film, a selective alpha-2 adrenergic receptor agonist effectively reduced symptoms of acute agitation associated with schizophrenia or bipolar disorder
- Statistically significant separation from placebo occurred as early as 10 minutes at the 180 mcg dose and 20 minutes at the 120 mcg dose.
- There were no treatment-related serious or severe adverse events.
- The most common TEAEs were somnolence, dry mouth, hypotension, dizziness, orthostatic hypotension, oral hypoesthesia, headache, nausea, and oral paresthesia.

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