Agitation Associated with Schizophrenia or Bipolar Disorder: Sublingual Dexmedetomidine Film Efficacy by Baseline Agitation Level

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PURPOSE

If behavioral de-escalation of agitation associated with schizophrenia or bipolar disorder is unsuccessful, ideal pharmacologic treatment reduces agitation without excess sedation.

Sublingual dexmedetomidine (DSF) is a mucoadhesive, orally absorbed film, approved to treat agitation in adults with schizophrenia or bipolar disorder I or II.

This post hoc analysis of data from 2 randomized, double-blind trials evaluates efficacy of DSF by baseline agitation severity.

METHODS

758 adults with agitation associated with schizophrenia or bipolar disorder who scored ≥14 on the Positive and Negative Symptom Scale-Excited Component (PEC) and ≥4 on ≥1 PEC item self-administered 180mcg, 120mcg or placebo.

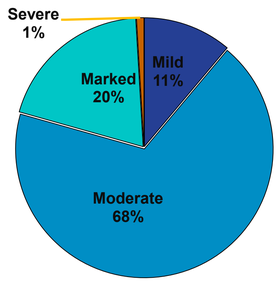
Primary outcome was 2-hour PEC change; secondary was time of separation from placebo. For this post hoc analysis, efficacy data were stratified into mild/moderate baseline agitation (CGI-S 3-4) and marked/severe baseline agitation (CGI-S 5-6).

RESULTS

- Significant improvement in agitation began as early as 10 minutes at 180 mcg and 20 minutes at 120 mcg (Fig 1)
- Baseline patient CGI-S ratings were mild/11%, moderate/68%, marked/20%, and severe/1%. Post hoc analysis showed statistically significant reduction in agitation with DSF in both baseline agitation groups (Figure 2)
- There were no severe or serious treatment-related adverse events. The most common pooled AEs were somnolence/21.5%, dry mouth/5.9%, hypotension/5.3%, dizziness/4.9%, orthostatic hypotension/4.0%, and oral hypoesthesia/3.8%. No patient was unarousable.

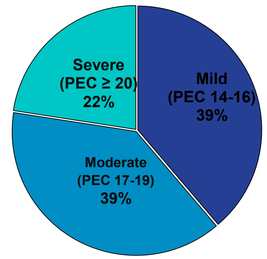
FIGURE 1. BASELINE AGITATION RATINGS: CGI-S AND PEC

CGI-S = Clinical Global Impression-Severity



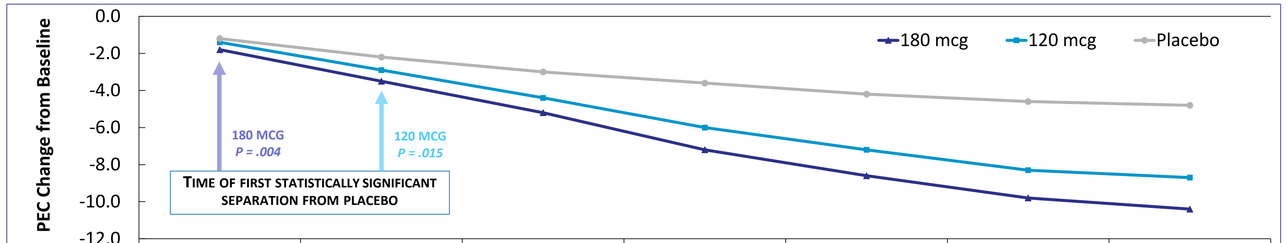
88% Rated as Moderate to Marked CGI-S Agitation Severity at Baseline

PEC = PANSS Excited Component



61% Rated as Moderate to Severe PEC Agitation Severity at Baseline

FIGURE 2. POOLED PEC CHANGE BY DOSE AND TIME – BASELINE TO 2 HOURS POSTDOSE



	10 mins Postdose	20 mins Postdose	30 mins Postdose	45 mins Postdose	1 hour Postdose	1.5 hours Postdose	2 hours Postdose
180 mcg	-1.8	-3.5	-5.2	-7.2	-8.6	-9.8	-10.4
120 mcg	-1.4	-2.9	-4.4	-6.0	-7.2	-8.3	-8.7
Placebo	-1.2	-2.2	-3.0	-3.6	-4.2	-4.6	-4.8

TABLE 1. POOLED ADVERSE EVENTS (AE) BY TREATMENT GROUP

	Sublingual Dexmedetomidine		
	180 mcg (n=252)*	**120 mcg (n=255)**	**Placebo (n=252)**
Any Treatment Emergent AE	92 (36.5)	95 (37.3)	41 (16.3)
Serious AE	0	1 (0.4)	0
Discontinuation due to AE	0	3 (1.2)	0
Somnolence	56 (22.2)	54 (21.2)	16 (6.3)
Dry Mouth	11 (4.4)	19 (7.5)	3 (1.2)
Hypotension	13 (5.2)	14 (5.5)	0
Dizziness	15 (6.0)	10 (3.9)	2 (0.8)
Orthostatic Hypotension	13 (5.2)	7 (2.7)	1 (0.4)
Oral Hypoesthesia	12 (4.8)	7 (2.7)	1 (0.4)
Headache	6 (2.4)	12 (4.7)	12 (4.8)
Nausea	7 (2.8)	6 (2.4)	4 (1.6)
Oral Paresthesia	6 (2.4)	7 (2.7)	1 (0.4)

Subjects were counted once within each adverse event preferred term. *Data for 1 subject enrolled in the study at two different sites in error (in the 120 mcg and the 180 mcg treatment groups) are reported in the 120 mcg and 180 mcg columns for adverse events.

SUMMARY

- Dexmedetomidine sublingual film reduced agitation symptoms as early as 10 minutes at 180 mcg group and 20 minutes at 120 mcg, regardless of baseline agitation severity
- The most common treatment emergent adverse events were somnolence, dry mouth, hypotension, dizziness, orthostatic hypotension, oral hypoesthesia
- Most somnolence was mild; all patients were awake or arousable

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