Raw scores for GEC, MI, and BRI (sum of 70, 40, and 30 items, respectively) were converted to a T-score (mean=50, standard deviation=10; T-score ≥ 65 considered abnormally elevated) and then to a change from (DB) baseline (CFB) T-score. The mean [±SE] CFB T-score was calculated for the GEC, MI, and BRI by study OLE visit, and the mean last on-study OLE visit was analyzed using a paired t-test.

**Results.** In the OLE trial, 157 subjects received viloxazine ER (first subject dosed, 24 Jan 2020; data cut, 30 MAR 2021). The mean [±SE (n)] T-score at DB baseline between placebo and viloxazine ER groups was similar for GEC [70.9 ± 0.82 (177) and 71.0 ± 0.77 (173)], MI [73.6 ± 0.86 (178) and 74.0 ± 0.83 (173)], and BRI [63.9 ± 0.85 (177) and 63.6 ± 0.77 (174)]. The CFB T-score decreased across OLE visits in all three measures. At last on-study OLE visit, the mean [±SE (n)] CFB T-score was significantly improved for the GEC [-12.4 ± 1.23 (121); P<0.0001], the MI (-12.6 ± 1.30 (121); P<0.0001], and the BRI [-10.0 ± 1.04 (122); P<0.0001]; median viloxazine ER dose was 400 mg/day.

**Conclusions.** Following the DB trial, improvement in executive function continued during viloxazine ER treatment in adults throughout the OLE trial, including a significant improvement at subjects' last on-study visit for overall functioning (GEC) and both indices (MI and BRI). Overall, the results suggest adults with ADHD may show improvement in executive function with viloxazine ER treatment.

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# Reliability of the Clinician's Tardive Inventory (CTI)

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**Abstract**

**Objectives.** Currently utilized clinician-rated symptom scales for tardive dyskinesia (TD) have not kept up with the expanding spectrum of TD phenomenology. The objective of this study was to develop and test the reliability of a new instrument, the CTI.

**Methods.** A movement disorder neurologist devised the outline of the scale. A steering committee (four neurologists and two psychiatrists) provided revisions until consensus was reached. The resulting instrument assesses frequency of abnormal movements of the eye/eyelid/face, tongue/mouth, jaw, limb/trunk, complex movements (e.g., handwringing, self-caressing), and vocalizations. The CTI rates symptoms from 0–3 with 0 = absent, 1 = infrequent/intermittent or only present with activating maneuvers, 2 = frequent intermittent, brief periods without movements, 3 = constant or nearly constant. Functional impairments including activities of daily living (ADL), social impairment, symptom bother, and harm are rated 0–3 with 0 = patient is unaware or unaffected, 1 = symptoms mildly impact patient, 2 = symptoms moderately impact patient, 3 = symptoms severely impact patient. Following institutional review board approval, the CTI underwent inter-rater and test-retest reliability testing. Videos of patient TD examinations were obtained and reviewed by two movement disorder specialists to confirm the diagnosis of TD by consensus and the adequacy to demonstrate a TD-consistent movement. Vignettes were created to include patients' symptom descriptions and functional, social, or occupational impairments/limitations. Four clinicians rated each video/vignette. Selected videos/vignettes were also subject to an intra-rater retest. Interrater agreement was analyzed via 2-way random-effects interclass correlation (ICC) and test-retest agreement assessment utilizing Kendall's tau-b.

**Results.** 45 video/vignettes were assessed for interrater reliability, and 16 for test-retest reliability. ICCs for movement frequency were as follows: abnormal eye movement .89; abnormal tongue/mouth movement .91; abnormal jaw movement .89; abnormal limb movement .76; complex movement .87; abnormal vocalization .77; and functional impairments including harm .82; social embarrassment .88; ADLs .83; and symptom bother .92. Retests were conducted on mean (SD) 15 (3) days later with scores ranging from .66–.87.

**Conclusions.** The CTI is a new instrument with good reliability in assessing TD symptoms and functional impacts. Future validation study is warranted.

**Funding.** Neurocrine Biosciences

# Mental Health Issues for Frontline Hospital Staff During Height of Covid Pandemic 2020

Diego Garces Gross, Yonatan Kaplan, Geoffrey Talis and Cheryl A. Kennedy

**Abstract**

**Introduction.** When the SARS-Cov2 virus hit the New York and New Jersey metropolitan area in Spring 2020, hospitals and hospital workers were hit hard with a new unknown pathogen that either killed people or made them very ill. There were large numbers of severely ill patients that strained resources. Hospital workers had extraordinary stress with multiple additional patients, the need to use personal protective equipment (PPE) in short supply, and faced with a pathogen that had no treatments beyond care and support initially.

**Methods.** We surveyed our hospital workers in late Spring 2020 to identify the main stressors and find out what measures were helpful. An online anonymous survey included questionnaires about sleep, mood, outside stressors, helpful measures, and how

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they coped generally. All levels of hospital workers were surveyed. Resources were provided to all respondents.
**Results.** Over 240 individuals responded to the survey; most respondents were women (76%). 'Workplace stressors' topped the chart for 98 of our respondents. The worst workplace stressor that was cited was 'irritable workforce,' but 'lack of 'protocols' and 'shortage of PPE' were also cited as stressors. 'Other' (not described) and 'taking care of an ill relative' were rated highly. Those who had 'symptoms everyday:' Anhedonia (loss of pleasure or interest), 13%; feeling down and hopeless, 12%; sleep disturbance, 41%; low energy, feeling tired, 29%; appetite disturbance, 26%; poor concentration and attention, 15%. Respondents told us what resources they used and what was most helpful; exercise was most frequently cited as helpful.
**Lessons Learned and Discussion.** Various resources for formal and informal mental health support were provided to all respondents at the time of survey. Our hospital mounted its own response with support services, as did our medical school and university. A "warm line" was available through the Department of Psychiatry from late March 2020; tip sheets and online groups were widely circulated; State Department of Health provided resources. There were formal peer support sessions and workers helped each other. Medical students provided child care, shopping, and transport. We learned that extra support for workers and more frequent rest and recharge time are important. A weekly "town hall" was instituted and a weekly update about the hospital and support in healthy activities are widely circulated to employees. Those with active PTSD (some were very disturbed by the number of deceased patients) were referred to professional providers. Hospitals need to be ready to deal with epidemics and pandemics more effectively in order to mitigate stress and support workers. Being prepared, not just with equipment, but with protocols in how to proceed should another pandemic come. We learned that listening to workers is important. Workers also need to know how valued they are.
**Funding.** Department of Psychiatry, New Jersey Medical School

# Safety and efficacy of KarXT (Xanomeline Trospium) in Schizophrenia in the Phase 3, Randomized, Double-Blind, Placebo-Controlled EMERGENT-2 Trial

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**Abstract**

**Introduction.** KarXT combines the $M_1/M_4$ preferring muscarinic receptor agonist xanomeline and the peripherally restricted anticholinergic trospium. In the phase 2 EMERGENT-1 study, KarXT met the primary endpoint of a significant reduction in Positive and Negative Syndrome Scale (PANSS) total score through week 5 vs placebo, improved other key secondary efficacy measures, and was generally well tolerated.
**Methods.** EMERGENT-2 was a phase 3, randomized, double-blind, placebo-controlled, 5-week trial of KarXT in acutely psychotic patients with schizophrenia in the inpatient setting. Eligible patients were randomized 1:1 to KarXT or matched placebo. Dosing of KarXT (mg xanomeline/mg trospium) started at 50 mg/20 mg BID and increased to a maximum of 125 mg/30 mg BID. The primary efficacy endpoint was change from baseline to week 5 in PANSS total score. Key secondary endpoints included change from baseline to week 5 in PANSS positive subscale, PANSS negative subscale, and PANSS negative Marder factor scores compared with placebo. Efficacy analyses were performed using the modified intent-to-treat population (patients with ≥1 dose of study medication, a baseline PANSS assessment, and ≥1 postbaseline PANSS assessment). All patients receiving ≥1 dose of study drug were included in safety analyses.
**Results.** 252 US patients were enrolled. KarXT demonstrated a statistically significant and clinically meaningful 9.6-point reduction from baseline to week 5 (effect size=0.61) in PANSS total score vs placebo ($p<0.0001$); a significant improvement in PANSS total score was demonstrated starting at week 2 (first postbaseline rating) and continued through the study end. KarXT also met key secondary endpoints. Results at week 5 included a 2.9-point reduction in PANSS positive subscale score with KarXT vs placebo ($p<0.0001$), a 1.8-point reduction in PANSS negative subscale score with KarXT vs placebo ($p=0.0055$), and a 2.2-point reduction in PANSS negative Marder factor score with KarXT vs placebo ($p=0.0022$). KarXT was generally well tolerated. Overall discontinuation rates were similar with KarXT (25%) and placebo (21%). The overall treatment-emergent adverse events (TEAEs) rate for KarXT and placebo was 75% and 58%, respectively. Discontinuation rates related to TEAEs were similar between KarXT (7%) and placebo (6%). Rates of serious TEAEs were similar with KarXT and placebo (2%, each group); no serious TEAEs were determined to be drug related. The most common TEAEs (≥5%) with KarXT were all mild to moderate in severity and included constipation, dyspepsia, nausea, vomiting, headache, blood pressure increases, dizziness, gastroesophageal reflux disease, abdominal discomfort, and diarrhea. KarXT was not associated with sedation/somnolence, weight gain, and extrapyramidal symptoms.
**Conclusions.** KarXT has the potential to be the first in a new class of treatments for patients with schizophrenia and a promising alternative to postsynaptic dopamine $D_2$ receptor antagonists.
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