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.
Funding. Karuna Therapeutics, Inc.

https://doi.org/10.1017/S1092852923001360 Published online by Cambridge University Press