CONCLUSIONS: This case report supports rTMS paired with cognitive training to be a safe and tolerable treatment for early-onset AD. However, more treatment cycles must be completed before conclusions about its efficacy can be determined.

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CME on Pharmacogenomics Testing Improves Knowledge, Competence, and Confidence Related to Implementing Testing in Practice

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ABSTRACT: Study Objective(s): Pharmacogenomics (PGx) testing, in particular combinatorial PGx testing, represents a potential means for delivering personalized treatment selection for patients with psychiatric disorders. The goal of this educational intervention was to educate clinicians about the role of PGx testing in neuropsychiatric conditions such as MDD, how these novel tests may be implemented into clinical practice, and how results may be used to inform decision-making.

METHOD: Psychiatrists (n=830) participated in an online enduring CME activity on PGx testing in psychiatric disorders

- The format was a 30-minute 2-person discussion (launched December 7, 2018)
- Data from this activity were collected for 30 days after launch
- Effectiveness of education for the CME activities was analyzed using 3 multiple-choice and 1 self-efficacy question (5-point Likert-type scale), presented as pre-/post-CME repeated pairs
- A paired samples t-test was conducted to examine improvements in mean confidence pre and post

Participant knowledge, competence, and confidence change in pre- to post-CME responses were calculated

RESULTS: Overall, 72% of psychiatrists (n=830) had knowledge or competence that was reinforced or improved as a result of education.

FOLLOWING EDUCATION:

* 56% and 12% of psychiatrists had reinforcement and improvement, respectively, in knowledge related to the clinical benefits of PGx-guided treatment strategies
- 61% and 8% of psychiatrists had reinforcement and improvement, respectively, in competence related to interpreting PGx tests for patients with neuropsychiatric disorders
- Within the group of psychiatrists with reinforced and improved knowledge/competence, there was a 30% increase in their confidence using PGx tests to help guide treatment decisions for patients with major depressive disorder (MDD) (M pre=2.14, post=2.77, scale 1 to 5)
- Confidence in the use of PGx testing was correlated with likelihood of considering PGx testing for patients with MDD

CONCLUSIONS: Online CME aided in psychiatrists' knowledge, competence, and confidence in using pharmacogenomics testing in patients with psychiatric disorders.
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Efficacy and Safety of SEP-363856, a Novel Psychotropic Agent with a Non-D2 Mechanism of Action, in the Treatment of Schizophrenia

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ABSTRACT: Background: SEP-363856 is a novel psychotropic agent that has shown broad efficacy in animal models of schizophrenia and depression. Its antipsychotic effects appear to be mediated by agonist activity at both trace amine-associated receptor 1 (TAAR1) and 5-HT1A receptors. Notably, SEP-363856 does not bind to any dopaminergic, serotonergic (except 5-HT1A), glutamatergic, or other neuroreceptors thought to mediate the effects of currently available antipsychotics. The aim of this study was to evaluate the efficacy and safety of SEP-363856 in acutely symptomatic patients with schizophrenia.

METHOD: Patients aged 18-40 years meeting DSM-5 criteria for schizophrenia (PANSS total score ≥80) were randomized, double-blind, to 4-weeks of flexible-dose SEP-363856 (50 or 75 mg/d) or placebo. Efficacy measures included the Positive and Negative Syndrome Scale (PANSS) total score (primary), PANSS subscale scores, and the Clinical Global Impressions-Severity (CGI-S) score. Change from baseline in primary and secondary measures were analyzed using a mixed model for repeated measures (MMRM) analysis.

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RESULTS: Study treatment groups were similar at baseline: SEP-363856 (N=120; male, 64.2%; mean age, 30.0 years; PANSS total score, 101.4) and placebo (N=125; male, 63.2%; mean age, 30.6 years; PANSS total score, 99.7). Least-squares (LS) mean reduction from baseline to week 4 was significantly greater for SEP-363856 vs. placebo on the PANSS total score (-17.2 vs. -9.7; P=0.001; effect size, 0.45), PANSS positive subscale score (-5.5 vs. -3.9; P=0.019; effect size, 0.32), PANSS negative subscale score (-3.1 vs. -1.6; P=0.008; effect size, 0.37), PANSS general psychopathology subscale score (-9.0 vs. -4.7; P<0.001; effect size, 0.51), and the CGI-Severity score (-1.0 vs. -0.5; P<0.001; effect size, 0.52). Discontinuation rates for SEP-363856 vs. placebo were similar overall (21.7% vs. 20.8%) and due to an adverse event (8.3% vs. 6.4%). Change in weight, lipids, glucose and prolactin was similar in SEP-363856 and placebo groups. Adverse events occurring with an incidence ≥2% on SEP-363856 or placebo (with SEP-363856 incidence higher than placebo) were: somnolence (6.7% vs. 4.8%), agitation (5.0% vs. 4.8%), nausea (5.0% vs. 3.2%), diarrhea (2.5% vs. 0.8%), and dyspepsia (2.5% vs. 0%). The proportion of patients who reported any extrapyramidal symptom was 3.3% on SEP-363856 and 3.2% on placebo.

CONCLUSION: In this placebo-controlled study, treatment with SEP-363856, a novel psychotropic agent, was associated with statistically significant and clinically meaningful improvement in schizophrenia symptoms as demonstrated by endpoint change in PANSS total and subscale scores, and CGI-Severity scores. Safety and tolerability findings for SEP-363856 were in general similar to placebo. In particular, SEP-363856 was not associated with extrapyramidal symptoms, akathisia, or hyperprolactinemia, consistent with its non-D2 mechanism of action.

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Early Response with Valbenazine and Long-Term Symptom Reduction in Patients with Tardive Dyskinesia: Post Hoc Analysis of the KINECT 3 Study

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ABSTRACT: Study Objective: Tardive dyskinesia (TD) is a persistent and potentially disabling movement disorder associated with prolonged exposure to antipsychotics and other dopamine receptor blocking agents. Valbenazine is a highly selective vesicular monoamine transporter 2 (VMAT2) inhibitor approved for the treatment of TD in adults. Using data from a long-term study (KINECT 3; NCT02274558), the effects of once-daily valbenazine (40 mg, 80 mg) on TD were assessed using the Abnormal Involuntary Movement Scale (AIMS) in participants who were early responders based on subjective measures, including patient self-report (Patient Global Impression of Change [PGIC]) or clinician judgment (Clinical Impression of Change-Tardive Dyskinesia [CGI-TD]).

METHODS: Data from KINECT 3 (6-week double-blind, placebo-controlled [DBPC] period; 42-week double-blind extension) were analyzed post hoc. Long-term outcomes included mean change from baseline to Week 48 in AIMS total score (sum of items 1-7) and AIMS response (≥50% total score improvement from baseline) at Week 48. These AIMS outcomes were assessed in participants who achieved early improvement, defined as a PGIC or CGI-TD score of ≤3 ("minimally improved" or better) at Week 2 (first post-baseline visit of the DBPC period). Participants who initially received placebo were not included in the analyses.

RESULTS: In participants who received only valbenazine (40 or 80 mg) during KINECT 3 and had available Week 2 assessment, 50% (72/143) had early PGIC improvement (score ≤3) and 43% (61/142) had early CGI-TD improvement (score ≤3). Baseline characteristics were generally similar between participants who achieved early PGIC or CGI-TD improvement and those who did not. Based on available assessments at Week 48, mean AIMS total score change from baseline in participants with early PGIC improvement was similar to those who did not reach the early PGIC improvement threshold (-4.1 [n=35] vs -3.5 [n=41]). Mean AIMS total score change from baseline in participants with early CGI-TD improvement was similar to those who did not achieve early CGI-TD improvement (-4.2 [n=31] vs -3.5 [n=45]). AIMS response at Week 48 was also similar in those who achieved early PGIC and CGI-TD improvement

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