following the original 30-day intervention. Prescription numbers continued to decrease over the next six months (to 92-93% of pre-intervention numbers), which indicates that the deprescribing intervention may have had a sustainable positive effect on provider prescribing behavior. This intervention is easy to implement and may decrease BZD prescribing, which addresses the overuse/misuse of BZD, a significant public health concern in the United States.

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Evaluation of Individual Items on the PHQ-9 and SDS in Patients with Treatment-Resistant Depression Treated with Esketamine Nasal Spray

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ABSTRACT: Introduction: Major depressive disorder (MDD) is a global long-term condition and is the leading cause for disability in most countries. The objective of this study was to evaluate individual items of the PHQ-9 and SDS to show differences by treatment arm over the course of treatment.

METHODS: The TRANSFORM-2 study (NCT02418585) was a Phase 3 short-term trial that evaluated efficacy and safety of flexible esketamine nasal spray (56 mg or 84 mg) doses in combination with newly initiated oral antidepressant (ESK+AD) vs oral AD + placebo nasal spray (AD+PBO) in patients with treatment resistant depression (TRD). The study population, men and women aged 18-64 years, who met the Diagnostic and Statistical Manual of Mental Disorders, Edition 5 diagnostic criteria for single-episode or recurrent MDD, but excluded subjects with suicidal ideation/intent to act within 6 months prior to study. Patient reported outcomes (PROs) were integrated to evaluate the patient perspective of treatment using instruments capturing concepts of importance. The 9-item Patient Health Questionnaire (PHQ-9) is a PRO instrument to assess self-reported depression symptoms, and the SDS a PRO instrument to assess function and disability. Individual items on each of these instruments represent a symptom or aspect of functioning. Respective items for PHQ-9 and SDS, are summed together to generate a total score: 0-27 for the PHQ-9 and 0-30 for SDS. Each total score reflects a single construct of depression severity for the PHQ-9 and functional disability for SDS. Change from baseline in SDS and PHQ-9 total scores at Day 28 were analyzed using a mixed-effects model using repeated measures based on observed case data. Generalized estimation equations of logistic regression models were used to estimate the likelihood of improvement by ≥ 1 point on the individual items of the PHQ-9 and SDS.

RESULTS: Full analysis set included 223 patients (ESK +AD: 114; AD+PBO: 109). Change in SDS total score from baseline to Day 28 numerically favored ESK+AD. The LS mean treatment difference (95% CI) was -4.0 (-6.28; -1.64). Change in PHQ-9 total score from baseline to Day 28 numerically favored treatment with ESK+AD. The LS mean difference (95%CI) was -2.4 (-4.18; -0.69). Most patients experienced improvement on all PHQ-9 items and more patients experienced greater improvement in the ESK+AD treatment arm compared to the AD+PBO arm (odds ratio range 1.367-2.767; favoring ESK+AD). Improvements were seen across all items of the Sheehan Disability Scale (odds ratio range from 1.994 – 3.378; favoring ESK+AD).

CONCLUSIONS: This study shows that while the magnitude of improvement varied on individual items, ESK+AD treatment leads to greater symptom improvement across the multiple symptoms included in the PHQ-9 and SDS compared to the AD+PBO. This assists interpretation of the total scores generated by these PRO measures since total scores on the two measures was not driven by a single item.

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HAM-D6 Outcomes in a Randomized, Controlled Trial Evaluating the Utility of Combinatorial Pharmacogenomics in Depression

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ABSTRACT: Background: The Genomics Used to Improve DEpresssion Decisions (GUIDED) trial assessed outcomes associated with combinatorial pharmacogenomic (PGx) testing in patients with major depressive disorder (MDD). Analyses used the 17-item Hamilton Depression (HAM-D17) rating scale; however, studies demonstrate that the abbreviated, core depression symptom-focused, HAM-D6 rating scale may have greater sensitivity toward detecting differences between treatment and placebo. However, the sensitivity of HAM-D6 has not been tested for two active treatment arms. Here, we evaluated the sensitivity of the HAM-D6 scale, relative to the HAM-D17 scale, when assessing outcomes for actively treated patients in the GUIDED trial.

METHODS: Outpatients (N=1,298) diagnosed with MDD and an inadequate treatment response to >1 psychotropic medication were randomized into treatment as usual (TAU) or combinatorial PGx-guided (guided-care) arms. Combinatorial PGx testing was performed on all patients, though test reports were only available to the guided-care arm. All patients and raters were blinded to study arm until after week 8. Medications on the combinatorial PGx test report were categorized based on the level of predicted gene-drug interactions: 'use as directed', 'moderate gene-drug interactions', or 'significant gene-drug interactions.' Patient outcomes were assessed by arm at week 8 using HAM-D6 and HAM-D17 rating scales, including symptom improvement (percent change in scale), response (≥50% decrease in scale), and remission (HAM-D6 ≤4 and HAM-D17 ≤7).

RESULTS: At week 8, the guided-care arm demonstrated statistically significant symptom improvement over TAU using HAM-D6 scale (Δ=4.4%, p=0.023), but not using the HAM-D17 scale (Δ=3.2%, p=0.069). The response rate increased significantly for guided-care compared with TAU using both HAM-D6 (Δ=7.0%, p=0.004) and HAM-D17 (Δ=6.3%, p=0.007). Remission rates were also significantly greater for guided-care versus TAU using both scales (HAM-D6 Δ=4.6%, p=0.031; HAM-D17 Δ=5.5%, p=0.005). Patients taking medication(s) predicted to have gene-drug interactions at baseline showed further increased benefit over TAU at week 8 using HAM-D6 for symptom improvement (Δ=7.3%, p=0.004) response (Δ=10.0%, p=0.001) and remission (Δ=7.9%, p=0.005). Comparatively, the magnitude of the differences in outcomes between arms at week 8 was lower using HAM-D17 (symptom improvement Δ=5.0%, p=0.029; response Δ=8.0%, p=0.008; remission Δ=7.5%, p=0.003).

CONCLUSIONS: Combinatorial PGx-guided care achieved significantly better patient outcomes compared with TAU when assessed using the HAM-D6 scale. These findings suggest that the HAM-D6 scale is better suited than is the HAM-D17 for evaluating change in randomized, controlled trials comparing active treatment arms.
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Confirmed Safety of Deutet.rabenazine for Tardive Dyskinesia in a 3-Year Open-Label Extension Study

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ABSTRACT: Background: Deutetrabenazine (Austedo) is approved by the FDA for treatment of tardive dyskinesia

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