

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 over-use/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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