METHOD: We present the case of a 32-year-old male with bipolar II disorder, who was initially went through elective cholecystectomy complicated by bowel perforation and septic shock. Patient had to be intubated and had complicated ICU stay. Various consultation services including Neurology, Infectious disease, psychiatry, Intensivist got involved to address the multiple medical comorbidities like sepsis, encephalopathy and apathy. In spite of improving EEG showing resolving encephalopathy patient remained mute, immobile, not following any instructions, with no oral intake. All imaging including CT scan and MRI repeated 3 times over the period of time were negative. Patient's psychiatric medications that includes Wellbutrin was held to minimize the risk of seizures. Patient's neuro exam had positive Babinski and pupils dilated. He also had autonomic dysfunction. There were no clear-cut symptoms to enable us differentiating hypoxic brain injury and Malignant catatonia. We considered the differential diagnosis of Catatonia and initiated Ativan IV challenge.

RESULTS: The patient was reassessed one hour after administration of lorazepam. He displayed slight response to Ativan by moving his fingers in the first 24 hrs. We had to continue to titrate the Ativan to very high doses in the period of 3 weeks with a very slow but good response.

CONCLUSION: This case reflects the intricacy in diagnosing Catatonia complicated by Encephalopathy and the challenges in its treatment. We want to add on to the current literature on Catatonia masked by multiple medical comorbidities and the challenges of treatment

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Determining Meaningful Change in Depression Symptoms Assessed with PHQ-9 and SDS in Treatment-resistant Depression Trials of Esketamine Nasal Spray

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ABSTRACT: Introduction: Major depressive disorder (MDD) has been ranked among the top causes worldwide of years lived with disability. In this study we assessed meaningful change for the PHQ-9 and the SDS and determined the meaningful change threshold (MCT) using anchor-based methods, which could be used to compare meaningful differences in patients within different treatment arms.

METHODS: TRANSFORM-1 (NCT02417064) and -2 (NCT0241858) were Phase 3 trials that evaluated the efficacy and safety of fixed and flexible doses of esketamine nasal spray (56 mg or 84 mg) in combination with newly initiated oral antidepressant (ESK+AD) vs oral antidepressant + placebo nasal spray (AD+PBO) in TRD patients. Patient Reported Outcomes (PROs) were integrated into these trials to evaluate the patient perspective of treatment using instruments capturing concepts of importance to patients. The 9-item Patient Health Questionnaire (PHQ-9) is a PRO instrument used to assess self-reported depression symptoms and the Sheehan Disability Scale (SDS) is a PRO for self-reported function and disability. Blinded trial data (combined treatment groups) from TRANSFORM-1 was used for the anchor-based analysis. The Clinical Global Impression - Severity (CGI-S) was used as an anchor and patients were classified into response groups depending on their level of change over the course of the study. Patients were classified among all possible change categories (15 levels, ranging from -7 to 7 where negative change scores indicate improvement). Cumulative Distribution Function (CDF) curves of change from baseline to day 28 were generated using unblinded data from TRANSFORM-2 to visualize the range of responses demonstrated in the respective treatment groups for the PHQ-9 and SDS. MCT values were used to as thresholds to evaluate percentage of responders in each treatment group.

RESULTS: In anchor-based analyses using TRANSFORM-1 combined treatment groups, the correlation between change on the CGI-S and change on the PHQ-9 at Day 28 was high (> 0.60) with anchor-based MCTs ranging from 5 to 8 points. The magnitude of change (standardized effect size estimate within-subject change) for patients improving was exceptionally high (> 0.80). Similar results were observed on the SDS: high correlation of

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CGI-S and SDS at Day 28 (0.75), moderate SES (0.66), with suggested MCT ranging from 3 to 7 with an MCT value of 5 pts. CDF curves from TRANSFORM-2 showed clear separation between the ESK+AD vs AD+PBO across a number of responder definitions inclusive of those identified with the anchor-based analyses.

CONCLUSIONS: The current study is the first to derive an MCT on the PHQ-9 and SDS in TRD to measure meaningful change from the perspective of the patient using regulatory-preferred psychometric anchor-based methodology. These analyses assist with interpretation of meaningfulness of esketamine phase 3 clinical trial results from the patient perspective.

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Treating Chronic Pain and Preventing Opioid Use Disorders in the Underserved: An Integrated Primary Care Model

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ABSTRACT: This poster builds on the CDC pain management guidelines and the current ASAM recommendations for substance use assessment to build an integrated primary care model for holistic chronic pain management in an urban, underserved primary care clinic. Using a case from our Federally Qualified Health Care Center, which operates in a southwest Denver clinic, a program of integrated care assessment, diagnosis, and holistic treatment planning is outlined for this client with chronic pain, physical, and behavioral health issues. Using a comprehensive care approach for complex clients, which are typical presentations for urban, underserved clients, we discuss the utilization of best practices in medication management for chronic pain (Alternatives to Opioids (ALTOS), prescribed and complementary and alternative practices (e.g., PT, acupuncture, etc), and behavioral health services (psychiatric assessment and treatment, psychotherapy, support groups, etc) to improve outcomes for our clients.

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Single-Dose Pharmacokinetics of Amphetamine Extended-Release Tablet Compared with Amphetamine Extended-Release Oral Suspension

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ABSTRACT: Objectives: Evaluate comparative bioavailability of single-dose amphetamine extended-release tablet (AMPH ER TAB, Tris Pharma, Inc., Monmouth Junction, NJ) 20 mg, swallowed whole or chewed and amphetamine extended-release oral suspension (AMPH EROS) 2.5 mg/mL; and evaluate whether a PK food effect exists on AMPH ER TAB (contains a 3.2:1 ratio of d- to l-amphetamine).

METHODS: Healthy volunteers (18-55 yr) were randomized to 1 dose of AMPH ER TAB 20 mg swallowed (fasted), chewed (fed/fasted), or 20 mg AMPH EROS (fasted).
A crossover design was used. Samples were collected each period pre-dose and at time points to 60 h post-dose. D-and l-amphetamine were measured, and PK was calculated (90% CIs of the ratios of the geometric mean plasma levels) for Cmax, AUCt, and AUC0∞. Comparative bioavailability was determined when ratios were within 80 and 125%. Safety was also assessed.

RESULTS: 32 subjects completed the study. Based on the calculated bioavailability ratios, for AMPH ER TAB swallowed vs. AMPH EROS fasted: d-amphetamine total and peak exposures were found to be similar: AUC0-t: 100.68-108.08%, AUC0-∞:101.47-109.52%, Cmax: 98.10-103.17%. For l-amphetamine, the total and peak exposures were similar: AUC0-t: 100.31-108.57%, AUC0-∞:101.27-111.09%, Cmax: 98.2-103.37%.
AMPH ER TAB chewed vs. AMPH EROS fasted: For d-amphetamine, the total and peak exposures were similar: AUC0-t: 99.23-106.62%, AUC0-∞: 99.58-107.59%, Cmax: 99.91-105.14%. For l-amphetamine, the total and peak exposure was similar: AUC0-t: 98.16-106.35%, AUC0-∞: 98.44-108.11%, Cmax: 99.53-104.75%.
Food effect: AMPH ER TAB, chewed, fasted vs. fed: For d-amphetamine, the total and peak exposure was similar: AUC0-t: 92.57-99.49%, AUC0-∞: 91.12-98.48%, Cmax: 94.22-99.17%.
For l-amphetamine, the total and peak exposure was similar: AUC0-t: 91.27-98.91%, AUC0-∞: 88.44-97.17%, Cmax: 94.52-99.50%).
No serious AEs were reported during the conduct of this study, and the AE profiles were observed to be similar in frequency of events and severity to other amphetamine formulations used in ADHD.

CONCLUSIONS: Bioavailability of single dose of AMPH ER TAB for both d- and l-amphetamine was comparable, swallowed whole or chewed, to an equivalent 20 mg dose of the reference product AMPH EROS, 2.5 mg/mL fasted, and showed equivalent peak and overall exposure.

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