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Efficacy and Safety of the Asenapine Transdermal Patch, HP-3070, for Schizophrenia: A Phase 3, Randomized, Placebo-Controlled, Inpatient Study

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ABSTRACT: Background: Asenapine is a 2nd-generation antipsychotic currently marketed as a sublingual (SL) tablet in the US for the treatment of schizophrenia. HP-3070, asenapine transdermal system, is a patch for treatment of schizophrenia in adults. Low- and high- HP-3070 doses deliver asenapine concentrations that are similar to SL asenapine 5 mg BID and 10 mg BID, respectively, but with fewer peak and trough fluctuations.

METHODS: In this Phase 3, randomized, double-blind, placebo (PBO)-controlled, 6-week inpatient study, adults with schizophrenia having baseline Positive and Negative Syndrome Scale (PANSS) total score ≥80 and Clinical Global Impression–Severity of Illness Scale (CGI-S) score ≥4 were randomized 1:1:1 to HP 3070 high-dose, HP-3070 low-dose, or PBO.
The primary efficacy objective was Week 6 PANSS score change from baseline (CFB) vs PBO.
The key secondary objective was Week 6 CGI-S CFB vs PBO.
Safety assessments included treatment-emergent adverse events (TEAEs), laboratory results, vital signs, dermal safety, and extrapyramidal symptoms (EPS) assessments.

RESULTS: A total of 616 patients were randomized, with 486 patients completing the study. Discontinuation rates were 23.3%, 18.6%, and 21.4% for HP-3070 high-dose, HP-3070 low-dose, and PBO, respectively; withdrawal of consent and AEs were the most common reasons for discontinuation. Demographics and baseline characteristics were well-balanced among treatment groups.
For PANSS total score, least squares mean (LSM) (standard error [SE]) estimates of the treatment comparison (HP-3070 vs PBO) for CFB at Week 6 were -4.8 (1.634; 95% CI: -8.06, -1.64; p=0.003) and -6.6 (1.630; 95% CI: 9.81, 3.40; p<0.001) for HP-3070 high- and low-dose, respectively. For CGI-S CFB at Week 6, LSM (SE) for the treatment comparison were 0.4 (0.100; 95% CI: 0.55, 0.16; p<0.001) for HP 3070 high-dose and 0.4 (0.099; 95% CI: 0.64, 0.25; p<0.001) for low-dose.
No deaths or serious TEAEs related to study treatment occurred. The HP-3070 safety profile was consistent with SL asenapine. Incidence of TEAEs at the patch application site was higher for HP-3070 (14.2% high-dose, 15.2% low-dose) than for PBO (4.4%); most of these events were mild or moderate in severity. PBO patients had higher rates of psychiatric disorders (24.3% vs 15.7% and 17.6% for HP-3070 high- and low-dose, respectively), with insomnia and anxiety as most common. Study treatment discontinuations due to application site reactions or skin disorders were low (≤0.5%) across treatment groups. There was no marked mean CFB for vital signs or electrocardiogram parameters, nor treatment differences observed on EPS assessments.

CONCLUSIONS: In this study, HP-3070 was efficacious, safe, and well-tolerated for treating schizophrenia in adults; both doses met primary and key secondary endpoints. As the first transdermal antipsychotic patch in the US, HP-3070 will provide patients a novel treatment option.
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Training Forgiveness. A Novel Approach to Reducing Physician Burnout

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ABSTRACT: Study Objective: Psychological risk factors that lead to impaired work performance, negatively impacting mental and physical health, have emerged as a concern across clinical settings. Although depression and anxiety are linked to poor physician mental health, physician burnout characterized by work related stress due to chronic exhaustion from clinical work, cynicism toward meaning of the medical profession, and feelings of inadequacy toward work related accomplishments, may be an even stronger indicator of well-being. Literature suggests

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that work satisfaction among physicians is rapidly deteriorating owing to high rates of burnout and poor mental health. Although the relationship between work burnout (WB) and negative affectivity has been well documented, the association with positive affect, such as trait forgiveness (TF) has been overlooked. On that note, research shows that lifetime stress severity and lower levels of forgiveness predict worse mental and physical health. Since TF has been linked strongly with healthy workplace relationships, positive occupational outcomes and general well-being, its association with WB remains to be investigated. Therefore, the aim of the present study was to explore the link between TF and WB among physicians. We hypothesized that TF would be associated with reduced levels of burnout.

METHOD: A total of 62 (F=23) medical residents at a Teaching Hospital consented for the study. Residents were administered surveys on WB (Maslach Burnout Inventory), workplace bullying, personal bullying (PB), interpersonal rejection sensitivity (IRS), perceived stress scale (PSS), TF, anxiety, and depression, all of which were anonymously submitted via electronically. Hierarchical multiple regression (HMR) models were used to determine the associations between WB, work environment social factors and TF. A p-value of <0.05 was considered significant.

RESULTS: The mean age 33.1 ± SD 4.2 years. HMR analysis using WB as main outcome contained 6 predictors: Model 1 contained depression and anxiety, Model 2 added PB, Model 3 added IRS and PSS, Model 4 added TF. Anxiety and TF were the only significant predictors ($p= >0.05$) accounting for 10.4% and 17.5% of the variance in WB scores, respectively.

CONCLUSIONS: The novel finding of the present study is that TF was associated with low levels of burnout. Additionally, WB was found to be linked to anxiety and depression which is in line with previous research. These data suggest that TF could be a potential resolution to the deleterious influence of burnout. Further exploration is needed in order to understand the psychology of forgiveness as a potential adjuvant and/or therapeutic intervention for physicians' burnout. These results suggest that strategies including forgiveness training aimed at decreasing WB while increasing job satisfaction among physicians warrant further exploration.

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Sustainability of a Benzodiazepine Deprescribing Intervention with Primary Care Providers in a University-Based Community Clinic

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ABSTRACT: Study Objectives: In light of the opioid crisis, less attention has been focused on the long-term misuse of benzodiazepines (BZD) for anxiety and sleep disorders. The purpose of this study was to determine the sustainability of positive results (an 80% decrease in BZD prescribing) following a deprescribing intervention with primary care providers working with a low-income population at a Midwestern university-based community clinic.

METHOD: All de-identified BZD prescriptions written by providers at the community clinic were captured using the electronic medical record. A BZD equivalency chart was used to compare the relative potencies of BZD commonly prescribed by the clinic. Each prescription was converted to a single number: the diazepam equivalent (DE). This number takes into account the potency of the drug (using diazepam as the standard), the dose of the drug, number of tablets dispensed and number of refills. The number of DE prescribed was tallied every 30 days for 6 months following the completion of a quality improvement BZD deprescribing intervention. The original intervention was implemented in 2018, with the goal of decreasing the prescription of BZD by clinic primary care providers to outpatients for insomnia or anxiety. The brief intervention combined academic detailing and pharmaceutical company detailing with a deprescribing message. Providers were given current evidence about alternatives to BZD, deprescribing schedules, and brain-storming opportunities about the management of patient concerns and resistance to change. Posters with alternatives to BZD were hung in the main provider office at the clinic. Food and "No Benzo" logo merchandise (mugs, pens) were provided to attendees of the intervention and clinic nurses. Thirty days after the intervention, the number of DE prescribed decreased by 80%.

RESULTS: Benzodiazepine prescribing (measured in DE) continued to decrease every 30 days for six months to 92-93% of pre-intervention numbers.

CONCLUSIONS: Follow up of a 2018 intervention revealed sustainability of the effect of a significant decrease in benzodiazepine (BZD) prescribing in a community clinic. A brief BZD deprescribing intervention using a combination of academic detailing and pharmaceutical company detailing designed to persuade prescribers to change their behavior was effective in influencing providers to decrease the amount of BZD they prescribe. The desired result (an 80% decrease in BZD prescribing) was achieved

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