ABSTRACT: Long acting injectable (LAI) antipsychotics are indicated for individuals suffering from schizophrenia, delusional disorder, schizoaffective disorder and bipolar disorder. Even though LAIs have traditionally been used for a subgroup of patients who were not compliant with oral treatments or who were a high risk to others, current trends are changing with increased options and availability of these treatments. A number of factors are implicated in the reversal of this trend including perspectives of patients and perspectives of providers. There is not abundant literature available regarding robust studies to examine these perspectives, but this presentation provides a current summary of available literature.

Some factors that influence perspectives of both patients and providers include knowledge about LAIs, cost of LAIs and the traditional views of these agents as being used under coercive circumstances. Altering perspectives has been a primary barrier to increase the use of these agents. Evidence clearly supports the use of early intervention for individuals with first episode psychosis, and poor medication compliance results in poorer treatment outcomes. With the potential improvement in quality of life and potentially decreasing the cost burden of this illness in society, this avenue for treatment must be a strong consideration for all involved in the treatment of the aforementioned disorders.

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Withdrawal Symptom Assessment in an Esketamine Safety Study in Patients with Treatment-resistant Depression

Leah Aluisio, PhD[1]; Lynn Yieh, PhD[1]; Ewa Wajs, MD, PhD[2]; Allitia DiBernardo, MD[3]; Andrew Krystal, MD[4]; Wayne Drevets, MD[1]; Yun Wu, PhD[5]; Jagadish Gogate, PhD[5]; Ella Daly, MD[3]; Peter Zannikos, PhD[3]; Valerie Curran, PhD[6]; Guang Chen, MD, PhD[1]; and Jaskaran Singh, MD[1]

[1] Janssen R&D, San Diego, CA US
[2] Janssen R&D, Beerse BE
[3] Janssen R&D, Titusville, NJ US
[4] UCSF, San Francisco, CA US
[5] Janssen R&D, Raritan, NJ US
[6] University College London, London UK

ABSTRACT: Background: SUSTAIN-2 (NCT02497287) was an open-label, phase III trial evaluating the safety of esketamine (ESK) nasal spray plus a newly initiated oral antidepressant (AD) for up to 1 year in adults with treatment-resistant depression (TRD). ESK is a schedule III drug that acts via glutamate receptor modulation. ESK is rapidly cleared from the plasma, and with intermittent dosing there is no accumulation. Thus, no withdrawal syndrome is expected. The current analysis assessed potential withdrawal symptoms in patients who discontinued ESK after long-term, intermittent use. In the absence of a glutamatergic-specific withdrawal scale, the Physicians Withdrawal Checklist1 (PWC-20) was used. The PWC-20 was designed to assess new or worsening benzodiazepine-like discontinuation symptoms after stopping non-SSRI anxiolytics.

METHODS: ESK nasal spray was administered two times per week during a 4-week induction phase (IND). Responders entered the optimization/maintenance phase (O/M) where ESK nasal spray was dosed either weekly or every two weeks for up to 48 weeks. Patients entered a 4-week follow up period (F/U) after discontinuation from either phase, during which continuation of the AD was recommended. PWC-20 assessments were conducted at the last ESK dosing (endpoint of IND or O/M) and at weeks 1, 2 and 4 of F/U. Symptoms were rated using a 0-3-point scale (Not present = 0, Mild = 1, Moderate = 2, Severe = 3). To account for worsening of underlying depression, subset calculations were performed for depressive symptoms (PWC-DS: loss of appetite; anxiety or nervousness; irritability; dysphoric mood or depression; insomnia; fatigue, lethargy or lack of energy; restlessness or agitation; headaches; muscle aches or stiffness; weakness; difficulty concentrating or remembering; depersonalization-derealization) and withdrawal symptoms (PWC-WS: nausea and/or vomiting; diarrhea; poor coordination; diaphoresis; tremor or tremulousness; dizziness or light-headedness; increased acuity of sound, smell, or touch; paresthesias).

RESULTS: Data on 357 patients entering F/U were included in the analysis (91 completed treatment during the IND phase and 141 were treated during O/M). The mean (SD) PWC-20 total scores (range 0-60) at treatment endpoint, Week 1, 2 and 4 were 7.2 (6.8), 7.5(7.0), 7.4 (7.1) and 7.2 (6.9), respectively. At these same assessment times, mean PWC-WS scores (range 0-24) were 0.9 (1.7), 1.0 (1.7), 1.0 (1.8), and 0.9 (1.8). Mean PWC-DS scores (range 0-36) were 6.3 (5.6), 6.5 (5.7), 6.5 (5.8), and 6.3 (5.7), respectively. Complete analysis of data from the entire SUSTAIN-2 dataset will be presented.

CONCLUSIONS: No indication of drug-specific withdrawal symptoms was seen after stopping up to 1-year of intermittent treatment with ESK nasal spray for TRD.

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