Abstract

Background. SEP-363856 is a novel psychotropic agent without dopamine D2 receptor occupancy. Although its mechanism of action has not been fully elucidated, preclinical data suggest that agonism at trace amine receptor 1 (TAAR1) and the serotonin 5-H1A receptor contributes to its efficacy. In a double-blind (DB), placebo-controlled study, SEP−363856 demonstrated significant efficacy in the treatment of an exacerbation of schizophrenia (Koblan et al, NEJM 2020; 82:1497–1506). We present results of a 6-month extension study whose aim was to evaluate the safety and effectiveness of longer-term treatment with SEP−363856.

Method. Patients with an acute exacerbation of schizophrenia who completed a 4-week, DB, placebo-controlled, flexible-dose (50 or 75 mg) study of SEP−363856 were given the option to enroll in an extension study in which they were treated, open-label (OL), with flexible doses (25/50/75 mg/d) of SEP−363856 for 26-weeks. The primary outcomes were safety measures; effectiveness outcomes were secondary and included the PANSS total score and the Brief Negative Symptom Scale (BNSS) total score.

Results. A total of 193 patients completed the 4-week DB study, and 156 (80.8%) were dosed in the OL extension study and received at least one dose of SEP−363856 (safety population). Study completer rate was 66.9%; reasons for discontinuation consisted of adverse event (11.5%), withdrawal of consent (10.2%), lack of efficacy (5.1%), and other (6.4%). 15 patients experienced an SAE: schizophrenia (n=11); acute psychosis (N=1); uterine hemorrhage and suicidal ideation (N=1 each); there were no deaths in the study. Individual AEs with an incidence =2% were schizophrenia (12.2%), headache (11.5%), insomnia (8.3%), anxiety (5.1%), somnolence (4.5%), nasopharyngitis (4.5%), nausea (3.8%), irritability (3.2%), influenza (3.2%), weight decreased (3.2%), and prolactin increased (2.6%). On movement scales, minimal mean change from OL-baseline to Week 26 occurred on the Barnes total score (−0.1), AIMS total score (0.0) and SAS score (−0.1). Mean month 6 change from DB baseline in weight was −0.3 kg. No clinically meaningful median changes were observed at week 26 in metabolic laboratory parameters (total and LDL cholesterol, triglycerides, hemoglobin A1c) or in prolactin levels. During 6 months of OL treatment, one patient had an increase in QTcF =60 msec; no patients had a QTcF interval =480 msec. Treatment with SEP−363856 was associated with significant improvement from OL baseline to week 26 in PANSS total score (−22.6) and BNSS total score (−11.3).

Conclusion. Treatment with SEP−363856 was associated with continued improvement from open-label baseline in the PANSS total (−22.6) and BNSS total (−11.3) scores. The most frequently reported adverse events (= 5%) were schizophrenia, headache, insomnia and anxiety. SEP−363856 had minimal effects on weight, lipids, glycemic indices, prolactin, and was associated with minimal risk of extrapyramidal symptom.

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Understanding the Evolving Continuing Medical Education Needs of Physicians Managing Patients with TD

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Abstract

This study sought to understand the evolving continuing medical education (CME) needs of physicians managing patients with tardive dyskinesia (TD). A case-based survey was developed, and later updated, to assess current practice, knowledge, and attitudes of neurologists and psychiatrists in the management of patients with TD. The original and updated survey were fielded in May 2018 and March 2020, respectively, to US-practicing psychiatrists and neurologists. Results were obtained from 213 psychiatrists and 187 neurologists in 2018 and from 125 psychiatrists and 128 neurologists in 2020. Less than half of physicians in both 2018 and 2020 were able to correctly identify the prevalence of TD in patients on maintenance antipsychotics, with many underestimating reported prevalence. Respondents reported moderate familiarity with VMAT2 inhibitor therapies for TD, with self-reported familiarity increasing more among neurologists than psychiatrists since the 2018 study. Psychiatrists are more likely than neurologists to take responsibility for medical management of TD symptoms and antipsychotic medication adjustment. Despite recommendations from APA guidelines and AAN reviews, 15% of physicians would use an anticholinergic to manage TD symptoms and only about half would opt for a VMAT2 inhibitor. There was a larger increase in VMAT inhibitor use between 2018 and 2020 among neurologists as compared to psychiatrists. The findings support the need for CME on TD focused toward specific provider groups. While both types of specialists would benefit from CME on the topic of TD epidemiology, there is an increased need for CME that includes treatment updates among psychiatrists.

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