METHODS: This was a Phase 3, 4-week, randomized, double-blind, active and placebo (PBO)-controlled study of ALKS 3831 in patients with acute exacerbation of schizophrenia (ClinicalTrials.gov: NCT02634346). Eligible patients (N = 403) were randomized 1:1:1 to receive ALKS 3831, OLZ, or PBO. Patients were treated in an inpatient setting for the first 2 weeks of the study and could be treated as inpatients or outpatients for the remaining 2 weeks. Patients were excluded if they received OLZ within 6 months prior to screening. Antipsychotic efficacy was assessed using the Positive and Negative Syndrome Scale (PANSS), and Clinical Global Impression–Severity (CGI-S) and CGI–Improvement (CGI-I) scales. Safety and tolerability were assessed as adverse events (AEs).

RESULTS: Of 401 randomized patients who received ALKS 3831, OLZ, or PBO, 91%, 89%, and 83% of patients, respectively, completed treatment. The most common reason for discontinuation was withdrawal by patient (6% in both the ALKS 3831and PBO groups, and 7% in the OLZ group). Baseline characteristics were generally similar between groups; however, baseline mean body mass index was higher in the OLZ group than in the ALKS 3831 group. Baseline mean ± standard deviation scores were 101.7 ± 11.9 for PANSS total score and 5.1 ± 0.7 for CGI-S scale score. The mean OLZ dose was 18.4 mg/day in both active treatment arms. Least squares (LS) mean difference ± standard error (SE) vs PBO from baseline to Week 4 in PANSS total score was −6.4 ± 1.8 (P < .001) for the ALKS 3831 group and −5.3 ± 1.8 (P = .004) for the OLZ group. LS mean difference ± SE vs PBO from baseline to Week 4 in CGI-S scale score was −0.4 ± 0.1 (P = .002) for the ALKS3831 group and −0.4 ± 0.1 (P < .001) for the OLZ group. The percentage of patients with improvement in PANSS response (≥30% from baseline) at Week 4 was 60%, 54%, and 38% in the ALKS 3831, OLZ, and PBO groups, respectively. The percentage of patients with an improvement in CGI-I scale response (score of ≤2) at Week 4 was 58%, 51%, and 33% in the ALKS 3831, OLZ, and PBO groups, respectively. Discontinuation due to AEs was low in all groups. Common AEs (≥5% in any group) included weight gain, somnolence, dry mouth, anxiety, headache, and schizophrenia.

DISCUSSION: Treatment with ALKS 3831 was more effective than PBO, as measured by the PANSS and CGI-S scale, and its antipsychotic efficacy was similar to the active control OLZ. The safety profile of ALKS 3831 was similar to OLZ.

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A New Method for Initiating Treatment with the Long-acting Antipsychotic Aripiprazole Lauroxil

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ABSTRACT: STUDY OBJECTIVE: Slow release is a fundamental feature of long-acting injectable (LAI) antipsychotics. This property allows continuous drug exposure between dosing intervals. However, there can be a significant delay between giving the first LAI dose and achievement of efficacious plasma concentrations. This time period requires additional pharmacologic intervention. Until now, this delay was addressed with one of two strategies: 1) continuing with supplemental oral antipsychotic, or 2) giving more LAI up front (e.g. loading dose). A third strategy has now been developed to reduce the time needed for oral supplementation when starting the LAI aripiprazole lauroxil (AL) from 21 days to 1 day. A nano-crystalline milled dispersion of AL (ALNCD; brand name ARISTADA INITIO™) was formulated by reducing the AL particle diameter from micron-size particles to nanometer- sized particles. ALNCD has faster dissolution and a shorter half-life than AL and is designed to be used as a single injection along with a single oral aripiprazole dose of 30 mg as a 1-day alternative to the 21 days of oral aripiprazole supplementation. Here we provide an overview of the new 1-day initiation regimen for starting AL treatment, and demonstrate the relative contributions of each of its components.

METHODS: A blinded, randomized, phase 1, pharmacokinetic (PK), and safety study compared the 1-day initiation regimen with the 21-day oral aripiprazole regimen. A combination of observed data, and population pharmacokinetic model–based simulations were used to plot plasma aripiprazole concentrations of single doses of ALNCD, 30 mg oral aripiprazole, and AL, individually, and all three combined.

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RESULTS: The PK profiles of the 1-day and 21-day initiation regimens (both in conjunction with either 441 mg or 882 mg doses of AL) were comparable, with therapeutically relevant aripiprazole levels achieved within 4 days of treatment initiation. The safety profile of the 1-day initiation regimen was similar to the 21-day initiation regimen, and consistent with that of AL. Aripiprazole concentration–time profiles demonstrated that each component delivered aripiprazole to the systemic circulation at different time periods, with the 30 mg dose of oral aripiprazole predominant in the first week, followed by ALNCD, and then AL.

CONCLUSIONS: The 1-day initiation regimen is well-tolerated and a suitable alternative to 21 days of oral aripiprazole supplementation for starting AL. Each component of the 1-day initiation regimen, together with AL, is necessary to provide continuous coverage from treatment initiation until the next regularly scheduled AL injection.

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How is Postpartum Depression Currently Diagnosed and Managed? Insights from a Virtual Patient Simulation

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ABSTRACT: Objectives: The goal of this study was to determine physician performance in diagnosis and management of postpartum depression (PPD) and to provide needed education in the consequence free environment of a virtual patient simulation (VPS).

METHODS:

- A continuing medical education activity was delivered via an online VPS learning platform that offers a lifelike clinical care experience with complete freedom of choice in clinical decision-making and expert personalized feedback to address learner's practice gaps
- Physicians including psychiatrists, primary care physicians (PCPs), and obstetricians/gynecologists (ob/gyns) were presented with two cases of PPD designed to model the experience of actual practice by including use of electronic health records
- Following virtual interactions with patients, physicians were asked to make decisions regarding assessments, diagnoses, and pharmacologic therapies. The clinical decisions were analyzed using a sophisticated decision engine, and clinical guidance (CG) based on current evidence-based recommendations was provided in response to learners' clinical decisions
- Impact of the education was measured by comparing participant decisions pre- and post-CG using a 2-tailed, paired t-test; $P < .05$ was considered statistically significant
- The activity launched on Medscape Education on April 26, 2018, and data were collected through to June 17, 2018.

RESULTS:

- From pre- to post-CG in the simulation, physicians were more likely to make evidence-based clinical decisions related to:
- Ordering appropriate baseline tests including tools/scales to screen for PPD: in case 1, psychiatrists ($n = 624$) improved from 34% to 42% on average ($P < .05$); PCPs ($n = 197$) improved from 38% to 48% on average ($P < .05$); and, ob/gyns ($n = 216$) improved from 30% to 38% on average ($P < .05$)
- Diagnosing moderate-to-severe PPD: in case 2, psychiatrists ($n = 531$) improved from 46% to 62% ($P < .05$); PCPs ($n = 154$) improved from 43% to 55% ($P < .05$); and, ob/gyns ($n = 137$) improved from 55% to 73% ($P < .05$)
- Ordering appropriate treatments for moderate-to-severe PPD such as selective serotonin-reuptake inhibitors: in case 2, psychiatrists ($n = 531$) improved from 47% CG to 75% ($P < .05$); PCPs ($n = 154$) improved from 55% to 74% ($P < .05$); and, ob/gyns ($n = 137$) improved from 51% to 78% ($P < .05$)
- Interestingly, a small percentage of physicians (average of 5%) chose investigational agents for PPD which were in clinical trials pre-CG, and this increased to an average of 9% post-CG

CONCLUSIONS: Physicians who participated in VPS-based education significantly improved their clinical decision-making in PPD, particularly in selection of validated screening tools/scales, diagnosis, and pharmacologic treatments based on severity. Given that VPS immerses physicians in an authentic, practical learning experience matching the scope of clinical practice, this type of intervention can be used to determine clinical practice gaps and translate knowledge into practice.

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