ADVANCE: adherence to antipsychotic and adjunctive pimavanserin in patients with negative symptoms of schizophrenia

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SUBMISSION DETAILS

What is the Methodological Question Being Addressed? Could checking medication adherence at screening potentially improve adherence in a clinical trial and improve overall quality and outcomes?

Introduction Nonadherence to antipsychotic (AP) treatment is problematic. In clinical trials, nonadherence complicates interpretation of results. Therefore, it is important to review adherence results after trial completion, regardless of study outcome.
Here we present adherence data (measured by blood levels) from the ADVANCE study, which demonstrated a significant effect of adjunctive pimavanserin, a 5-hydroxytryptamine (5-HT)2A inverse agonist/antagonist, on negative symptoms of schizophrenia.

Methods ADVANCE (NCT02970305) was a phase 2, 26-week, randomized, double-blind, placebo-controlled study of stable outpatients with schizophrenia and predominant negative symptoms. Outpatients were eligible immediately after their most recent hospitalization provided their AP treatment was stable for ≥8 weeks before screening with no dose changes ≥4 weeks prior to screening for oral AP or ≥16 weeks prior to screening for depot AP. During screening, patients provided documentation showing AP treatment stability, a blood sample was tested for presence or absence of the AP, and a telemedicine interview was completed with an independent clinician. Blood sampling occurred at baseline and Weeks (W) 2, 8, 14 and 26 for pharmacokinetic assessments of the main AP and pimavanserin. A post-hoc analysis of adherence used descriptive statistics to examine the proportion of patients who were adherent to AP at screening and AP and pimavanserin during the study.

Results Overall, 608 patients were screened with 36 rescreens, for a total of 644 screenings. One of the most common reasons for screen failure was failure to detect AP levels (13.3% of all screen failures). One of these screen failures was allowed to rescreen after the patient switched to a different generic version of AP and was subsequently randomized. Other reasons for screen failure included patients not meeting study inclusion criteria and withdrawal of consent. At baseline, 95.0% of patients were considered adherent to their main AP; a substantial improvement over the theoretical adherence rate of 88.0% had nonadherent patients been randomized. High adherence rates for both the main AP and adjunctive pimavanserin were found at W2, W8, W14 and W26. Overall, 201 patients were randomized to receive pimavanserin, of whom 191 (W2), 184 (W8), and 177 (W14) patients provided blood samples with 186 (97.4%) (W2), 183 (99.5%) (W8), and 173 (97.7%) (W14) patients showing measurable levels of pimavanserin. At study exit (W26 or early termination), 190 of 200 (95.0%) patients were considered adherent based on measurable

pimavanserin levels. Furthermore, 91.7% of measured pimavanserin concentrations post-baseline were at or above the lower limit of the 90% prediction interval of the model-predicted median expected level.

Conclusion Adherence results complement the positive efficacy and safety results previously reported for ADVANCE. Patients showed high adherence to 26 weeks of adjunctive pimavanserin treatment with little to no impact on adherence to main AP. High adherence is likely a result of both the rigorous screening procedures employed in ADVANCE, including testing for measurable levels of AP and pimavanserin, and the tolerability of the combination.

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Guidelines I have read and understand the Poster Guidelines

Disclosures if applicable One or more authors report potential conflicts which are described in the program.

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