Study Design and Patient Population
The study was a double-blind, parallel-group, multicenter, multiple-dose study (NCT02720263) to evaluate adult patients (aged 18–60) with schizophrenia or schizoaffective disorder if they had low to moderate positive symptom scores and moderate positive symptom severity (Clinical Global Impressions-Positive). The remaining cohorts received 15-mg (Cohort B), 50-mg (Cohort C), or 150-mg (Cohort D) doses of ASP4345. Patients were assigned to one of four dose cohorts and randomized 3:1 within each cohort, resulting in 27 active patients and 9 placebo patients per cohort. The dose groups were: 3-mg, 15-mg, 50-mg, or 150-mg of ASP4345.

As part of the study, patients were randomized to receive a 10-mg dose of active drug or placebo followed by a 3-mg, 15-mg, 50-mg, or 150-mg dose of active drug or placebo. The primary objective of the study was to evaluate the safety and tolerability profile of ASP4345 in patients with schizophrenia or schizoaffective disorder who are on antipsychotics. Here we present the primary objective of the safety and tolerability profile of multiple-dose active drug as well as the exploratory objective of the study, which was to assess the changes in neurophysiological biomarkers associated with hearing, decision making, and information processing in patients with stable schizophrenia or schizoaffective disorder.

METHODS

Study Design and Patient Population
This was a double-blind, randomized, placebo-controlled, multiple-dose study (NCT02720263) to evaluate adult patients who were on stable doses of risperidone, olanzapine, or aripiprazole at the time of screening for the study. The study population included patients who were aged 18–60 years, had a diagnosis of schizophrenia or schizoaffective disorder, and were on stable doses of risperidone, olanzapine, or aripiprazole. The remaining cohorts received 15-mg (Cohort B), 50-mg (Cohort C), or 150-mg (Cohort D) doses of ASP4345. Patients were assigned to one of four dose cohorts and randomized 3:1 within each cohort, resulting in 27 active patients and 9 placebo patients per cohort. The dose groups were: 3-mg, 15-mg, 50-mg, or 150-mg of ASP4345.

Pharmacodynamic Effects of ASP4345 for the Treatment of Cognitive Impairment in Patients With Schizophrenia

Background

Studies have shown that early intervention with antipsychotics, such as risperidone, olanzapine, or aripiprazole, can improve cognitive function in patients with schizophrenia. However, these treatments can also lead to adverse effects, including weight gain, metabolic disturbances, and extrapyramidal side effects. Therefore, there is a need for new treatments that can improve cognitive function without causing these adverse effects.

Objective

The primary objective of this study was to evaluate the safety and tolerability profile of ASP4345 in patients with schizophrenia or schizoaffective disorder who are on antipsychotics. The secondary objectives were to assess the changes in neurophysiological biomarkers associated with hearing, decision making, and information processing in patients with stable schizophrenia or schizoaffective disorder.

Methods

The study was a double-blind, randomized, placebo-controlled, multiple-dose study to evaluate adult patients who were on stable doses of risperidone, olanzapine, or aripiprazole at the time of screening for the study. The study population included patients who were aged 18–60 years, had a diagnosis of schizophrenia or schizoaffective disorder, and were on stable doses of risperidone, olanzapine, or aripiprazole.

Results

The results of this study highlight the importance of further development of ASP4345 for the treatment of cognitive impairment in patients with schizophrenia or schizoaffective disorder. The study found that all doses of ASP4345 (3-mg, 15-mg, 50-mg, 150-mg) were found to be well-tolerated with mostly mild TEAs and drug-related AEs of confusion, headache, and somnolence.

Conclusions

The results of this study highlight the importance of further development of ASP4345 for the treatment of cognitive impairment in patients with schizophrenia or schizoaffective disorder. The study found that all doses of ASP4345 (3-mg, 15-mg, 50-mg, 150-mg) were found to be well-tolerated with mostly mild TEAs and drug-related AEs of confusion, headache, and somnolence.

References


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There were no signs of abuse liability or effect on mood that could lead to suicidal ideation or behavior. Improvement in performance on the cognitive tests suggests that treatment with ASP4345 was associated with a beneficial effect on psychomotor function, information processing, and visual attention.

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