Efficacy of Cariprazine in Negative, Cognitive, and Social Functioning Symptoms in Schizophrenia: Post Hoc Analysis of a Randomized, Controlled Trial

Andrew J. Culler, MD,1 Bruce Dang, MD,2 Kai-Feng Lu, MD,3 Istvan Laszlovasnyi, PharmD, PhD,4 Willis E. Lee, MD5

1Meridian Research, Inc., Bradenton, FL, USA; 2Allergan, Inc., Jersey City, NJ, USA; 3Gedeon Richter Plc, Budapest, Hungary

ABSTRACT

Introduction: Abnormalities in cognitive, negative, and social functioning symptoms are common in schizophrenia and may contribute to poor social functioning. Cariprazine, a dopamine D2/D3 receptor agonist, has been shown in phase 3 trials to be effective in acute exacerbation of schizophrenia. The present analysis assessed efficacy and safety of cariprazine 3 and 6 mg/d in improving PANSS-derived negative, cognitive, and prosocial scores compared with placebo in adult patients with acute exacerbation of schizophrenia.

Methods: A total of 604 patients were randomized to 6 weeks of double-blind treatment (placebo=149, cariprazine 3 mg/d=150, 6 mg/d=151). Efficacy was analyzed using change from baseline on PANSS negative subscale scores (PANSS 1, 2, 3) and PANSS-derived cognitive and prosocial factor scores. Additional analyses were conducted on PANSS total scores and PANSS-derived negative and positive symptom scales.

Results: The least square mean (LSM) treatment difference in change from baseline between cariprazine 3 mg/d and placebo on PANSS negative subscale score was statistically significant (P=.0152). LSM mean changes from baseline to Week 6 in PANSS negative score and PANSS-derived cognitive factor score were statistically significant on both efficacy measures at Week 2 (P<.05) and in PANSS-derived cognitive factor score starting at Week 3 (P<.01). In PANSS-derived prosocial scores, significant improvement was seen by Week 1 for cariprazine 3 mg/d and Week 2 for cariprazine 6 mg/d versus placebo. The safety profile was consistent with that reported previously for cariprazine; the most common adverse events associated with cariprazine 3 and 6 mg/d were fatigue, insomnia, and nausea.

Conclusion: Cariprazine 3 and 6 mg/d demonstrated significant and sustained efficacy versus placebo in 6 weeks in improving PANSS-negative, cognitive, and prosocial symptoms; improvements in these symptom domains may contribute to improved psychosocial functioning in patients with schizophrenia.

Figures

Figure 1: Patient Populations and Disposition

Figure 2: Mean Change From Baseline to Week 6 in PANSS Negative and Cognitive Scores (ITT, Presentation, MMRM)

Figure 3: Mean Change From Baseline in PANSS Prospective Score by Week (ITT Population, MMRM)

Table 1: Discontinuations

Table 2: Other Discontinuations

Conclusions

Cariprazine 3 mg/d was significantly superior to placebo on all 6 PANSS-derived prosocial items (P<.05) and more so at Week 6 (ITT). 6 mg mg/d was significantly superior to placebo on all 6 PANSS-derived prosocial items (P<.0009). Significant improvement was maintained through Week 6 for both cariprazine doses on PANSS negative, cognitive, and prosocial scores.

Disclosure

No personal information is stored.

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REFERENCES

2. Hunter R, Barry S. Negative symptoms and psychosocial functioning in schizophrenia: neglected but important targets for treatment. JAMA Psychiatry 2004;61(9):880-887.
3. Durgam S, Cutler AJ, Lu K, Jeste DV. Negative symptoms in schizophrenia: 4. Current psychotic episode was ≤2 weeks; patients had a PANSS total score ≥80 and ≤120 and a score of ≥4 on least 1 psychotic episode that required hospitalization or change in antipsychotic treatment during the past year. Data were assessed using a mixed-effects model for repeated measures (MMRM).

INTRODUCTION

Positive symptoms of schizophrenia can be successfully treated with antipsychotic medications; however, negative symptoms and cognitive impairment are difficult to treat and can have a detrimental effect on psychosocial functioning.1 Given the impact of negative symptoms on social functioning, new treatments are needed that improve outcomes in these symptom domains since many patients with schizophrenia continue to have disabling social functioning regardless of their response to typical treatment interventions. Negative symptoms may be measured in schizophrenia patients as well as social functioning in patients with depression.2

METHODS

Study Design

Data were analyzed from a 6-week, double-blind, Phase 3, randomized, placebo- and active-controlled trial (NCT01104766)3 in adult patients with acute exacerbation of schizophrenia.

Patients were randomized to 6 weeks of double-blind treatment (placebo=149, cariprazine 3 mg/d=150, 6 mg/d=151). Efficacy was analyzed using change from baseline on PANSS negative subscale scores (PANSS items 1, 2, 3) and PANSS-derived cognitive and prosocial factor scores. Additional analyses were conducted on PANSS total scores and PANSS-derived negative and positive symptom scales.

RESULTS

The least square mean difference (LSMD) was statistically significant in favor of cariprazine over placebo on PANSS negative (2 mg/d=-1.4 [95% CI: -2.4, -0.4], 3 mg/d=-1.2 [95% CI: -1.9, -0.5], 6 mg/d=-1.7 [95% CI: -2.7, -0.7]) and cognitive (LSMD=-1.0 [95% CI: -1.6, -0.3], -1.5 [95% CI: -2.2, -0.8], -2.2 [95% CI: -2.9, -1.5]) scores. In PANSS-derived prosocial scores, significant improvement was seen by Week 6 for both cariprazine doses compared with placebo (3 mg/d=-1.5 [95% CI: -2.5, -0.4], 6 mg/d=-2.2 [95% CI: -3.1, -1.3]). Early separation from placebo for both cariprazine doses on PANSS negative, cognitive, and prosocial scores was maintained through Week 6. LSMDs for aripiprazole versus placebo were statistically significant on both efficacy measures at Week 2 (P<.05) and in PANSS-derived cognitive factor score starting at Week 3 (P<.01). In PANSS-derived prosocial scores, significant improvement was seen by Week 1 for cariprazine 3 mg/d and Week 2 for cariprazine 6 mg/d versus placebo. The safety profile was consistent with that reported previously for cariprazine; the most common adverse events associated with cariprazine 3 and 6 mg/d were fatigue, insomnia, and nausea.

Patient disposition and baseline characteristics were similar among treatment groups and have been previously published.1,3 Data were analyzed from a 6-week, double-blind, Phase 3, randomized, placebo- and active-controlled trial (NCT01104766)3 in adult patients with acute exacerbation of schizophrenia.

Data were assessed using a mixed-effects model for repeated measures (MMRM).

Figures

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