# Efficacy of Cariprazine in the Early Stage of Schizophrenia: A Pooled, Post-hoc Analysis of 3 Phase II/III Double-blind Placebo-controlled Trials

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## INTRODUCTION

Schizophrenia is a life-long neurodevelopmental disorder that is characterized by significant alterations in patient's thoughts, behaviour, mood and perception[1]. Diagnosis and treatment start from the early stage of schizophrenia that is predominantly characterized by negative symptoms like amotivation, positive symptoms such as hallucinations as well as high levels of hostility, lasting up to 5 years[2,3]. As successful treatment in this period is necessary to prevent relapse into a second episode, finding the right antipsychotic medication is crucial[4]. Cariprazine, a potent dopamine $D_3/D_2$ receptor partial agonist was found to be generally safe and effective in the treatment of acute schizophrenia, however patients in the early stage have not been specifically analysed yet[5–7].

## STUDY OBJECTIVE

This poster aims to summarise the evidence of cariprazine's efficacy in the early stage of schizophrenia treatment with special focus to those symptoms that are prevalent in this period of the disorder.

## METHODS

Data from 3 randomized, double-blind, placebo-controlled trials (NCT01104766, NCT01104779, NCT00694707) with identical design (1 week of wash out period, 6 weeks of cariprazine treatment and 2 weeks of follow-up) were pooled. The primary efficacy measure in all studies was the Positive and Negative Syndrome Scale (PANSS). For the post-hoc analyses, patients with early stage of schizophrenia (defined as having a disease duration of less than 5 years) were extracted from the whole IIT population, and cariprazine dose groups (1.5 mg to 6.0 mg/day) were combined. Primary efficacy was evaluated using PANSS Total Scores. In addition, PANSS-derived Marder Factor groupings relevant to this disease stage (Positive, Negative and Uncontrolled Hostility/Excitement Symptom Factor scores) were analysed. Change from baseline in total and factor scores were evaluated based on least squares mean differences (LSMDs) between cariprazine and placebo using a mixed-effects model for repeated measures (MMRM) approach.

## RESULTS

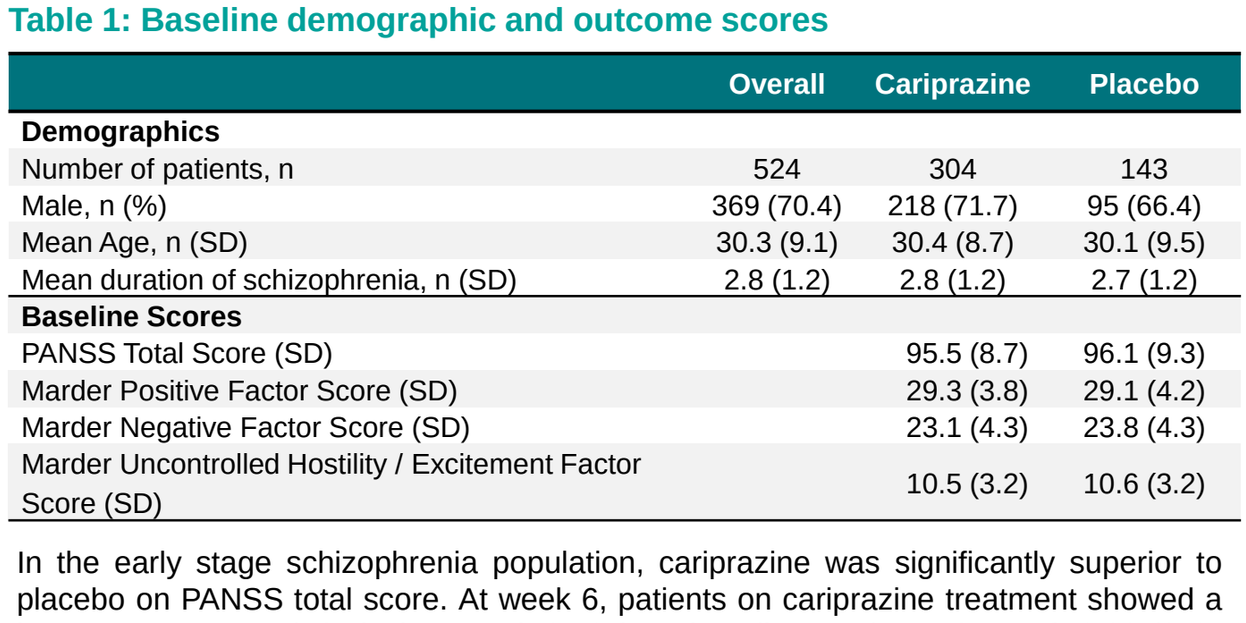
Overall, data from 143 placebo and 304 cariprazine treated patients were identified as having schizophrenia for less than 5 years. The mean age was around 30 years with about 3 years duration of schizophrenia. The baseline PANSS scores were similar in the two groups.

### Table 1: Baseline demographic and outcome scores

| | Overall | Cariprazine | Placebo |
|---|---|---|---|
| **Demographics** | | | |
| Number of patients, n | 524 | 304 | 143 |
| Male, n (%) | 369 (70.4) | 218 (71.7) | 95 (66.4) |
| Mean Age, n (SD) | 30.3 (9.1) | 30.4 (8.7) | 30.1 (9.5) |
| Mean duration of schizophrenia, n (SD) | 2.8 (1.2) | 2.8 (1.2) | 2.7 (1.2) |
| **Baseline Scores** | | | |
| PANSS Total Score (SD) | | 95.5 (8.7) | 96.1 (9.3) |
| Marder Positive Factor Score (SD) | | 29.3 (3.8) | 29.1 (4.2) |
| Marder Negative Factor Score (SD) | | 23.1 (4.3) | 23.8 (4.3) |
| Marder Uncontrolled Hostility / Excitement Factor Score (SD) | | 10.5 (3.2) | 10.6 (3.2) |

In the early stage schizophrenia population, cariprazine was significantly superior to placebo on PANSS total score. At week 6, patients on cariprazine treatment showed a least square mean (LSM) change of -24.2 from baseline, and an LSMD of -6.28 (95% CI: -10.30 to -2.26; p=0.002) compared to placebo. In comparison to the rest of the study population (not early stage), early stage schizophrenia patients responded better to cariprazine treatment with bigger change from baseline.

### Figure 1: Change from Baseline in PANSS Total Score

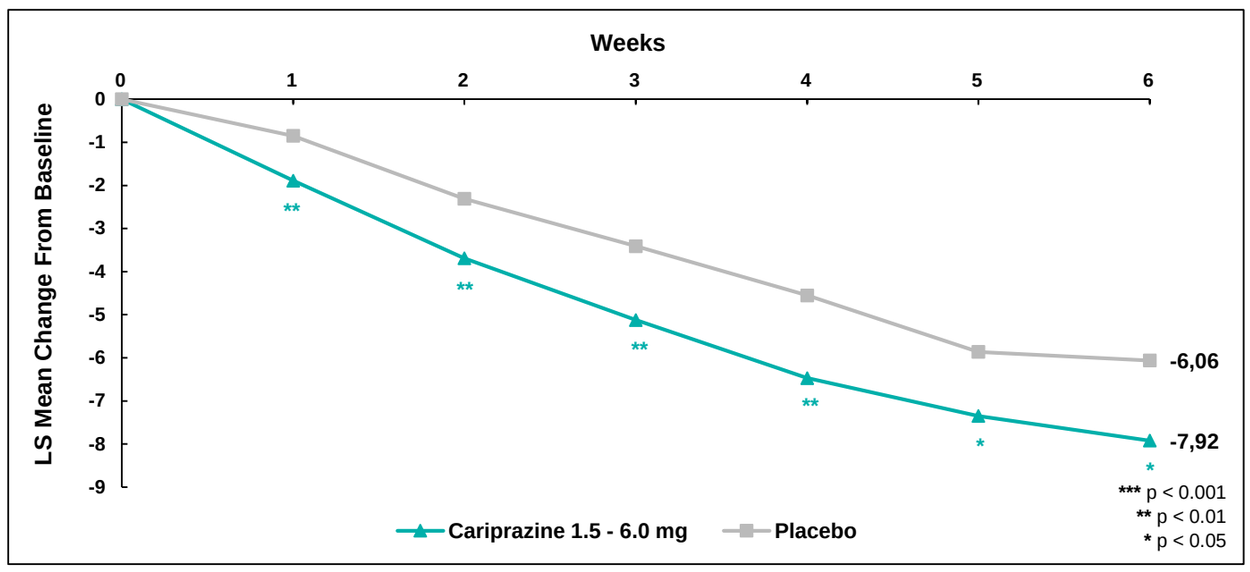



Decreases in Marder Positive Symptom Factor scores were significantly greater in the cariprazine group versus placebo; at week 6 the LSM change from baseline was -7.92 (LSMD: -1.86; 95% CI: -3.33 to -0.39; p=0.013).

## CONCLUSIONS

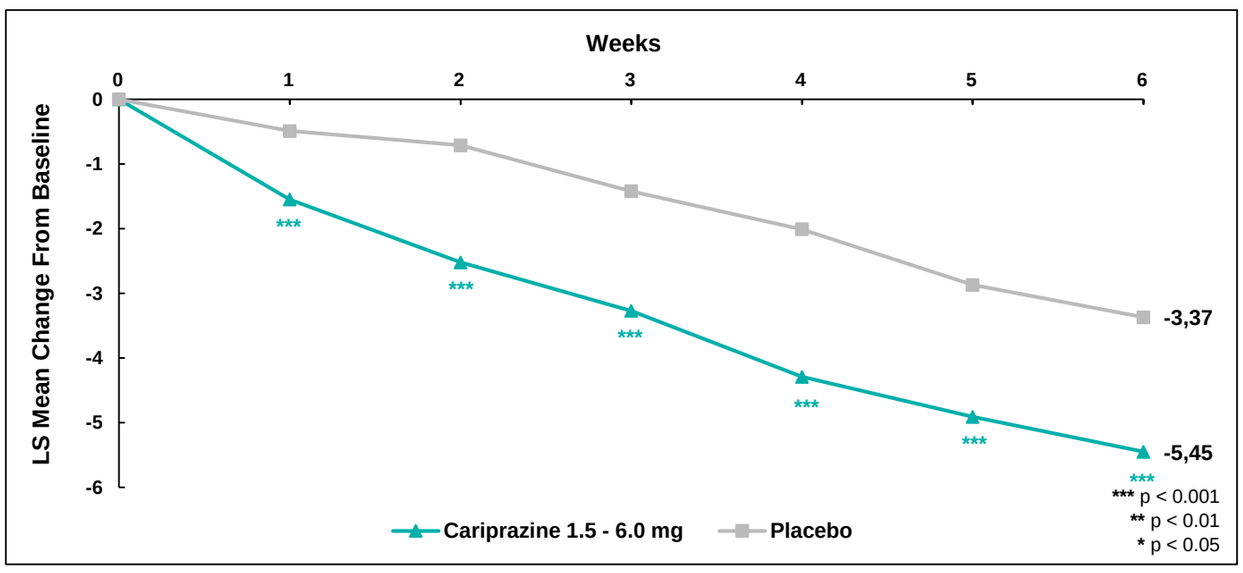
**Cariprazine was efficacious in treating patients in the early stage of schizophrenia. Significant efficacy was observed in the overall symptomatology, as well as in the positive, negative and hostility-related symptoms which are highly characteristic in this period of the disorder.**

### Figure 2: Change from Baseline in Marder Positive Symptom Factor Scores



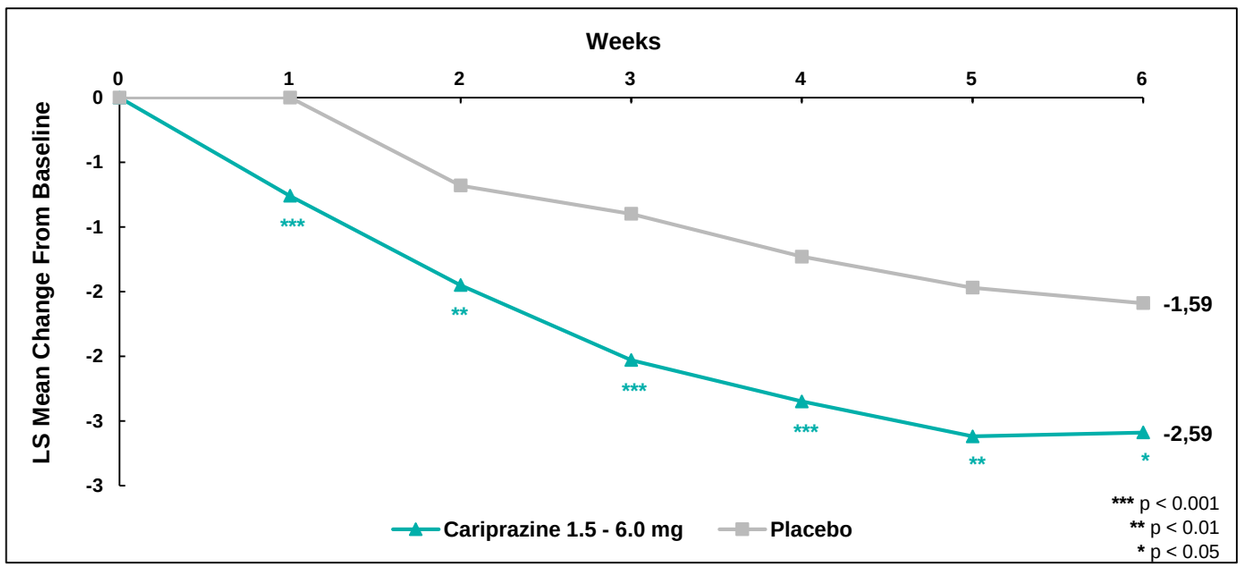

A significant decrease of -5.45 from baseline to week 6 in the Marder Negative Symptom Factor scores was also detected, with an LSMD of -2.01 (95% CI: -3.18 to -1.00; p<0.001) compared to placebo.

### Figure 3: Change from Baseline in Marder Negative Symptom Factor Scores




Finally, the Marder Uncontrolled Hostility/Excitement Factor scores also decreased from baseline significantly versus placebo, with an LSM change of -2.59 (LSMD: -0.99; 95% CI: -1.79 to -0.20; p=0.014) at week 6 in patients on cariprazine treatment.

### Figure 4: Change from Baseline in Marder Uncontrolled Hostility/Excitement Symptom Factor Scores

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