Tolerability of Cariprazine in the Early Stage of Schizophrenia: A Pooled, Post-hoc Analysis of 4 Phase II/III Double-blind Placebo-controlled Trials

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INTRODUCTION

Schizophrenia is a chronic disorder characterized by disruption of thoughts, behaviour, mood and perception. In the early stage of schizophrenia (which consists of the first 3-5 years of the disorder[1]) the most important clinical target besides the alleviation of psychotic symptoms and the stabilisation of the patient is relapse prevention, as each relapse significantly decreases the possibility of preferable long-term outcomes[2].

Early discontinuation of antipsychotic medication due to intolerable side-effects is one of the most common causes of relapse[3]. When asked, the most important side-effects for patients in terms of medication adherence were weight gain, akathisia and somnolence[4]. Furthermore, sexual problems are also considered to be highly relevant and known to affect treatment adherence negatively[5]. Cariprazine, a potent dopamine D3 receptor preferring D3/D2 partial agonist was found to be generally well-tolerated in acute schizophrenia[6], however patients in the early stage have not been specifically analysed yet.

STUDY OBJECTIVES

This poster aims to present the safety and tolerability of cariprazine in patients in the early stage of schizophrenia by presenting data on treatment-emergent adverse events (TEAEs), discontinuation and relapse rates.

METHODS

Data from 4 randomized, double-blind, placebo-controlled trials (NCT00404573, NCT01104766, NCT01104779, NCT00694707) with similar design (1 week of wash out period, 6 weeks of treatment and 2-4 weeks of follow-up) were pooled.

For the post-hoc analysis, patients with early stage of schizophrenia (defined as having a disease duration of less than 5 years) were extracted from the whole safety population, and approved doses of cariprazine (1.5-6.0 mg/day) were combined. TEAEs, relapse and discontinuation rates were analysed versus placebo.

RESULTS

Overall, 169 placebo- (PBO) and 322 cariprazine-treated (CAR) patients were identified as having schizophrenia for less than 5 years (Table 1). The mean duration of having schizophrenia in the CAR and PBO groups was 2.8 years. The majority of the patients involved were male and the mean age of the patients was around 30 years.

Table 1: Baseline demographics

	Overall	CAR	PBO
Number of patients	491	322	169
Male, n (%)	347 (70.7)	232 (72.0)	115 (68.0)
Mean Age, n (SD)	30.4 (9.0)	30.5 (8.7)	30.2 (9.5)
Mean duration of disorder, n (SD)	2.8 (1.2)	2.8 (1.2)	2.8 (1.2)

Altogether, 67.7% CAR and 56.2% PBO-treated patients reported at least one TEAE throughout the treatment period (Table 2). The most frequent TEAEs were insomnia (10.9 % CAR; 12.4% PBO), akathisia (9.6% CAR; 2.4% PBO) and extrapyramidal symptoms (9.3% CAR; 1.8% PBO). Although akathisia and extrapyramidal symptoms were the second most common TEAE experienced in the cariprazine group, it is a side effect that can be managed by adjusting dosage and providing additional drug treatments.

Importantly, weight-gain and sexual problems, one of the most important side-effects for patients in the early stage of schizophrenia, affected less than 2% of patients who took cariprazine.

Table 2: % of TEAEs

TEAE	CAR, n (%)	PBO, n (%)
All	218 (67.7)	95 (56.2)
Insomnia	35 (10.9)	21 (12.4)
Akathisia	31 (9.6)	4 (2.4)
Extrapyramidal symptoms	30 (9.3)	3 (1.8)
Headache	24 (7.5)	16 (9.5)
Anxiety	19 (5.9)	7 (4.1)
Constipation	15 (4.7)	2 (1.2)
Dizziness	13 (4.0)	2 (1.2)
Schizophrenia	10 (3.1)	9 (5.3)
Weight-gain	6 (1.9)	2 (1.2)
Sexual problems	5 (1.6)	0 (0)
Agitation	5 (1.6)	7 (4.1)
Abdominal discomfort	5 (1.6)	2 (1.2)

Discontinuation due to adverse events was reported in only 8.4% of cariprazine- and 14.8% of placebo-treated patients (Table 3). Importantly, this suggests that side effects of cariprazine were similar to placebo. Among those who did continue the treatment, relapse occurred only in 3.1% of cariprazine- and 5.3% of placebo-treated patients

Table 3: % of discontinuation

Discontinuation	CAR, n (%)	PBO, n (%)
Total	124 (34.3)	74 (48.8)
Adverse Event	27 (8.4)	25 (14.8)

CONCLUSION

- **Cariprazine was well-tolerated in the early stage of schizophrenia.**
- **Discontinuation rates due to unbearable side-effects were low.**
- **Relapse occurred in only a low percentage of patients.**

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DISCLOSURE

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ABSTRACT

Introduction

In the early stage of schizophrenia (first 5 years), the most important clinical target besides symptom control is relapse prevention as each relapse significantly decreases the possibility of preferable long-term outcomes (1). Early discontinuation of antipsychotic medication due to intolerable side-effects is one of the most common causes of relapse (2).

Objectives

This poster aims to present cariprazine's tolerability in the early stage of schizophrenia.

Methods

Data from 4 randomized, double-blind, placebo-controlled trials (NCT00404573, NCT01104766, NCT01104779, NCT00694707) with similar design (1 week of wash out period, 6 weeks of treatment and 2-4 weeks of follow-up) were pooled. For the post-hoc analysis, patients with early stage of schizophrenia (defined as having a disease duration of less than 5 years) were extracted from the whole safety population, and approved doses of cariprazine (1.5-6.0 mg/day) were combined. Treatment-emergent adverse events (TEAEs) and discontinuation rates were analysed versus placebo.

Results

Overall, 169 placebo- (PBO) and 322 cariprazine-treated (CAR) patients were identified as having schizophrenia for less than 5 years. 67.7% cariprazine- and 56.2% placebo-treated patients reported at least one TEAE; most frequently insomnia (10.9 % CAR; 12.4% PBO), akathisia (9.6% CAR; 2.4% PBO) and extrapyramidal symptoms (9.3% CAR; 1.8% PBO). Discontinuation due to adverse events was reported in only 8.4% of cariprazine- and 14.8% of placebo-treated patients. Relapse occurred in 3.1% of cariprazine- and 5.3% of placebo-treated patients.

Conclusion

Cariprazine was generally well-tolerated in the early stage of schizophrenia; given the limitations of this analysis, additional research is warranted.

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