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Safety with or without treatment: a post-hoc analysis comparing stable patients discontinuing cariprazine treatment versus patients taking cariprazine long-term

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INTRODUCTION

Non-adherence with drug therapy is the leading cause of relapse in schizophrenia patients.[1] Nonetheless, about 50% of patients are non-adherent to their medication, thus increasing the risk for hospitalization, suicide and poorer prognosis.[2] Non-adherence is most common when side effects are unbearable or unacceptable for patients, and there is a tendency for patients to discontinue taking their medication after symptom remission is achieved.[3,4,5,6] Consequently, a drug's side effect profile should be considered when selecting long-term treatment in schizophrenia; therapists are encouraged to choose an antipsychotic that exhibits only few and/or acceptable side effects.

STUDY OBJECTIVE

The aim of the present post-hoc analysis is to examine safety parameters in patients achieving symptom remission with cariprazine, and then either discontinuing their treatment or continuing to take it long-term.

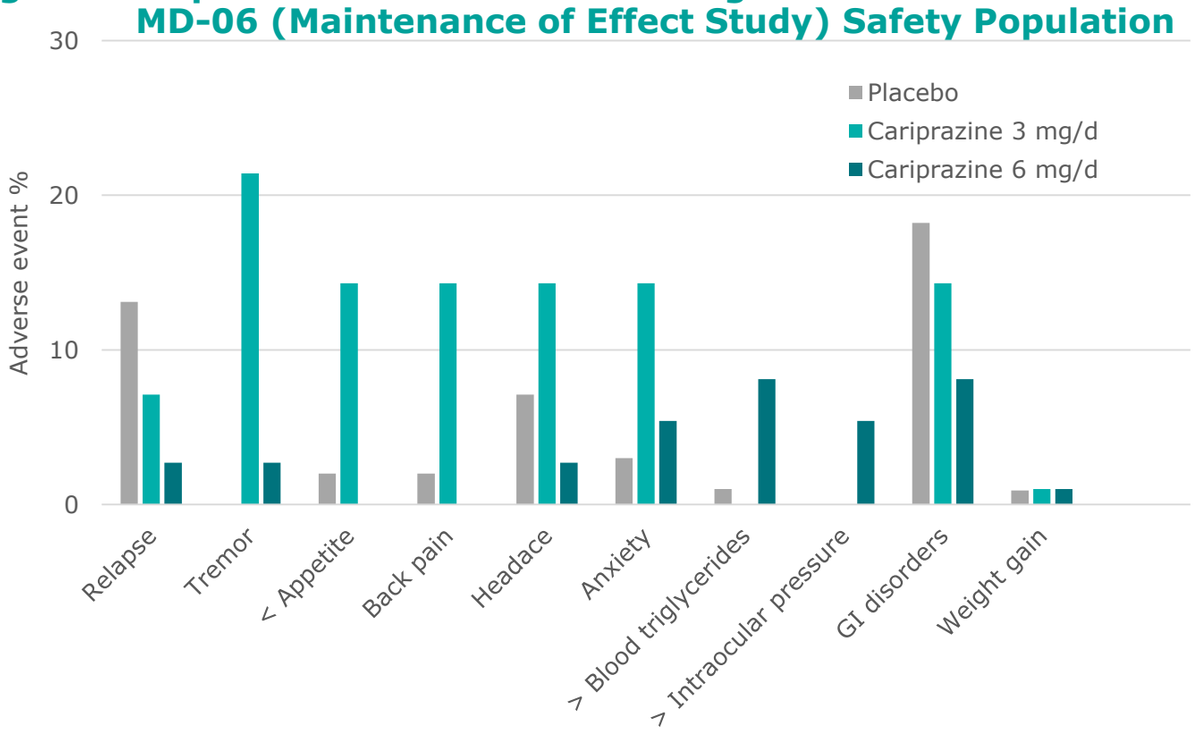
METHODS

- Adverse event data from a multinational, randomized, double-blind, placebo-controlled, parallel-group trial (NCT01412060) of adult patients with schizophrenia diagnosis was examined. In the study, acute symptoms of schizophrenia were stabilized during a 20-week open-label, cariprazine treatment (3-9 mg/d), after which patients were randomized to continue on either cariprazine (CAR) or switch to placebo (PBO) for up to 72 weeks of double-blind treatment. The present post-hoc analysis examined the safety profile of patients taking placebo (n = 99) versus patients taking either 3 mg/day (n = 14) or 6 mg/day (n = 37) cariprazine. Safety parameters were summarized using descriptive statistics.

RESULTS

- Adverse events were reported in 64.6% of the PBO treated patients versus 71.4% of the 3 mg/day CAR and 64.9% of the 6 mg/day CAR treated patients. The most often reported adverse event in the PBO group was relapse to schizophrenia symptoms (13.1%) which was significantly lower in the CAR groups (7.1% and 2.7% in the 3 and 6mg/day, respectively). In contrast, the most often reported adverse event in the 3 mg/day CAR group was tremor (21.4% versus 0% in PBO). Tremor and extrapyramidal side effects (EPS) are common in antipsychotic treatment. Cariprazine is comparable to other atypical antipsychotics in causing EPS.[7]
- In the 6 mg/day group there was no adverse event occurring in more than 10% of patients. Differences between PBO and the 6 mg/day CAR group were found in increased blood triglycerides (8.1% vs 1.0%) and heightened intraocular pressure (5.4% vs 0%). There were no clinically significant changes in intraocular pressure in a previous 48-week, single-arm, open-label extension study on the safety and tolerability of cariprazine in the long-term treatment of schizophrenia.
- Gastrointestinal disorders such as abdominal pain, constipation, diarrhea, dry mouth and vomiting were less prominent in the CAR groups (3 mg/day: 14.3% and 6 mg/day: 8.1%) than in PBO (18.2%).

Figure 1 Reported Adverse Events during Treatment Period. RGH-MD-06 (Maintenance of Effect Study) Safety Population



CONCLUSIONS

- **Cariprazine was generally safe and well tolerated**
- **Schizophrenia relapse occurred significantly less with cariprazine treatment than with placebo, while many safety parameters were comparable to placebo**
- **Overall, the results suggest that adherence might be improved with cariprazine treatment**

Table 1 Incidence of Treatment Emergent Adverse Events (TEAEs) during Treatment Period by System Organ Class, Preferred Term. RGH-MD-06 (Maintenance of Effect Study) Safety Population

		Cariprazine Fix Doses: Double-Blind Phase	
System Organ Class Preferred term	Placebo (N=99) n (%)	Cariprazine 3.0 mg (N=14) n (%)	Cariprazine 6.0 mg (N=37) n (%)
Patients with at least one TEAE	64 (64.6)	10 (71.4)	24 (64.9)
Discontinuation due to TEAE	5 (5.1%)	1 (7.1%)	3 (8.1%)
Eye disorders	3 (3.0)	1 (7.1)	3 (8.1)
Gastrointestinal disorders	18 (18.2)	2 (14.3)	3 (8.1)
Constipation	3 (3.0)	1 (7.1)	1 (2.7)
General disorders & administration site conditions (i.e. fatigue, pain, pyrexia)	6 (6.1)	1 (7.1)	1 (2.7)
Infections and infestations	14 (14.1)	1 (7.1)	6 (16.2)
Nasopharyngitis	5 (5.1)	1 (7.1)	3 (8.1)
Injury, poisoning and procedural complications	2 (2.0)	1 (7.1)	2 (5.4)
Investigations	9 (9.1)	0 (0.0)	9 (24.3)
Blood triglycerides increased	1 (1.0)	0 (0.0)	3 (8.1)
Intraocular pressure increased	0 (0.0)	0 (0.0)	2 (5.4)
Metabolism and nutrition disorders	6 (6.1)	3 (21.4)	1 (2.7)
Decreased appetite	2 (2.0)	2 (14.3)	0 (0.0)
Type 2 diabetes mellitus	0 (0.0)	1 (7.1)	1 (2.7)
Musculoskeletal and connective tissue disorders	12 (12.1)	2 (14.3)	2 (5.4)
Back pain	2 (2.0)	2 (14.3)	0 (0.0)
Nervous system disorders	19 (19.2)	5 (35.7)	5 (13.5)
Akathisia	2 (2.0)	0 (0.0)	1 (2.7)
Headache	7 (7.1)	2 (14.3)	1 (2.7)
Tremor	0 (0.0)	3 (21.4)	1 (2.7)
Psychiatric disorders	27 (27.3)	4 (28.6)	7 (18.9)
Anxiety	3 (3.0)	2 (14.3)	2 (5.4)
Insomnia	6 (6.1)	1 (7.1)	3 (8.1)
Schizophrenia	13 (13.1)	1 (7.1)	1 (2.7)
Respiratory, thoracic and mediastinal disorders	6 (6.1)	2 (14.3)	3 (8.1)
Cough	2 (2.0)	1 (7.1)	2 (5.4)

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