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Short- and long-term changes in metabolic parameters and body weight in cariprazine-treated patients with schizophrenia

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INTRODUCTION

Metabolic side effects and weight gain are major problems with antipsychotic treatment. They increase the incidence of cardiovascular risks and contribute to vascular consequences, diabetes, poor adherence and impaired treatment response. Therefore, antipsychotics with favorable metabolic profile are preferred [1,2]. Cariprazine is a recently approved antipsychotic for schizophrenia. Understanding its metabolic profile is essential to be able to make the right therapeutic choice for patients.

STUDY OBJECTIVE

To analyze short and long-term effects of cariprazine (CAR) treatment on metabolic parameters and weight changes in adult patients with schizophrenia.

METHODS

Pooled data of 1114 CAR and 584 placebo (PBO) treated patients with schizophrenia from four short-term (6 week), studies [3], and 1122 CAR and 99 PBO patients from four long-term (26-96 week) studies was analyzed using descriptive statistics [4,5,6,7].

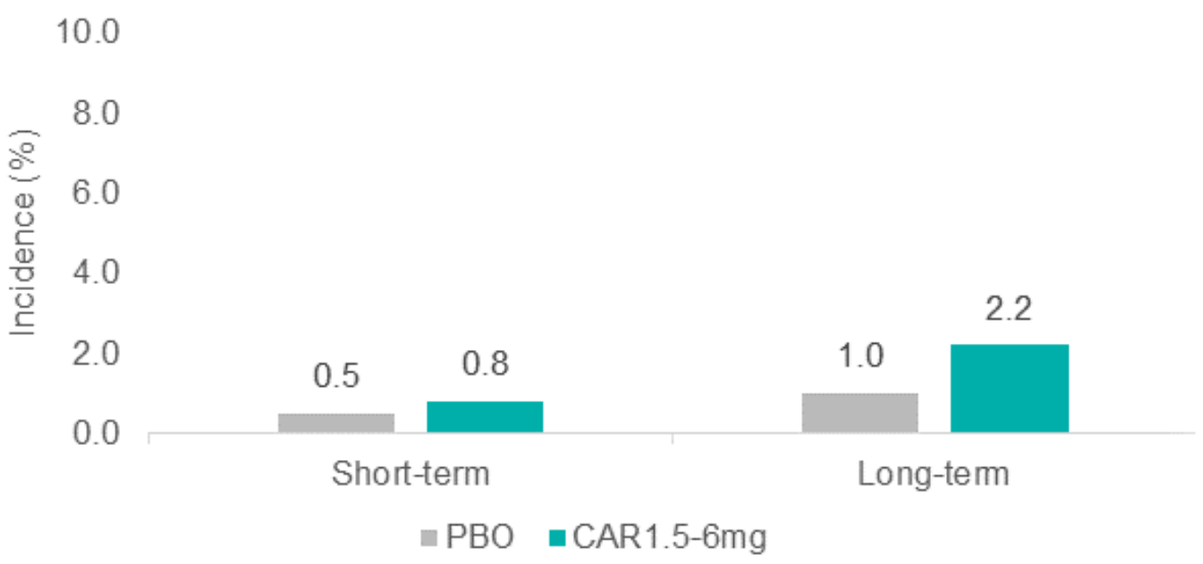
Cariprazine data is presented within the approved dose range from 1.5 to 6 mg/day. Safety parameters included assessment of treatment emergent adverse events (TEAEs), clinical laboratory values and body weight measures. Hyperlipidemia and hypergycemia were defined as the sum of dislipidemia or hyperglycemia and diabetes mellitus related TAEs coded by Medical Dictionary of Regulatory Activities (MEDRA).

RESULTS

Hyperlipidemia in short and long-term studies (*Figure 1*)

In short-term studies there was no significant difference (p=0.49) between PBO and CAR regarding the incidence of hyperlipidemia (CAR=0.8%; PBO=0.5%), simillary to long-term treatment (p=0.42), where it was observed in 2.2% of the cariprazine, and in 1.0% of the placebo-treated patients.

Figure 1 Incidence of dyslipidemia related TEAEs in short and long-term studies

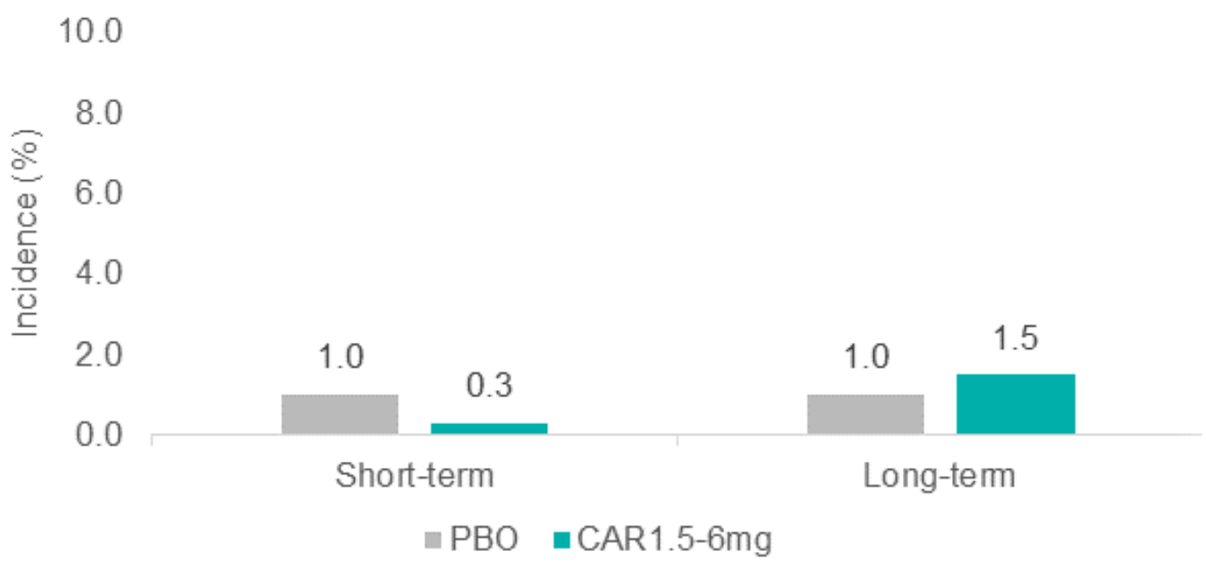


Dyslipidemia related TEAEs: blood triglycerides increased, blood cholesterol increased, dyslipidemia, hypercholesterolemia, hypertriglyceridemia, hyperlipidemia

Hyperglycemia in short and long-term studies *(Figure 2)*

Hyperglycemia was significantly (p=0.04) less frequent with cariprazine (0.3%), than with placebo (1.0%) in the short-term studies. With long-term treatment, there was no significant difference (p=0.69) between the two groups (PBO=1.0%;CAR=1.5%).

Figure 2 Incidence of Hyperglycemia and Diabetes Mellitus related TEAEs in short and long-term studies



Blood glucose increased, hyperglycemia, diabetes mellitus, diabetes mellitus inadequate control, glucose tolerance impaired, metabolic syndrome, type 2 diabetes mellitus, hypoglycemia, blood insulin increased, glucose urine present, glycosylated hemoglobin increased

CONCLUSIONS

- **Cariprazine was metabolically neutral and well tolerated in patients with schizophrenia.**
- **Incidence of any unfavorable metabolic change was low during both short-term and long-term cariprazine treatment.**
- **Minimal weight change was observed early in treatment which maintained stable over time.**
- **Its overall metabolic effects were modest, offering an alternative with favorable metabolic profile both in acute and long-term management of schizophrenia.**

Shifts from normal to high in LDL-cholesterol, triglycerides and fasting glucose *(Table 1)*

Shifts from normal to high level in cholesterol and triglycerides occurred less frequent in the CAR group. The incidence of glucose level shifts from normal to high was higher in the CAR group both in short and log-term trials, however it stayed stable over time.

Table 1 Incidences of treatment-emergent shifts from normal to high in LDL-cholesterol, triglycerides and fasting glucose from baseline to any time post-baseline during short and long-term studies

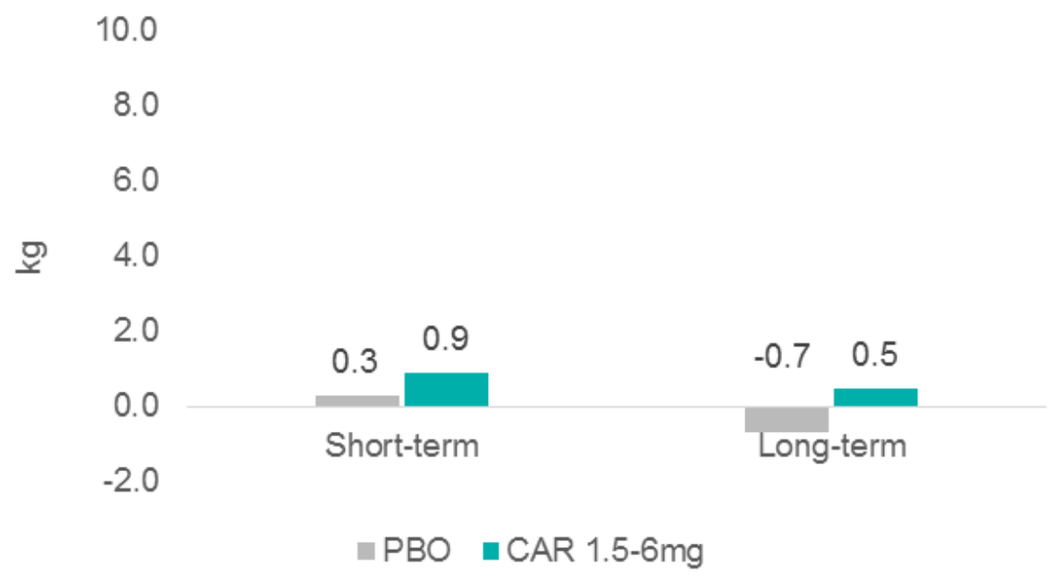
	Short-term studies		Long-term studies	
	PBO N=584	CAR1.5-6mg N=1114	PBO N=99	CAR 1.5-6mg N=1122
LDL-cholesterol	4.9%	2.9%	2.0%	2.0%
Fasting triglycerides	8.3%	6.7%	12.5%	10.7%
Fasting glucose	3.6%	6.7%	1.0%	6.2%

LDL-cholesterol: Normal <3.4 mmol/l; High >4.1 mmol/l
Fasting TG: Normal <1.7 mmol/l; High >2.2 mmol/l
Fasting Glucose: Normal <5.6 mmol/l; High >7.0 mmol/l

Weight change in short and long-term studies *(Figure 3)*

Mean weight increase over short term treatment was 0.9kg with CAR and 0.3kg with PBO, and on long-term treatment it was 1.0kg in both groups.

Figure 3 Weight change from baseline over short and long-term treatment



Metabolic discontinuation

0.1% of patients in the CAR group discontinued due to metabolic side effects and 0% in the PBO group.

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