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Clinical improvement of patients with predominant negative symptoms of schizophrenia: post-hoc analysis of cariprazine versus risperidone

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INTRODUCTION

Schizophrenia is a complex mental disorder embracing positive, negative, cognitive, and mood symptoms; and is associated with an impaired functioning and quality of life. [1] Antipsychotic treatment is efficacious for positive symptoms, but often not efficacious against negative symptoms, which are known to impair functioning more. [2,3] In a Phase III, double-blind, randomized, active-controlled trial, cariprazine (CAR) was significantly more effective than risperidone (RISP) in treating predominantly negative symptoms (PNS) of schizophrenia and improving patients' functioning. Functionality assessment was carried out with the Personal and Social Performance scale (secondary outcome parameter); and was also reflected in the Clinical Global Impression Severity (CGI-S) and Clinical Global Impression Improvement (CGI-I) scales (additional outcome parameters).Improvement on these scales is known to correspond with a better functionality and quality of life. [4]

STUDY OBJECTIVE

The aim of the current post-hoc analysis is to present clinical improvement and its distribution based on the CGI-I scale in patients with predominantly negative symptoms of schizophrenia during cariprazine and risperidone treatments.

METHODS

The study was an international, 26-week, randomized, double-blind, active-controlled, fixed-flexible-dose trial in adults with predominantly negative symptoms of schizophrenia who had a score of 24 or higher on the Factor Score for Negative Symptoms of the Positive and Negative Symptom Score (PANSS-FSNS) and no pseudospecific factors, like high positive symptoms, extrapyramidal symptoms or depression: Factor Score for Positive Symptoms of the Positive and Negative Symptom Score (PANSS-FSPS) ≤19, Calgary Depression Scale Score ≤6, Simpson Angus Scale first 8 items ≤3. Patients were randomized 1:1 to a target dose of 4.5 mg/d cariprazine (n=227) or 4 mg/d risperidone (n=229) for 26 weeks. Clinical condition was scored by the CGI-I: at each visit patient's state was compared to the baseline severity given by the Clinical Global Impression-Severity (CGI-S) score, and scored 1=very much improved; 2=much improved; 3=minimally improved; 4=no change; 5=minimally worse; 6= much worse; 7=very much worse. Results are shown with descriptive statistics at the end of treatment (week 26). Probability of patients being in different CGI-I categories during the study was modeled by ordinal logistic regression for repeated data with treatment, week and treatment x week interaction effects. Patients with CGI-I scores >4 are not presented in this analysis to improve parameter estimation in the logistic regression.

RESULTS

CGI-I score results by treatment group (Table 1)

CGI-I as an efficacy outcome parameter of the study showed statistically significantly better improvement in the cariprazine group versus risperidone.

Table 1 CGI-I scores by treatment at week 26

	CAR	RISP
CGI-I score (standard deviation)	2.53 (0.07)	2.89 (0.07)
p	*<0.0001*	

Distribution of different CGI-I categories by treatment-group (Table 2)

The observed distribution over CGI-I categories was significantly different between the two groups, given by chi-square statistics. Much and very much improvement was achieved by more cariprazine-treated patients, while categories with less improvement were more likely in the risperidone group. Maximal clinical improvement (CGI-I=1) was reached by significantly more patients in the cariprazine group *(p=0.0010).* The highest proportion of cariprazine-treated patients was considered much improved (CGI-I=2), while the biggest ratio of risperidone-treated patients improved only minimally (CGI-I=3).

Table 2 Distribution of clinical improvement categories at week 26

	CAR	RISP
CGI-I=4 (n)	39	54
CGI-I=3 (n)	63	81
CGI-I=2 (n)	82	69
CGI-I=1 (n)	28	9
Degree of freedom	5	
p (chi- square statistics)	*0.0059*	

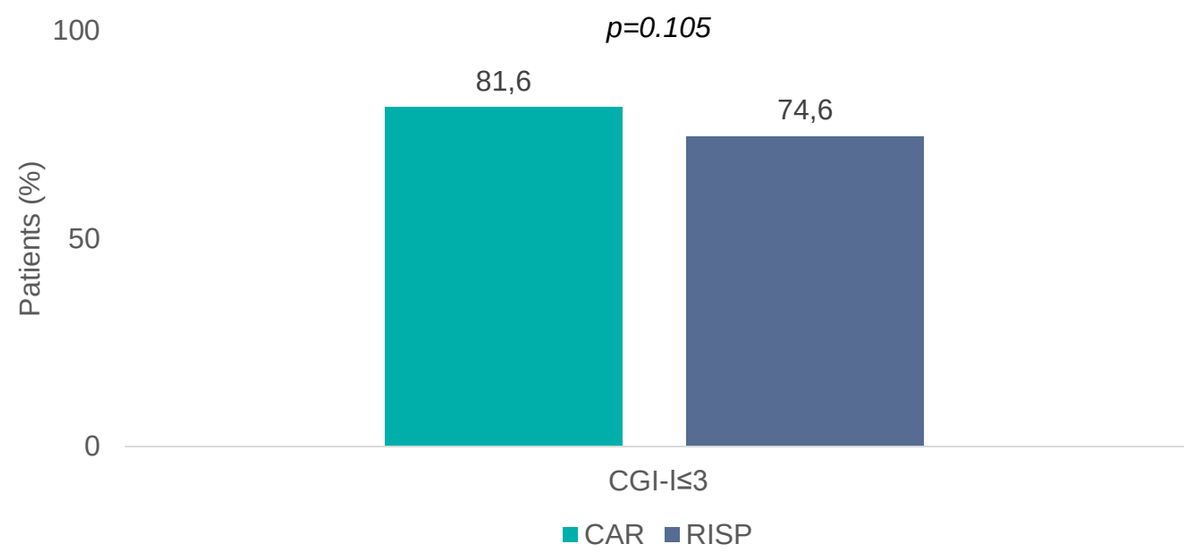
CONCLUSIONS

- **Clinical improvement of patients with predominant negative symptoms of schizophrenia was significantly better with cariprazine, compared with risperidone treatment.**
- **Distribution of clinical improvement categories was significantly different between the two treatment groups in favor of cariprazine.**
- **While response rates were similar in the two treatment groups, higher degrees of clinical improvement were more likely to achieve with cariprazine treatment.**

Clinical response rate (Figure 1)

The ratio of patients with any clinical response (CGI-I≤3) was numerically higher (81.6%) in the cariprazine group compared with risperidone-treated patients (74.6%).

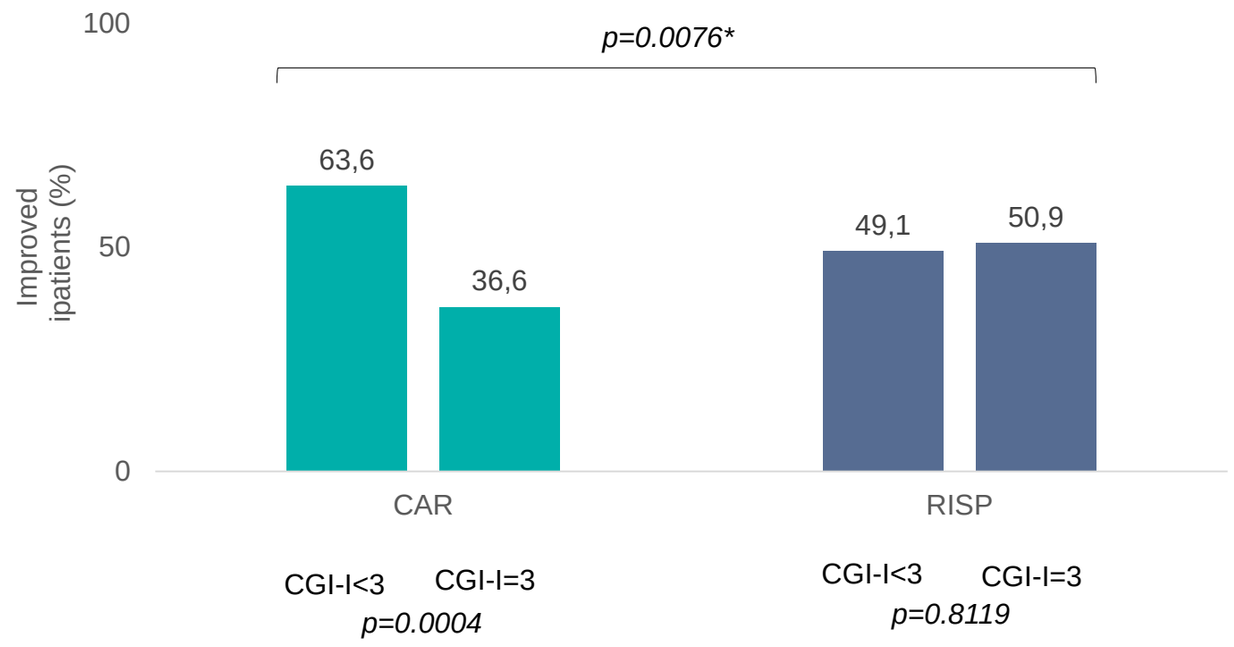
Figure 1 Proportion of patients with clinical improvement at week 26



Distribution of clinically improved patients (Figure 2)

Given by chi-square statistics, greater improvement was *significantly (p=0.0004)* more likely, compared with minimal improvement within the cariprazine-responder group. Within the risperidone-responder group, the ratio of greater progression was similar to minimal improvement *(p=0.8119).* Between group differences resulted in a significantly higher proportion *(p=0.0076)* of patients achieving greater improvement, favoring cariprazine.

Figure 2 Distribution of higher (CGI-I<3) and minimal (CGI-I=3) clinical response at week 26 among responders



** Chi-square statistics comparing the distribution of CGI-I<3 and CGI-I=3 between CAR and RISP.*

Estimated probabilities of clinical improvement

The observed distribution of clinical improvement was transformed into estimated probabilities. The estimated probabilities for CGI-I=4; CGI-I=3; CGI-I=2; CGI-I=1 were 0.09 and 0.17; 0.27 and 0.38; 0.51 and 0.39; 0.12 and 0.06 in the cariprazine and risperidone groups, respectively.

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DISCLOSURES & FUNDING STATEMENT

This study was funded by Gedeon Richter Plc.
Dr. Sebe, Dr. Barabássy, Dr. Laszlovszky, Szatmári, Dr. Harsányi, Acsai and Dr. Németh are employees of Gedeon Richter Plc.
Dr. Earley and Dr. Patel are empoyees of Allergan.