THE EFFICACY OF CARIPRAZINE IN LIGHT OF ITS RECEPTOR PROFILE

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INTRODUCTION

The complex neurochemical dysfunction of schizophrenia manifests in positive, negative, cognitive and affective symptoms. Optimal treatment requires not only the management of positive symptoms but favourable effects in all these dimensions.[1] Cariprazine is a partial agonist antipsychotic, approved for schizophrenia and symptoms of bipolar disorder I.[2,3] Cariprazine's broad therapeutic effect is mediated by its partial agonist activity at dopamine D3/D2/5-HT2B receptors.[4]

STUDY OBJECTIVES

This poster's objective is to present the efficacy of cariprazine in schizophrenia in light of its receptor profile.

METHODS

The in vitro receptor binding profile of cariprazine was characterized. Data from five Phase 3, efficacy studies (NCT00694707, NCT01104766, NCT01104779, EudraCT2012-005485-36, NCT01412060) in patients with schizophrenia were analyzed.

RESULTS

Cariprazine has the highest affinity to D3 receptors (Ki 0.085-0.3nM), reflecting strong efficacy against negative cognitive symptoms versus risperidone in a predominantly negative symptom (PNS) population. Its D2 activity (Ki 0.49-0.71nM) translates into strong efficacy against positive symptoms and relapse prevention as demonstrated in acute and stable patients. Its affinity to 5-HT1A (Ki 1.4-2.6nM), 5-HT2B (Ki 0.58-1.1nM) and 5-HT2A (Ki 18.8nM) receptors may be responsible for its effects on affective symptoms.

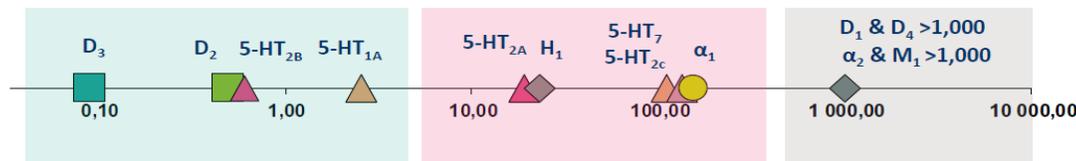### Figure 1. Cariprazine's in vitro receptor affinities (Ki values, nM)

Table 1 Efficacy measures

Efficacy measures			Potentially related receptors
PNS population			
Negative symptoms vs risperidone (PANSS, Marder Negative Symptom Factor)	LSMD -1.46 (95% CI:-2.39, -0.53)	p=0.0022	D3
Cognitive symptoms vs risperidone (PANSS, Marder Disorganized Thought Factor)	LSMD -0.63 (95% CI:-1.26, 0.0)	p=0.05	
Acute population			
Positive symptoms vs placebo (PANSS, Marder Positive Symptom Factor)	LSMD -2.23 (95% CI: 3.00,-1.45)	p<0.0001	D2, 5-HT2B
Affective symptoms vs placebo (PANSS, Marder Anxiety/Depression Factor)	LSMD -0.60 (95% CI:-0.97, -0.23);	p<0.0015	5-HT1A, 5-HT2B, 5-HT2A
Stable patients			
Relapse prevention vs placebo (Relapse rate)	CAR=24.8%, PBO=47.5%, (95% CI:0.28, 0.73)	Hazard Ratio= 0.45	D2

CONCLUSION

Due to its unique receptor profile, cariprazine is an effective antipsychotic for broad symptoms of schizophrenia.

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DISCLOSURE