

PW01-188 - CHARACTERIZATION OF CARIPRAZINE (RGH-188) D₃/D₂ RECEPTOR OCCUPANCY IN HEALTHY VOLUNTEERS AND SCHIZOPHRENIC PATIENTS BY POSITRON EMISSION TOMOGRAPHY (PET)

I. Laszlovszky¹, A. Gage², M. Kapas³, P. Ghahramani⁴

¹Medical Division, Gedeon Richter, Plc., Budapest, Hungary, ²Clinical Research, CNS, Forest Research Institute, Inc., Jersey City, NJ, USA, ³Pharmacological and Drug Safety Research, Gedeon Richter, Plc., Budapest, Hungary, ⁴Clinical Pharmacology and Drug Dynamics, Forest Research Institute, Inc., Jersey City, NJ, USA

Objectives: To evaluate the striatal D₃/D₂ receptor occupancy of cariprazine (RGH-188) in healthy volunteers and schizophrenic patients, and assess the correlation between cariprazine plasma concentration and receptor occupancy.

Methods: Single- (0.5 mg) or multiple-dose (1 mg/day, 14 days) cariprazine was administered to healthy adult males (N=5) in an open-label positron emission tomography (PET) study. In a separate open-label PET study, multiple-dose cariprazine (0.5-3.0 mg/day, 14 days) was administered to adult male schizophrenic patients (N=8). Healthy volunteers had 1 predose and 1 postdose raclopride PET scan; schizophrenic patients had 1 predose and up to 3 postdose fallypride scans. Cariprazine plasma concentrations were determined by LC-MS/MS.

Results: In healthy volunteers, single-dose cariprazine 0.5 mg resulted in low plasma concentration (0.1 ng/ml) and was associated with 12% maximum D₃/D₂ receptor occupancy; cariprazine 1 mg/day for 14 days resulted in cariprazine plasma concentrations of 2.3-3.4 ng/ml and >70% D₃/D₂ receptor occupancy. In schizophrenic patients, cariprazine 1.5 mg/day for 14 days resulted in cariprazine plasma concentrations of 2.5-3.4 ng/ml and >70% receptor occupancy; cariprazine 3.0 mg/day resulted in ≥90% occupancy. Predicted E_{max} values in schizophrenic patients approached 100% D₃/D₂ occupancy for dorsal and ventral striatum.

Conclusions: D₃/D₂ receptor occupancy in dorsal and ventral striatum was similar for cariprazine 1.0 mg/day in healthy volunteers and cariprazine 1.5 mg/day in schizophrenic patients. In both, higher receptor occupancy was associated with higher cariprazine plasma concentration. Cariprazine at 1.5 to 3.0 mg/day showed D₃/D₂ receptor occupancy within the predicted effective antipsychotic range.