P01-79 - **PET-MEASURED OCCUPANCY OF THE D2 RECEPTOR: A COMPARISON OF QUETIAPINE FUMARATE IMMEDIATE- AND EXTENDED-RELEASE FORMULATIONS IN HEALTHY SUBJECTS**

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Objectives: Developed as an antipsychotic, quetiapine displays moderate, transient occupancy of dopamine D2 receptors. Characterization of norquetiapine indicates this major human metabolite potently inhibits the norepinephrine transporter and binds to D2 receptors with affinity similar to quetiapine. Clinical pharmacology studies indicate pharmacodynamic differences between the immediate-release (IR) and the recently developed extended-release (XR) quetiapine formulation. The objectives of this study were to further investigate the pharmacokinetics of these formulations, and to relate D2-receptor occupancy to quetiapine and norquetiapine exposures.

Methods: Eleven healthy male volunteers, aged 20-45 years, underwent PET using the radioligand [11C]raclopride. After baseline measurements, quetiapine XR was administered once-daily for 8 days, with titration to 300 mg on Days 5-8. Quetiapine IR was administered at 300 mg daily on Days 9-12. PET measurements were repeated after the last doses of XR and IR at predicted times of Cmax. D2-receptor occupancy was calculated using a reference tissue model. Concomitant pharmacokinetic measurements were performed.

Results: For quetiapine XR, mean D2-receptor occupancy at Cmax was 32% (SD ±11%; n=11). For quetiapine IR, mean D2-receptor occupancy at Cmax was 47% (SD ±9%; n=10). Quetiapine XR produced lower peak D2 occupancy than quetiapine IR in all subjects.

Conclusions: Pharmacokinetic differences between quetiapine XR and IR formulations translate to different profiles of brain receptor occupancy. Quetiapine XR was associated with lower peak D2-receptor occupancy than quetiapine IR at corresponding doses. This observation may provide important mechanistic underpinnings for emerging clinical data comparing the 2 quetiapine formulations.

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