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**CHANGES IN PSYCHOTROPIC PRESCRIPTION DURING HOSPITALIZATION OF
DEPRESSED PATIENTS CORRELATED WITH INNATE CYP2D6 FUNCTION**

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Objective: Many psychotropic medications are known substrates for metabolism by the cytochrome p450 2D6 isoenzyme (CYP2D6) encoded by the *CYP2D6* gene. Well-characterized sequence alterations in the *CYP2D6* gene occur with significant frequency in psychiatric populations. These include 15 loss-of-function alleles encoding a null or deficient metabolizer isoenzyme and 3 gain-of-function alleles encoding a rapid metabolizer isoenzyme. We hypothesized that innate CYP2D6 functional status is related to psychotropic prescription patterns during hospitalization of patients with major depressive disorder (MDD).

Methods: CYP2D6 functional status was determined by genotyping 18 *CYP2D6* alleles in 150 psychiatric inpatients with MDD admitted to the Hartford Hospital Institute of Living. We quantified CYP2D6 *Metabolic Reserve (MR)* based on the genotype of null, deficient, functional, and rapid alleles for each patient. Patients were grouped (*I* to *VI*) according to CYP2D6 MR as follows: *I*: 0 or 0.5 [*null or poor*, N=8]; *II*: 1.0 [*deficient*, N=36]; *III*: 1.5 [*deficient*, N=22]; *IV*: 2.0 [*functional*, N=41]; *V*: 2.5 [*functional*, N=29]; *VI*: 3.0 [*rapid*, N=13]. A total of 17 CYP2D6-substrate (11 major, 6 minor) psychotropic drugs were taken by these patients (10 antidepressants, 7 antipsychotics). We compared the number of CYP2D6-substrate medications prescribed at admission and during hospitalization to those prescribed at discharge for each patient to determine prescription changes during hospitalization. We assessed the effect of CYP2D6 MR on prescription changes using one-way ANOVA (linear model) and Sidak post hoc tests.

Results: A mean of 2.1 ± 0.1 SE CYP2D6-substrate drugs were prescribed at admission or during the index hospitalization and 1.9 ± 0.1 SE CYP2D6-substrate drugs at discharge ($p < 0.0001$). During hospitalization, *CYP2D6* genotypes were not available, and prescription changes were made on clinical considerations alone. When genotyping results and MR are applied, Group membership significantly affected prescription changes ($p < 0.002$). Group *I* had the most prescription changes (0.88 drugs ± 0.30 SE). It differed significantly from Group *IV* (0.20 drugs ± 0.06 SE, $p < 0.02$) and from Group *V* (0.03 drugs ± 0.03 SE, $p < 0.002$). Groups *II* (0.42 drugs ± 0.12 SE), Group *III* (0.36 drugs ± 0.14 SE) and Group *VI* (0.31 drugs ± 0.13 SE) were intermediate between Group *I* and Groups *IV-V*.

Conclusion: There was a significantly greater reduction in the number of CYP2D6-substrate drugs prescribed to MDD patients with null or poor CYP2D6 MR during hospitalization, compared to patients with functional MR. Patients with deficient and rapid MR were intermediate. Empirical psychotropic management during hospitalization is more intricate in patients with altered (sub- or supra-normal) CYP2D6 MR. Determination of CYP2D6 functional status at admission could improve psychotropic prescription during hospitalization and optimize overall utilization of psychiatric services.

Educational Objectives: At the conclusion of this presentation, participants will be able to (1) describe the prevalence and significance of CYP2D6 drug metabolism deficiencies, (2) assess the utility of CYP2D6 Metabolic Reserve in characterizing and individual's metabolic phenotype and (3) utilize CYP2D6 MR to improve psychotropic management.

Disclosures: Dr. Ruaño is President and Ms. Gorowski an employee of Genomas Inc. Dr. Goethe, Dr. Seip, Dr. Schwartz, and Ms. Szarek have no disclosures.