The value of Pharmacogenomics for White and Indigenous Americans after Kidney Transplant

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Introduction: Kidney transplant recipients (KTR) have a significant medication burden with risk for drug-drug and gene-drug interactions. The objective of this study is to define the value of pharmacogenomics (PGx) testing comparing a cohort of White versus Indigenous American (IA) KTR.

Methods: A prospective cohort study of 26 IA and 50 White KTR patients with OneOme22 PGx gene panel.

Results: Mean age 53 (SD14.5 years), 50% female, 75% required dialysis prior to transplant. Mean number of medications at the time of the OneOme test was 13 (SD4.6), 54% were on beta blockers, 31% on antidepressants, 17% on anticoagulation, 50% on pain medications and 25% on statin therapy. Significant differences in CYP2C19 and CYP2D6 were noted between IA and White patients (p0.05). IA patients had more low or intermediate activity of VKORC (vs normal) compared to White (p=0.018) and more normal activity (vs reduced) of CYP4F2 compared to Whites (p=0.005), both are critical for warfarin drug dosing and efficacy. More IA patients had increased metabolism of NUDT15 (2% vs8%) and TMPT phenotypes compared to Whites (27% vs14%) which has significant dosing implications for Azathioprine. SLC6A4 phenotype, significant for antidepressant metabolism, was reduced in 39% of IA patients compared to 20% of whites suggesting delayed or lack of response to therapy (p=0.07). 12% of Whites had increased F2 phenotype associated with increased risk of thrombosis. 34% of patients had recommended change in medication and 19% had drug-gene interactions identified based on current medication.

Conclusions: KTR have a high rate of identified drug-gene interactions and over a third of patients would benefit from modification in medication based on PGx results.