**INTRODUCTION**

Application of pharmacogenomics is used commonly to inform clinical therapeutic decisions in cancer, psychiatry, cardiovascular disease, and to prevent serious drug-related adverse reactions. Pharmacogenomic testing has not been routinely adopted in transplantation despite the availability of genomically biomarkers for multiple medications that transplant recipients may receive. Aside from tacrolimus which has a strong evidence for the effect of genetic variants in the cytochrome P450 (CYP) 3A4 gene on its pharmacokinetics, transplant recipients often require cardiovascular therapies and many other drugs which have clinically relevant pharmacogenomic markers.

**OBJECTIVE**

The objective of this work was to determine the frequency of actionable variants in kidney transplant recipients.

**METHODS**

**Study Participants**
Kidney allograft recipients enrolled in the multi-center, prospective, observational Genomics of Kidney Transplantation (GEN03) study (NCT01714440) (Table 1). Participants were selected for the current analysis if they were enrolled in the GEN03 study and had GWAS genotypes available.

**DNA Collection and Genotyping**
Genomic DNA was collected on the Affymetrix Transplant Array chip. The chip produced ~767,000 high quality genomic markers. Imputation of unmeasured variants was conducted using 1000 Genomes Phase 3 and Genom of the Netherlands v5.5 reference panels, and high quality control ~40M genotyped and imputed variants were available.

**Identification of Actionable Pharmacogenomic Diplotypes**
Actionable diplotypes and corresponding pharmacotypes for this study were identified by searching the Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines, Dutch Pharmacogenetics Working Group (DPWG) guidelines and PharmGKB. Actionable variants were selected for the analysis if they had CPIC or DPWG guidelines.

**RESULTS CONTD**

Diabetes (20.9%) and glomerular disease (28.5%) were the most common actionable causes of kidney disease. The presence of cardiovascular disease was common among transplant recipients; 88.5% had hypertension and 50.3% had hyperlipidemia that required treatment at transplant. Other cardiovascular disorders were present in lower frequencies (<11%). A majority of the kidney transplant population (91%) was on tacrolimus.

Thirty-three variants within 14 genes were present on our chip: CYP2B6*5,*18; CYP2C9*2,*3; CYP2C19*2,*3;*17, CYP4F2*4; CYP4F2*3; DPD*2A2,*5A9,*DA499V,*13, HapB3; F5; HLA-B*37; IFNL3 CC, CT, TT, NUDT1*3; SLC22A1*1b,*15,*17, PTMP2*3A,*3B,*3C; FMR1*1-C1639 G-A; Frequencies of actionable diplotypes in European and African ancestry recipients are shown in Table 2. Every individual had at least 1 actionable pharmacogenomic phenotype, while the majority (58%) of patients had three or four among the 14 genes (Figure 1). About 1% of recipients carried 7 or 8 actionable phenotypes.

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