

OP-24: The design and implementation of a novel pharmacogenomic assay to study the distribution of *CYP3A53 (rs776746) and *CYP3A5**1E (rs4646453) polymorphisms and its implications to predict the response to the immunosuppressive drug tacrolimus**

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Introduction: Tacrolimus is a first-line immunosuppressive agent for solid organ transplantations. Due to its narrow therapeutic index, tacrolimus demonstrates a wide inter-individual variability in pharmacokinetics. Genetic polymorphisms in *CYP3A5* are significant determinants of tacrolimus efficacy.

Methods: A total of 100 healthy individuals from the Sri Lankan population were screened for the *CYP3A5* single nucleotide polymorphisms (SNPs), *CYP3A5**3 (rs776746) and *CYP3A5**1E (rs4646453) using a novel single variant tetra-primer amplification refractory mutation system (ARMS) polymerase chain reaction (PCR) assay and the results were validated by DNA sequencing.

Results: The *CYP3A5**3 variant was the most frequent allele detected in 82% of the Sri Lankan population, while the *CYP3A5**1E C allele was found in 66.5% of the population. The observed *CYP3A5* genotype frequency distributions for the *CYP3A5**3 (rs776746) and *CYP3A5**1E (rs4646453) variants in the study population were consistent with the Hardy–Weinberg equilibrium ($p > 0.05$). The expected phenotype frequency for the clinically significant *CYP3A5**3 (rs776746) variant was reported as T/T [extensive metabolizer] 4.0%, C/T [intermediate metabolizer] 28.0% and C/C [poor metabolizer] 68.0%. As 68.0% of the Sri Lankan population were identified to be poor metabolizers (*CYP3A5**3/*3), lower doses of tacrolimus would be required to reach therapeutic concentrations.

Conclusions: A novel tetra-primer ARMS PCR assay was successfully designed for genotyping the *CYP3A5* variants *CYP3A5**3 (rs776746) and *CYP3A5**1E (rs4646453). Further studies comprising a larger number of samples and more related genes are recommended.

Keywords: tacrolimus, *CYP3A5*, tetra-primer ARMS polymerase chain reaction, pharmacogenomic assay