Title: Summary of genetic guideline for use of Tacrolimus in Transplantation

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The *CYP3A5* genotype and tacrolimus dosing guidelines were published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) in March 2015 to provide recommendations on how to use *CYP3A5* genotype information, if it is known, to guide tacrolimus dosing. A brief summary of the recommendations follow.

Tacrolimus is a widely used immunosuppressive medication with a narrow therapeutic index; enzymes in the cytochrome P450 (CYP) 3A family are responsible for the oxidative metabolism of tacrolimus. CYP3A5 genotype-guided dosing quickly achieves initial target tacrolimus concentrations after transplantation but cannot replace therapeutic drug monitoring (TDM).Currently there is no definitive evidence to indicate that genotype-guided dosing for tacrolimus affects long-term clinical outcomes, however, there is strong evidence to support its effect on achieving target tacrolimus trough whole blood concentrations. There are various types of metabolizers and the recommendations for each are below:

- CYP3A5 Extensive metabolizer carries two functional alleles (*1). Will require 1.5-2 times The recommended starting dose, total dose not to exceed 0.3/kg/day, followed by TDM
- CYP3A5 Intermediate metabolizer, carries one functional allele (*1), and one non-functional allele (*3-*6-*7).Will require 1.5-2 times The recommended starting dose, total dose not to exceed 0.3/kg/day, followed by TDM
- CYP3A5 Non-expresser Poor metabolizer carries two non-functional alleles (*3-*6 *7).Initiate therapy with standard recommended dose, followed by TDM.
- Additional rare variants such as *CYP3A5*2, *8,* and **9* may be found which are of unknown functional significance. However, if a copy of **1* is present, the expected phenotype would be an Intermediate metabolizer.
- Further dose adjustments or selection of alternative therapy may be necessary due to other

clinical factors (Birdwell et al., 2015).

References

Birdwell, K. A., Decker, B., Barbarino, J. M., Peterson, J. F., Stein, C. M., Sadee, W., ... MacPhee, I. A. (2015, March 18). Clinical pharmacogenetics implementation consortium (CPIC) guidelines for CYP3A5 genotype and tacrolimus dosing. *Clinical Pharmacology & Therapeutics*, *98*, 19-24. http://dx.doi.org/10.1002/cpt.113