Web-based app for mycophenolate mofetil dosing recommendation in pediatric and adult transplant patients

Danna Chan, Pharm.D.¹,², Janel Long-Boyle, Pharm.D., Ph.D.², Vijay Ivaturi, M.S., Ph.D.¹

Institutions:
University of Maryland, Baltimore; ²University of California, San Francisco

Objectives:
Transplantation is a life-saving procedure for patients with organ failure, hematologic disorders, and nonmalignant genetic conditions and is associated with high rates of morbidity and mortality in pediatric and adult populations. Mycophenolate mofetil (MMF) is an immunosuppressant that prevents organ rejection in solid organ transplant and graft-vs-host disease in hematopoietic cell transplantation. Successful MMF therapy improves quality-of-life and survival but is contingent on maintaining therapeutic concentrations. The purpose of this project is to create a web-based app for therapeutic drug monitoring to optimize MMF dosing.

Methods:
We conducted a primary literature search for adult MMF population pharmacokinetic (PopPK) models. We replicated 5 models in R using mrgsolve package and externally evaluated the models with the observed (digitized) pharmacokinetic (PK) profiles from these publications. Allometric-scaling was used to extrapolate the models to a pediatric population followed by internal validation using 5 pediatric MPA studies from the literature. Quantitative model evaluation was performed using residual-based metrics. Lastly, we selected the least unbiased model to build a web-based shiny application.

Results:
Of the 5 MMF model from adults, the Staatz¹ model best explained the profiles in all other adult studies. Addition of allometric-scaling to this model resulted in a system that well predicted literature MPA PK studies. This model was then used to develop a simple web-based application in R-shiny that facilitated dosing recommendations based on achieving concentrations in the therapeutic range (AUC₀-12h 30-60mg*hr/L)

Conclusions:
We evaluated and established a MMF model that can predict PK profiles in adult and pediatric populations. The model was then used to build a web-based MMF dosing recommendation application to facilitate decision-making in the clinic.

References: