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Pharmaceutical Sciences Seminar

Wednesday, November 11, 2020
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https://umich-health.zoom.us/j/97003058475
4:00-5:00 pm

"Population pharmacokinetics model of mycophenolic acid in liver transplant recipients and its implication for experimental design"

Presented by:

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Abstract: Mycophenolic acid (MPA), the active compound of the pre-systemically hydrolysed prodrug mycophenolate mofetil (MMF, CellCept), has been widely used for the prophylaxis of acute allograft rejection in solid organ transplantation as a powerful immunosuppressive agent. However, the great inter- and intra- individual pharmacokinetic (PK) variability is one of biggest hurdles in optimizing therapeutic drug monitoring (TDM) of MPA therapy. As both MMF and MPA are classified as Biopharmaceutics Classification System (BCS) class II drugs, the variability arising from the absorption process, which involves physiology, dissolution, enterohepatic circulation (EHC)-related metabolism, presumably contributes to the remarkable MPA variability to some great extent. In this study, a population pharmacokinetics model of MPA focusing on the absorption process was developed based on the 0-12 hr plasma concentration of MPA after MMF administration among 64 Chinese adult liver transplant subjects in a long-term treatment up to 672 days. The PK profiles were best characterized by a two-compartment disposition model with zero inter-individual variability in terms of elimination (K20), lag time (Tlag) but considerable inter-occasion variability in terms of systemic appearance (Ka), K20 and Tlag. The results supported the previous finding that the migrating motor complex (MMC) in fasted state and irregular pattern in fed state within the subject variability played a much more significant role than the inter-individual variability from the population PK model perspectives. This implies a smaller sample size but better simulated gastrointestinal physiological dynamics is needed for oral systemic availability (absorption) in drug bioequivalence study.

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