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## Population pharmacokinetics of mycophenolic acid during the first week after renal transplantation.

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Abstract: To investigate the population pharmacokinetics of mycophenolic acid (MPA) in adult kidney transplant recipients during the crucial first week after transplantation.

Data were collected from 117 patients. MPA plasma concentrations were determined at t=0, 1, 2, 3 and 4 h after mycophenolate mofetil dosing on days 3, 5 and 7. Population analysis was performed using NONMEM. Covariates screened were sex, age, body weight, serum creatinine, creatinine clearance, serum albumin, days of therapy, diabetes mellitus, organ source (live or cadaveric) and co-therapy (tacrolimus or cyclosporine). Final model validity was evaluated using 200 boot strapped samples from the original data. Bias and precision were determined through comparison of observed and predicted concentrations.

Individual concentration-time profiles showed evidence of an absorption lag time and enterohepatic recirculation of MPA in some patients on some occasions. The best base model had bi-exponential elimination with a typical population (SE%) apparent clearance (CL/F) of 29 l/h (5%) and apparent volume of the central compartment of 65 l (7%). CL/F decreased significantly with increasing serum albumin (1.42 l/h reduction in total plasma CL/F with each 1 g/l increase in albumin) and was 27% greater in patients receiving cyclosporine than in those receiving tacrolimus. Evaluation of the final model showed close agreement between pairs of boot strapped and final model parameter estimates (all differences

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