Supplemental Table 1. Summary of covariate model selection

Covariate	Model parameter	ΔOFV	ΔIIV/ ΔIOV[a]
Forward selection			
Step 1. Basic model (without any covariate)			
Age (year)	CL	-12.21	-0.25%
Serum albumin (g/dL)	CL	-68.79	-4.75%
Serum albumin (g/dL)	V_c	-1.37	+3.2%
Serum albumin (g/dL)	Q	-6.20	+1.6%
Serum albumin (g/dL)	Vp	-0.10	-2.4%
Serum total bilirubin (μmol/L)	CL	-30.75	-6.65%
Serum direct bilirubin (μmol/L)	CL	-31.34	-2.36%
Serum creatinine (mg/dL)	CL	-14.32	-0.14%
Serum aspartate aminotransferase (U/L)	CL	-2.08	-0.14%
Serum alanine aminotransferase (U/L)	CL	-2.73	-0.14%
Serum alkaline phosphatase (U/L)	CL	-12.50	-0.54%
Serum lactate dehydrogenase (U/L)	CL	-3.99	-0.14%
Fludarabine administration	CL	-0.64	0%
Fludarabine administration	K_a	-16.63	-3.23% / +3.04%
Gender	CL	+0.11	0%
Cyclosporine administration	CL	-46.02	-3.09%
Conditioning regimen (myeloablative vs. nonmyeloablative)	CL	-20.42	-0.41%
Conditioning regimen	K_a	-8.82	-15.77%
Donor type	CL	-2.38	0%
Donor type	K_a	-8.71	+0.51%
Step 2. Intermediate model (albumin as covariate to CL)			
Age (year)	CL	-12.91	-0.33% / +0.07%
Serum total bilirubin (μmol/L)	CL	-18.29	-0.80% / -0.32%
Serum direct bilirubin (μmol/L)	CL	-16.70	-1.10% / -0.20%
Serum creatinine (mg/dL)	CL	-10.93	-0.20% / -0.20%
Serum alkaline phosphatase (U/L)	CL	-6.60	-0.10%/-0.06%
Fludarabine administration	K_a	-10.06	-1.71% /+0.6%
Cyclosporine administration	CL	-50.11	-3.04%/-0.03%
Conditioning regimen	CL	-9.52	+0.25% / +0.01%
Conditioning regimen	K_a	-7.01	-3.06% / +1.09%
Step 3. Intermediate model (albumin and cyclosporine as covariate to CL)			
Serum total bilirubin (μmol/L)	CL	-4.40	+0.02% / -0.25%
Serum direct bilirubin (μmol/L)	CL	-2.41	-0.07% / -0.14%
Fludarabine administration	K_a	+40.40	+2.25% /+0.6%
Conditioning regimen	K_a	+43.13	+0.92% /+1.1%
Backward elimination			
Step 4. Intermediate model (albumin and cyclosporine as covariate to CL)			
Serum albumin (g/dL)	CL	+50.14	+3.03% / +0.03%
Cyclosporine administration	CL	+64.94	+4.18% / -0.8%

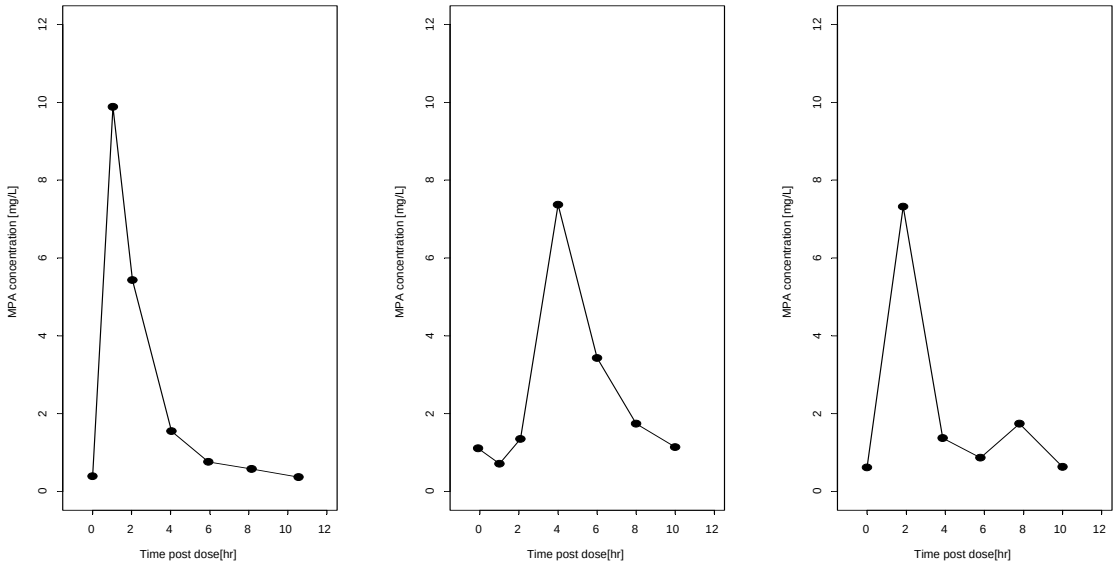
[a]Change in the objective function value (OFV) was compared to the base structural model (Figure 1). The final covariate model incorporated albumin and cyclosporine as covariates to MPA clearance (CL). K_a: first-order rate constant representing both formation and

absorption process; V_c: volume of central compartment; IIV: inter-individual variability; IOV: Inter-occasion variability. Due to extensive running time, FO method was used for covariate model exploration (step 1). FOCE method was used for model validation (step 2 to step 4).

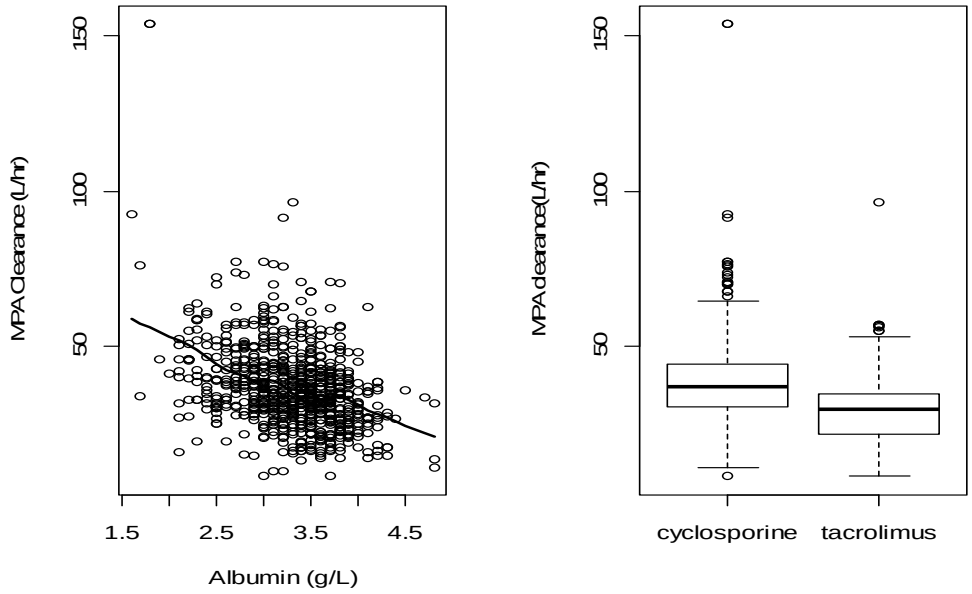
Supplemental Table 2. Five-sample LSS of 4 hr duration sampling after oral MMF administration

Q12 hr oral MMF dosing					
RMSE ($AUC_{0\text{-}12hr}$)%	**Proposed Sampling Time (hr)**				
	#1	#2	#3	#4	#5
16.24	-0.1	0.25	1.25	2	4
16.30	-0.1	0.25	1.25	2	3
16.30	-0.1	0.25	1	2	4
16.30	-0.1	0.25	1.25	3	4
16.32	-0.1	0.25	0.5	2	4
16.34	-0.1	0.25	0.5	3	4
16.35	-0.1	0.25	1	3	4
16.39	-0.1	0.25	1	2	3
16.40	-0.1	0.25	1	1.25	4
16.40	-0.1	0.25	1.25	2.5	4
Q8 hr oral MMF dosing					
RMSE ($AUC_{0\text{-}8hr}$)%	**Proposed Sampling Time (hr)**				
	#1	#2	#3	#4	#5
16.59	-0.1	0.25	1.25	2	3
16.61	-0.1	0.25	1	1.25	3
16.64	-0.1	0.25	1	1.25	4
16.68	-0.1	0.25	1.25	2	2.5
16.69	-0.1	0.25	1	2	3
16.69	-0.1	0.25	0.5	1.25	3
16.69	-0.1	0.25	1	1.25	2
16.69	-0.1	0.25	1.25	2	4
16.71	-0.1	0.25	1	2	2.5
16.72	-0.1	0.25	0.5	2	3

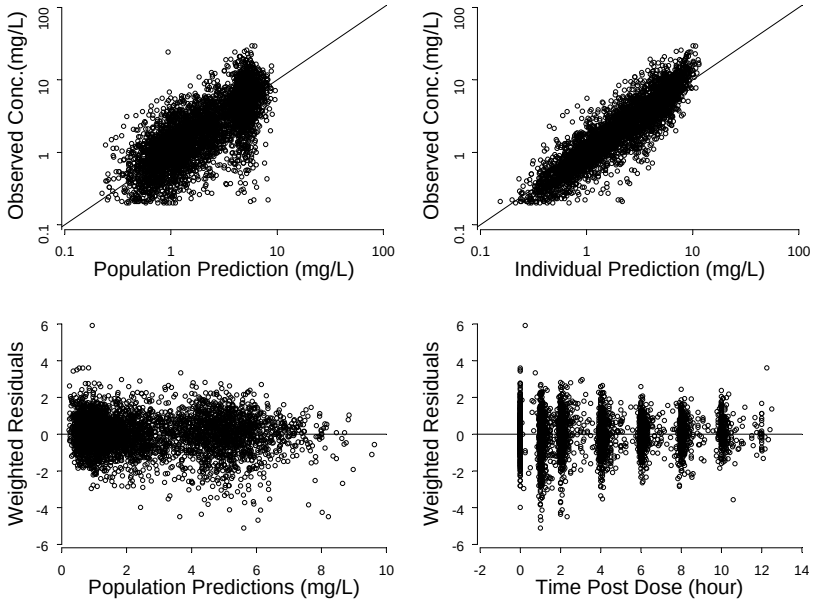
Supplemental Figure 1. Representative individual MPA concentration-time profiles.



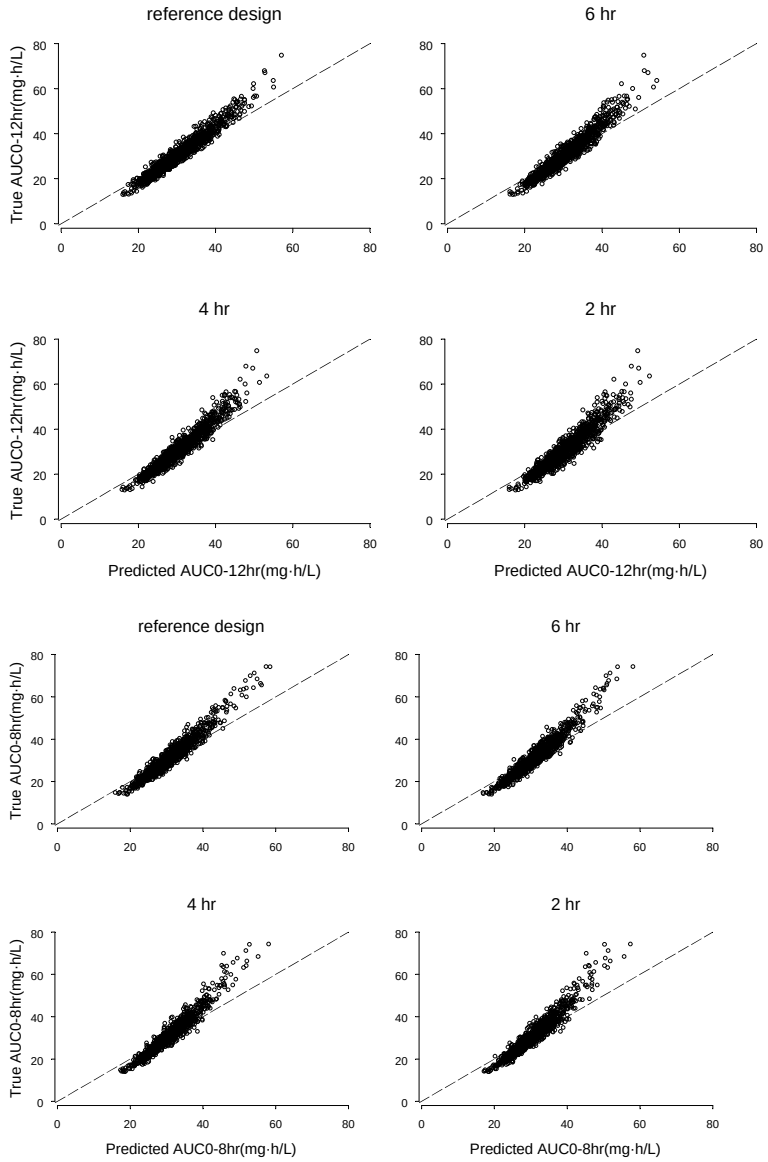
Supplemental Figure 2. Individual Bayesian estimates of clearance from the base structural model as a function of albumin concentration (left panel) and concomitant calcineurin inhibitor (right panel). Solid line in the left panel is the regression line.



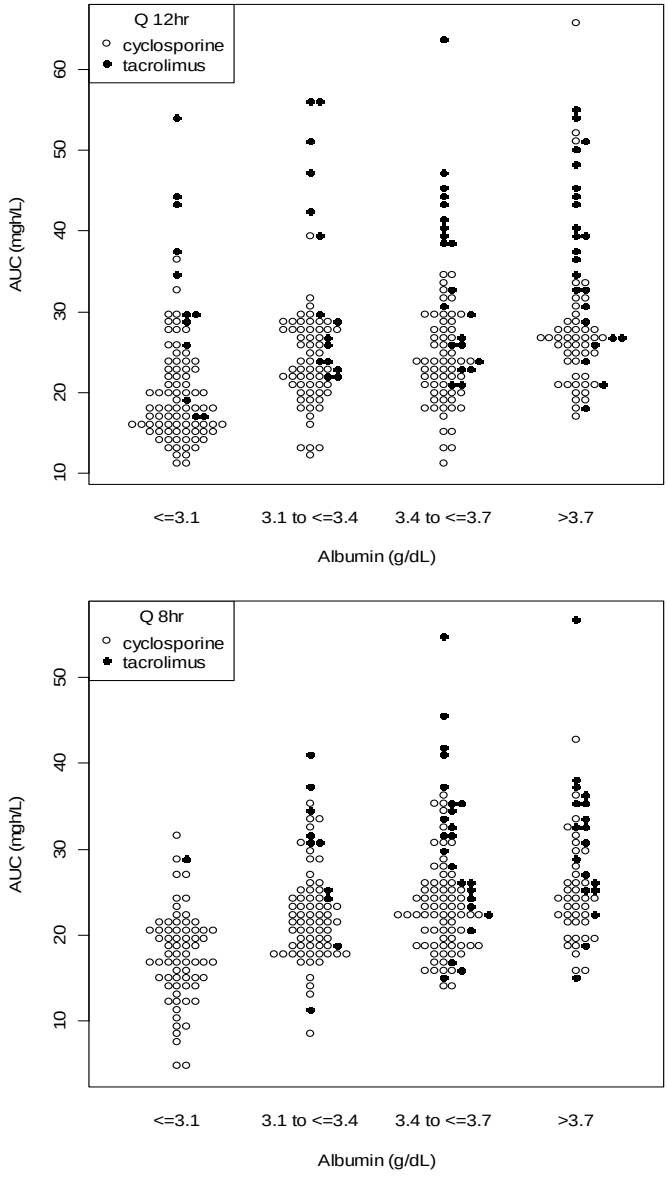
Supplemental Figure 3. Goodness-of-fit plots. Upper left panel: Observed vs. population predicted MPA concentrations. Upper right panel: Observed vs. and individual predicted MPA concentrations. Lower left panel: weighted residuals vs. population predicted MPA concentrations. Lower right panel: weighted residuals vs. time after MMF dose. Solid lines in the upper panels represent lines of identity; solid lines in the lower panels represent WRSE = 0.



Supplemental Figure 4. Precision of various pharmacokinetic sampling schedules to predict the actual AUC for oral MMF administered every 12 hr (top panel) and every 8 hr (bottom panel).



Supplemental Figure 5. Maximum a posteriori Bayesian estimates of total MPA AUC by covariates for Q12hr (top panel) and Q8hr (bottom panel) oral MMF dosing. Data presented by quartiles of albumin concentration. Solid and open circles represent patients receiving tacrolimus and cyclosporine, respectively.



Supplemental Figure 6. Simulated total MPA Css (μg/mL) values in subjects weighing less than 50 kg and serum albumin concentration of 3.4 g/dL for oral administration of MMF every 8 hr at 1250 mg, 1750 mg, 15 mg/kg, and 20 mg/kg with a calcineurin inhibitor, either cyclosporine and tacrolimus. Dashed line represents the lower therapeutic Css of 3 μg/mL.