

Supplemental Material

Supplemental Table 1. Target tacrolimus trough levels based on time post-transplant. Higher tacrolimus trough levels are targeted immediately after transplant to avoid acute rejection of the kidney graft

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Supplemental Figure 1. Percentile curves for tacrolimus CV by time post-transplant, stratified by age at time of transplant. (A) Patients transplanted at age 1-12 years and (B) patients transplanted at age 13-25 years.

Supplemental Table 1. Target tacrolimus trough levels based on time post-transplant. Higher tacrolimus trough levels are targeted immediately after transplant to avoid acute rejection of the kidney graft

Time post-transplant	Target trough levels (ng/mL)
Day 0 to week 2 (day 0 to 14 days)	12-15
Day 15 to week 8 (days 15 to 56)	10-12
Week 9 to week 12 (days 57 to 84)	7-10
After 12 weeks (≥85 days)	5-7
After 6-month biopsy if calcineurin inhibitor toxicity	4-6
After 12-month biopsy if calcineurin inhibitor toxicity	3-5

Supplemental Table 2. Routine post-transplant surveillance as per Lucile Packard Children’s Hospital Kidney Transplant Protocol

Routine post-transplant surveillance	Number of months post-transplant													
	0	1	2	3	4	5	6	7	8	9	10	11	12	24
Protocol kidney allograft biopsies, reviewed by pathologists							✓						✓	✓
Measurement of donor-specific antibodies (serum)	✓	✓	✓	✓			✓						✓	
Transplant clinic visits (twice/week to monthly)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Supplemental Table 3. Results of Mann-Whitney U test comparing tacrolimus inpatient variability in patients who formed C1q-binding *de novo* DSA with non-DSA formers for all ages and for each age group

	De novo DSA-	De novo DSA+	P value
Age group	Tacrolimus IPV (%)	Tacrolimus IPV (%)	
All ages	27.6 (19.7-38.0)	37.9 (28.2-47.8)	<0.001
1-6 years	30.6 (21.7-40.2)	38.2 (27.9-47.4)	<0.001
7-12 years	28.5 (20.5-38.8)	38.8 (27.5-47.7)	<0.001
13-17 years	25.0 (17.5-35.4)	37.7 (28.4-47.7)	<0.001
18+ years	23.1 (17.6-28.5)	38.6 (29.9-60.8)	<0.001

DSA, Donor-specific antibodies

IPV, Inpatient variability

Tacrolimus IPV is presented as median (interquartile range) and was calculated using tacrolimus values after 10 months post-transplant.

Supplemental Table 4. Association between graft loss and other variables in the outcome cohort (n=220)

Variable	Bivariate analyses	Multivariate analysis	
		Model 1 ^a HR (95% CI)	Model 2 ^b HR (95% CI)
Age at transplant, years	1.21 (1.05-1.39)		
Age at tacrolimus measurement, years	1.20 (1.05-1.36)		
Sex, male	0.65 (0.21-1.96)		
Living donor	2.55 (0.61-10.65)		
HLA match	0.67 (0.42-1.07)		
Peak PRA	1.00 (0.98-1.02)		
Tacrolimus level, ng/mL	0.95 (0.75-1.21)		
Presence of C1q-binding de novo DSA	36.35 (4.73-279.5)		
Tacrolimus IPV (continuous variable)	1.03 (1.01-1.04)		
Tacrolimus IPV >30% (high vs. low)	8.69 (1.89-40.00)	3.91 (0.75-20.36)	
Tacrolimus IPV by quartiles*			
1 st quartile	-		-
2 nd quartile	2.14 (0.29-15.62)		2.76 (1.06-7.17)
3 rd quartile	16.68 (0.06-3.44)		2.30 (0.61-8.70)
4 th quartile	6.35 (1.06-38.15)		2.94 (0.86-10.02)

Bold text denotes p<0.05

^a Model 1: Adjusted for presence of C1q-binding de novo DSA and tacrolimus IPV categorized as below or over 30%

^b Model 2: Adjusted for presence of proteinuria and tacrolimus IPV categorized by quartiles.

* Tacrolimus IPV cutoffs by quartiles calculated from entire cohort: 1st quartile (25th percentile) 20.6%; 2nd quartile (50th percentile) 29.5%; 3rd quartile (75th percentile) 41.1%; 4th quartile (100th percentile) 173.2%.

HR, *Hazard ratio*

CI, *Confidence interval*

IPV, *tacrolimus intrapatient variability*

HLA, *Human leukocyte antigen*

Peak PRA, *Historic peak panel reactive antibodies*

DSA, *Donor-specific antibodies*

Supplemental Figure 1. Percentile curves for tacrolimus CV by time post-transplant, stratified by age at time of transplant. (A) Patients transplanted at age 1-12 years and (B) patients transplanted at age 13-25 years.

