



*Differences in Kidney Allograft Outcomes
Between Ethnicities when Converting to
Sirolimus Based Immunosuppression*

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Background

- Acute rejection rates are less than 15% at most transplant centers
- Chronic allograft nephropathy (CAN) is one of the primary contributors to graft loss
- Toxicity of calcineurin inhibitors (CNI) may contribute to CAN
- African-Americans (AAs) are at increased risk of acute rejection and CAN
 - Require higher doses of immunosuppression
 - More likely to be presensitized to HLA antigens
 - Longer mean time on dialysis

Purpose

- Determine if ethnicity impacts graft outcomes in kidney transplant patients converted to sirolimus and either maintained on a calcineurin inhibitor or mycophenolate mofetil with steroids

- Single-center evaluation of patients >18 years of age who received a kidney transplant between 7/91 and 4/07 and underwent SRL conversion
- Reasons for Conversion
 - Acute persistent rejections
 - Chronic CNI (calciuneurin inhibitors) nephrotoxicity
 - Hemolytic uremic syndrome (HUS)
 - Intolerable adverse effects to CNI
 - Malignancy

Objectives

- Primary Objective
 - Incidence of acute rejection after SRL conversion
 - Overall graft survival
- Secondary Objective
 - Comparison of SrCr and CrCl at time and post-conversion

- Differences between groups were tested using Student's T-test and Fisher's Exact test
- Kaplan Meier survival analysis was used to assess overall differences in graft survival
- P-values <0.05 were considered significant

Study Groups

	Group 1: N=113	Group 2: N= 42	Group3: N=70	Group 4: N=32
Ethnicity	African Americans (AA)	African Americans (AA)	Non-African Americans (non-AA)	Non-African Americans (non-AA)
Drug Regimen	Sirolimus (SRL) + Calcineurin inhibitor (CNI) (Cyclosporine – CSA or tacrolimus - TAC)	SRL + Mycophenolate mofetil (MMF)	SRL +CNI	SRL + MMF

Baseline Characteristics

	Group 1 (n=113)	Group 2 (n=42)	Group 3 (n=70)	Group 4 (n=32)
Mean age	46±12	47±14	47±13	47±13
Males	57 (50%)*	33 (79%)*	35 (50%)	20 (63%)
Living donor	20 (18%)	1 (2.3%)	24 (34%)	12 (38%)
PRA (panel reactive antibody) >20%	13 (11.5%)	5 (9%)	7 (10%)	3 (9%)
HD within 7 days post-transplant	20 (18%)	9 (21%)	7 (10%)	5 (16%)

*p<0.05

Immunosuppression

	Group 1	Group 2	P-Value between Group 1 and 2	Group 3	Group 4	P-Value between Groups 1 and 2
Calcineurin Inhibitor			0.0001			0.036
CSA	79 (75%)	15 (36%)		51 (75%)	16 (52%)	
TAC	27 (25%)	27 (64%)		17 (25%)	15 (48%)	
Induction			0.002			NS
IL-2	43 (45%)	26 (67%)		34 (69%)	19 (61%)	
ALA	20 (21%)	11 (28%)		15 (31%)	10 (32%)	
None	33 (34%)	2 (5%)		0 (0%)	2 (7%)	

Results

	Group 1	Group 2	P-Value between Groups 1 and 2	Group 3	Group 4	P-Value between Groups 3 and 4
Acute Rejection before SRL	49 (43%)	9 (21%)	0.015	28 (40%)	3 (9%)	0.002
Acute Rejection after SRL conversion	8 (7%)	3 (7%)	NS	4 (6%)	1 (3%)	NS
Mean days to graft failure	649 ±444	393 ±189	0.0004	574±423	198±N/ A	N/A

Results

	Group 1	Group 2	P-Value between Groups 1 and 2	Group 3	Group 4	P-Value between Groups 3 and 4
SrCr at time of conversion	2.5 ± 1.0	2.1 ± 1.0	0.03	2.1 ± 1.0	2.2 ± 1.0	NS
Last Follow-Up SrCr	3.5 ± 2.8	2.4 ± 1.6	0.02	2.4 ± 1.6	2.3 ± 1.6	NS

Conclusions

- AAs converted to SRL + CNI had a significantly longer time to graft failure compared to AA converted to SRL + MMF
- No difference in incidence of proteinuria or acute rejection rates after conversion to SRL between all groups
- Trend toward improved graft survival in AA converted to SRL+CI and non-AA converted to SRL+MMF
 - Further investigation is warranted to confirm this finding

Limitations

- Retrospective study
- Each group was not well matched
 - More rejection pre conversion in SRL+CI group
 - Longer time to conversion
- Transplanted during two different time periods

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