

Table S1. Association between CNl trough level and treatment adherence assessed by the Morisky scale

	Non adherent patients*	Adherent patients*	p-value [‡]
Treatment by tacrolimus			
At 3 months	8.7 (2.0)	9.2 (2.7)	0.33
At 6 months	8.4 (2.0)	8.2 (2.1)	0.58
At 12 months	7.6 (2.4)	7.9 (2.6)	0.55
At 24 months	7.9 (2.5)	7.6 (2.4)	0.44
Treatment by cyclosporine			
At 3 months	147.3 (30.0)	164 (46.0)	0.31
At 6 months	147.1 (42.3)	147.3 (52.6)	0.99
At 12 months	123.1 (41.9)	127.3 (45.6)	0.77
At 24 months	87.8 (34.2)	98.4 (46.4)	0.52

*assessed by the Morisky scale at the time of CNl trough levels measures

[‡]assessed by Student test

Table S2. Factors associated with occurrence of acute rejection over the 5 years post transplantation.

	N	No rejection (n=228)	At least one rejection (n=73)	P value
Age (years), mean (SD)	301	50.0 (12.3)	47.8 (15.4)	0.27
Male , n (%)	301	154 (67.5)	54 (74.0)	0.30
Primary kidney disease	295			0.42
Vascular, n (%)		8 (3.6)	2 (2.8)	
Diabetics, n (%)		32 (9.4)	3 (4.2)	
Glomerulonephritis, n (%)		62 (27.8)	20 (27.8)	
Tubulo-interstitial, n (%)		24 (10.8)	7 (9.7)	
Hereditary (including polycystic kidney disease), n (%)		51 (22.9)	13 (18.1)	
Other or undetermined, n (%)		57 (25.6)	27 (37.5)	
Number of previous graft(s)	271			0.71
0, n (%)		167 (81.9)	57 (85.1)	
1, n (%)		31 (15.2)	10 (14.9)	
≥ 2, n (%)		6 (2.9)	0 (0.0)	
Sensitized patients , n (%)	226	45 (27.1)	16 (26.7)	0.95
Donor age (years), mean (SD)	278	49.0 (15.6)	49.7 (16.8)	0.76
Living donor , n (%)	298	8 (3.5)	1 (1.4)	0.69
Expanded criteria donor , n (%)	274	86 (41.8)	30 (44.1)	0.73
Number of HLA mismatches (A-B-DR)	295			0.22
0 - 1, n (%)		11 (4.9)	2 (2.9)	
2 - 4, n (%)		131 (58.2)	34 (48.6)	
5 - 6, n (%)		83 (36.9)	34 (48.6)	
Total ischemia time (hours), mean (SD)	269	16.2 (6.4)	16.5 (5.7)	0.72
Induction treatment	276			0.60
Basiliximab, n (%)		126 (60.0)	42 (63.6)	
rATG, n (%)		84 (40.0)	24 (36.4)	
Delayed graft function , n (%)	292	46 (20.6)	15 (21.7)	0.84
Maintenance treatment at 3 months post-transplant	271			0.002
Cyclosporine		42 (18.6)	18 (40.0)	
Tacrolimus		181 (80.1)	25 (55.6)	
Without CNI		3 (1.3)	2 (4.4)	
Maintenance treatment at 6 months post-transplant	255			0.01
Cyclosporine		45 (20.1)	10 (32.3)	
Tacrolimus		175 (78.1)	18 (58.1)	
Without CNI		4 (1.8)	3 (9.7)	
Maintenance treatment at 12 months post-transplant	241			0.005
Cyclosporine		42 (19.0)	9 (45.0)	
Tacrolimus		171 (77.4)	9 (45.0)	
Without CNI		8 (3.6)	2 (10.0)	
Maintenance treatment at 24 months post-transplant	227			0.39
Cyclosporine		41 (19.0)	3 (27.3)	
Tacrolimus		164 (75.9)	7 (63.6)	
Without CNI		11 (5.1)	1 (9.1)	
Corticosteroids at 3 months	301			0.06
Continued		188 (82.5)	67 (91.8)	
Discontinued		40 (17.5)	6 (8.2)	

N : subjects with available data ; SD : standard deviation ; HLA : Human Leucocyte Antigen

Table S3. Effect of non-adherence measured by the Morisky scale and immunosuppression regimen on the hazard of acute rejection. Results of Cox proportional hazard model. Multivariable analysis.

	3 months (N = 246)			6 months (N = 228)			12 months (N = 220)			24 months (N = 189)		
	HR*	CI 95%	p-value	HR*	CI 95%	p-value	HR*	CI 95%	p-value	HR*	CI 95%	p-value
Non adherent vs adherent[†]	0.93	0.40- 2.15	0.94	1.19	0.52- 2.75	0.77	0.52	0.17- 1.59	0.27	0.57	0.11- 2.91	0.60
Maintenance treatment			0.001			0.0008			0.005			0.52
Tacrolimus	1			1			1			1		
Cyclosporine	2.68	1.42- 5.08		2.08	0.92- 4.71		4.07	1.57- 10.57		1.60	0.31- 8.27	
Without anticalcineurin	4.48	1.27- 17.7		6.97	1.99- 24.41		5.78	1.21- 27.5		2.99	0.34- 26.4	

HR: Hazard ratio ; CI: Confidence Interval ; N = Subjects with complete data, with a functioning graft at time of measure of NA and without acute rejection before this time ; [†]Subjects with at least one positive response to Morisky scale at time of measure. * adjusted for adherence status and maintenance treatment measured at the time mentioned above

Table S4. Factors associated with risk of graft failure defined as death, return to dialysis or retransplantation. Results of univariate Cox model.

	N	HR	CI 95%	p-value
Recipient age, per year	297	1.02	0.99-1.03	0.08
Female sex	297	0.71	0.43-1.16	0.17
Primary kidney disease	292			0.98
Vascular, n (%)		1		
Diabetics, n (%)		1.10	0.28-4.25	
Glomerulonephritis, n (%)		1.10	0.33-3.65	
Tubulo-interstitial, n (%)		0.87	0.23-3.28	
Hereditary (including PKD), n (%)		0.81	0.24-2.79	
Other, n (%)		0.91	0.26-3.22	
Undetermined, n (%)		1.14	0.32-4.15	
Multiples, n (%)		0.76	0.08-7.25	
Number of previous grafts, per unit	269	0.93	0.57-1.51	0.77
Preemptive transplantation	296	0.59	0.24-1.47	0.26
Transplant with a living donor	295	0.33	0.05-2.41	0.28
Donor age, per year	275	1.02	1.01-1.04	0.007
Transplant with an expanded criteria donor	271	1.48	0.95-2.30	0.08
Number of HLA mismatches, per unit	292	1.00	0.85-1.18	0.968
Induction treatment	272			0.47
Basiliximab, n (%)		1		
rATG, n (%)		1.19	0.74-1.91	
Total ischemia time, per hour	266	1.02	0.98-1.05	0.38
Occurrence of a delayed graft function	289	1.38	0.83-2.29	0.21
Maintenance treatment at 3 months	296			0.08
Tacrolimus		1		
Cyclosporine		1.68	1.06-2.66	
Without CNI		0.73	0.10-5.26	
Maintenance treatment at 6 months	294			0.10
Tacrolimus		1		
Cyclosporine		1.62	1.01-2.60	
Without CNI		0.50	0.07-3.62	
Maintenance treatment at 12 months	291			0.24
Tacrolimus		1		
Cyclosporine		1.51	0.91-2.51	
Without CNI		1.53	0.55-4.22	
Maintenance treatment at 24 months	282			0.23
Tacrolimus		1		
Cyclosporine		1.51	0.88-2.59	
Without CNI		1.64	0.65-4.12	
CNI trough levels at 3 months	239			0.93
Standard CNI through levels		1		
Low CNI through levels		1.09	0.34-3.46	
Without CNI		0.71	0.10-5.13	
CNI trough levels at 6 months	253			0.66
Standard CNI through levels		1		
Low CNI through levels		1.22	0.56-2.67	
Without CNI		0.48	0.07-3.44	
CNI trough levels at 12 months	253			0.25
Standard CNI through levels		1		
Low CNI through levels		1.62	0.84-3.12	
Without CNI		1.66	0.60-4.60	
CNI trough levels at 24 months	248			0.007
Standard CNI through levels		1		
Low CNI through levels		2.36	1.37-4.07	
Without CNI		1.84	0.73-4.67	
Corticosteroids discontinued at 3 months post transplant	296	0.99	0.55-1.78	0.96

Occurrence of <i>de novo</i> DSA between 2 and 3 years post transplantation	219	3.26	1.70-6.28	0.0004
Occurrence of acute rejection	297	2.10	1.35-3.26	0.001

N : number of available data ; HR : Hazard Ratio ;

Table S5. Effect of non-adherence measured by the Morisky scale and immunosuppression regimen (standard CNI trough level / low CNI trough level / any anticalcineurin) on the hazard of graft failure since the third year post transplantation. Results of Cox proportional hazard model. Multivariable analysis.

	3 months (N [‡] = 155)			6 months (N [‡] = 158)			12 months (N [‡] = 168)			24 months (N [‡] = 149)		
	HR*	CI 95%	p-value	HR*	CI 95%	p-value	HR*	CI 95%	p-value	HR*	CI 95%	p-value
Non adherent vs adherent[†]	1.03	0.40 – 2.62	0.98	1.01	0.45 – 2.24	0.85	0.77	0.37 – 1.62	0.45	0.97	0.49 – 1.92	0.99
Recipient age (<i>per year</i>)	0.99	0.96 – 1.04	0.75	1.01	0.97 – 1.05	0.68	1.02	0.98 – 1.05	0.42	0.99	0.96 – 1.03	0.79
Donor age			0.54			0.77			0.88			0.25
	1			1			1			1		
	1.53	0.50 – 4.62		1.23	0.41 – 3.66		1.19	0.42 – 3.34		2.11	0.62 – 7.17	
	2.43	0.72 – 8.15		1.75	0.58 – 5.31		1.52	0.50 – 4.66		2.87	0.80 – 10.29	
	2.70	0.63 – 11.61		1.32	0.34 – 5.18		1.63	0.43 – 6.08		4.41	1.05 – 18.57	
Maintenance treatment			0.42			0.29			0.78			0.20
Standard CNI trough level ©	1			1			1			1		
Low CNI trough level ®	0.48	0.10 – 2.40		1.17	0.39 – 3.50		0.87	0.39 – 1.96		1.88	0.94 – 3.76	
Without anticalcineurin	0.55	0.07 – 4.50		0.26	0.03 – 1.98		0.84	0.25 – 2.86		1.98	0.71 – 5.51	
Occurrence of acute rejection (time-dependent variable)	2.13	1.04 – 4.35	0.03	2.25	1.14 – 4.44	0.01	1.93	1.01 – 3.68	0.04	1.90	0.98 – 3.67	0.08
Occurrence of <i>dn</i> DSA between 2 and 3 years post-transplant	2.66	1.09 – 6.45	0.03	3.74	1.55 – 9.04	0.001	2.39	1.07 – 5.37	0.03	1.84	0.74 – 4.53	0.17

HR: Hazard ratio ; CI: Confidence Interval ; [‡]Subjects with complete data and with a functioning graft at 3 years post-transplant; [†]Subjects with at least one positive response to Morisky scale at time of measure. © defined as tacrolimus trough levels ≥ 5 ng/ml or ciclosporin trough levels ≥ 100 ng/ml. ® defined as tacrolimus trough levels ≤ 5 ng/ml or ciclosporin trough levels ≤ 100 ng/ml. *adjusted for recipient and donor age, maintenance treatment at time of measure of NA, occurrence of acute rejection (time dependent variable) and occurrence of *dn*DSA between 2 and 3 years post transplant