

SUPPLEMENTAL TABLE 1. Comparison of the number of indication biopsies and the histological appearance of these indication biopsies, according to whether a protocol biopsy was performed. P values were calculated using one-way ANOVA or Fisher exact test.

	Protocol biopsy at 6 months		
	Done	Not done	P value
Number of indication biopsies (mean ± standard deviation)	1.09 ± 1.43	0.83 ± 1.09	0.3659
At least one indication biopsy	50/100 (50.0%)	14/30 (46.7%)	0.8361
At least one indication biopsy with acute rejection	16/100 (16.0%)	6/30 (20.0%)	0.5883
At least one indication biopsy with acute rejection or borderline changes	26/100 (26.0%)	10/30 (33.3%)	0.4874
	Protocol biopsy at 12 months		
	Done	Not done	P value
Number of indication biopsies (mean ± standard deviation)	0.96 ± 1.32	1.14 ± 1.43	0.4663
At least one indication biopsy	38/81 (46.9%)	26/49 (53.1%)	0.5877
At least one indication biopsy with acute rejection	12/81 (14.8%)	10/49 (20.4%)	0.4721
At least one indication biopsy with acute rejection or borderline changes	21/81 (25.9%)	15/49 (30.6%)	0.6862
	Protocol biopsy at 24 months		
	Done	Not done	P value
Number of indication biopsies (mean ± standard deviation)	1.15 ± 1.55	0.87 ± 1.04	0.2574
At least one indication biopsy	36/75 (47.6%)	28/55 (50.9%)	0.8592
At least one indication biopsy with acute rejection	11/75 (14.7%)	11/55 (20.0%)	0.4816
At least one indication biopsy with acute rejection or borderline changes	20/75 (26.7%)	16/55 (29.1%)	0.8434

SUPPLEMENTAL TABLE 2. Histological characteristics (% prevalence) of the renal allograft protocol biopsies at implantation and at 6,12 and 24 months after transplantation. Already in the first 2 years after transplantation, there was an increase in interstitial fibrosis and tubular atrophy, which was present in almost 50% of biopsies performed at 1 year after transplantation. In addition, there was a significant increase in the prevalence and extent of vascular intimal thickening by time after transplantation, mainly in the first 3 months after transplantation. The prevalence of tubular microcalcifications increased only in the first 3 months after transplantation. Also the prevalence of ischemic glomerular changes, glomerulosclerosis, lymphoid aggregates, CD20 positive infiltration and inflammation in atrophic areas increased in the first 2 years after transplantation. There was no significant increase in arteriolar hyalinosis, C4d deposition or transplant glomerulopathy. P-values were obtained using Cochran-Mantel-Haenszel statistics (non-zero correlation). *The subclinical rejection evolution P-value was calculated with exclusion of implantation biopsies.

		Implantation	6 months	12 months	24 months	P-value
	N	112	100	81	75	
Subclinical T-cell mediated rejection	Absent	-	80 (80%)	71 (78%)	68 (91%)	0.015*
	Borderline	-	9 (9%)	8 (9.9%)	5 (6.7%)	
	Acute	-	11 (11%)	2 (2.5%)	2 (2.7%)	
Subclinical antibody-mediated rejection	Absent	-	85/86 (99%)	75/75 (100%)	72/72 (100%)	0.31
	Present	-	1/86 (1.2%)	0/75 (0%)	0/72 (0%)	
Interstitial fibrosis (Banff "ci" score)	0-5%	110 (98%)	66 (66%)	40 (49%)	33 (44%)	<0.0001
	6-25%	2 (1.8%)	25 (25%)	29 (36%)	23 (31%)	
	26-50%	0 (0%)	6 (6%)	7 (8.6%)	10 (13%)	
	>50%	0 (0%)	3 (3%)	5 (6.2%)	9 (12%)	
Tubular atrophy (Banff "ct" score)	0%	90 (80.4%)	32 (32%)	18 (22%)	23 (31%)	<0.0001
	1-25%	22 (20%)	61 (61%)	52 (64%)	34 (45%)	
	26-50%	0 (0%)	4 (4%)	7 (8.6%)	8 (11%)	

	>50%	0 (0%)	3 (3%)	4 (4.9%)	10 (13%)	
Banff "IFTA" grade	grade 0	110 (98%)	67 (67%)	40 (49%)	33 (44%)	<0.0001
	grade 1	2 (1.8%)	26 (26%)	30 (37%)	24 (32%)	
	grade 2	0 (0%)	4 (4%)	7 (8.6%)	9 (12%)	
	grade 3	0 (0%)	3 (3%)	4 (4.9%)	9 (12%)	
Percentage globally sclerosed glomeruli	Absent	83/112 (74%)	75/96 (78%)	55/78 (71%)	39/74 (53%)	<0.0001
	1-25%	29/112 (26%)	21/96 (22%)	20/78 (26%)	25/74 (34%)	
	> 25%	0/112 (0%)	0/96 (0%)	3/78 (3.9%)	10/74 (24%)	
Vascular intimal thickening (Banff "cv" score)	Absent	108 (96%)	77 (77%)	66 (81%)	59 (79%)	0.0098
	Present with <25% luminal narrowing	4 (3.6%)	14 (14%)	10 (12%)	13 (17%)	
	Present with 25-50% luminal narrowing	0 (0%)	7 (7%)	4 (4.9%)	3 (4%)	
	Present with >50% luminal narrowing	0 (0%)	2 (2%)	1 (1.2%)	0 (0%)	
Mesangial matrix increase (Banff "mm" score)	Absent	112 (100%)	99 (99%)	81 (100%)	71 (95%)	0.0098
	Present	0 (0%)	1 (1%)	0 (0%)	4 (5.3%)	
Tubular microcalcifications	Absent	110 (98%)	85 (85%)	65 (80%)	59 (79%)	<0.0001
	Present	2 (1.8%)	15 (15%)	16 (20%)	16 (21%)	
Peripheral arteriolar hyalinosis (Banff "ah" score)	Absent	107 (96%)	92 (92%)	75 (93%)	70 (93%)	0.39
	Present	4 (3.6%)	8 (8%)	6 (7.4%)	5 (6.7%)	

Ischemic glomerular changes	Absent	100 (89%)	78 (78%)	43 (53%)	30 (40%)	<0.0001
	Present	12 (11%)	22 (22%)	38 (47%)	45 (60%)	
Diffuse C4d deposition in peritubular capillaries (>50%)	Absent	104/104 (100%)	85/86 (99%)	75/75 (100%)	72/72 (100%)	0.82
	Present	0 (0%)	1/86 (1%)	0/75 (0%)	0/73 (0%)	
Glomerulitis (Banff "g" score)	Absent	112 (100%)	1 (1.0%)	1 (1.2%)	3 (4.0%)	0.0217
	Present	0 (0%)	99 (99%)	80 (98.8%)	72 (96%)	
Peritubular capillaritis	Absent	112 (100%)	95 (95%)	83 (100%)	68 (91%)	0.008
	Present	0 (0%)	5 (5%)	0 (0%)	7 (9.3%)	
Transplant glomerulopathy (Banff "cg" score)	Absent	112 (100%)	99 (99%)	80 (99%)	73 (97%)	0.09
	Present	0 (0%)	1 (1%)	1 (1.2%)	2 (2.7%)	
CD20 positive infiltrates	Absent	99/99 (100%)	75/83 (90%)	65/75 (87%)	53/72 (74%)	<0.0001
	Present	0 (0%)	8/83 (9.6%)	10/75 (13%)	19/72 (26%)	
Inflammation in atrophic areas	0	108 (96%)	58 (58%)	32 (40%)	28 (37.3%)	<0.0001
	1	4 (3.6%)	32 (32%)	32 (40%)	22 (29%)	
	2	0 (0%)	6 (6%)	10 (13%)	8 (11%)	
	3	0 (0%)	4 (4%)	7 (8.8%)	17 (23%)	
Lymphoid aggregates	Absent	112 (100%)	74 (74%)	51 (63%)	44 (59%)	<0.0001
	Present	0 (0%)	26 (26%)	30 (37%)	31 (41%)	

CADI score	0-1	96 (86%)	45 (45%)	30 (37%)	26 (35%)	<0.0001
	2-4	16 (14%)	43 (43%)	40 (49%)	31 (41%)	
	5-7	0 (0%)	12 (12%)	11 (14%)	13 (17%)	
	>7	0 (0%)	0 (0%)	0 (0%)	5 (6.7%)	
cCNIT score	0-1	98 (88%)	53 (53%)	33 (41%)	29 (39%)	<0.0001
	2-4	14 (13%)	39 (39%)	40 (49%)	28 (37%)	
	5-7	0 (0%)	8 (8%)	8 (9.9%)	16 (21%)	
	>7	0 (0%)	0 (0%)	0 (0%)	2 (2.7%)	

SUPPLEMENTAL TABLE 3

*Analyses were performed using the GENMOD procedure with generalized-estimating-equations (GEE).

		Determinants of higher grade of interstitial fibrosis/tubular atrophy*			
		Univariate odds ratio	Univariate p-value	Multivariate p-value after backward elimination	Multivariate adjusted odds ratio after backward elimination
Treatment group					
	Steroid-based	1			
	Steroid-free	1.14 (0.71-1.83)	0.5967		
Recipient sex					
	Female	1			
	Male	1.44 (0.88-2.38)	0.1499		
Donor sex					
	Female	1			
	Male	0.99 (0.61-1.60)	0.9667		
Recipient age					
	< 5 years	2.30 (1.44-3.69)	0.0005		
	5 - 12 years	1.44 (0.80-2.59)	0.2183		
	> 12 years	1			
Donor source					
	Living	1			
	Deceased	0.73 (0.45-1.18)	0.1999		
Recipient size					
	BSA < 0.75 m²	3.42 (1.77-6.64)	0.0003	4.52 (2.02-10.1)	0.0002
	BSA 0.75 - 1.5 m²	1.99 (1.02-3.89)	0.0436	2.22 (0.99-4.95)	0.0516

	BSA > 1.5 m²	1		1	
Time after transplantation					
	Implantation	1		1	
	6 months	26.7 (6.4-111)	<0.0001	29.1 (6.89-123)	<0.0001
	12 months	54.0 (12.5-233)	<0.0001	60.0 (13.6-264)	<0.0001
	24 months	78.5 (19.1-323)	<0.0001	87.5 (21.0-364)	<0.0001
Prior acute rejection episode					
	No	1			
	Prior AR	2.25 (1.24-4.11)	0.0079		
Pristine kidney at implantation					
	Yes	1			
	No	1.21 (0.75-1.95)	0.4296		
Donor age					
	< 25 years	1			
	25 - 35 years	1.50 (0.87-2.60)	0.1464		
	> 35 years	1.63 (0.90-2.96)	0.1061		

*Analyses were performed using the GENMOD procedure with generalized-estimating-equations (GEE).

		Determinants of higher grade of cCNIT score*			
		Univariate odds ratio	Univariate p-value	Multivariate p-value after backward elimination	Multivariate adjusted odds ratio after backward elimination
Treatment group					
	Steroid-based	1			
	Steroid-free	1.11 (0.70-1.75)	0.6571		
Recipient sex					
	Female	1			
	Male	1.23 (0.78-1.94)	0.3686		
Donor sex					
	Female	1			
	Male	0.83 (0.53-1.31)	0.4308		
Recipient age					
	< 5 years	2.06 (1.35-3.15)	0.0008		
	5 - 12 years	1.28 (0.71-2.28)	0.4097		
	> 12 years	1			
Donor source					
	Living	1			
	Deceased	0.59 (0.38-0.92)	0.0203		
Recipient size					
	BSA < 0.75 m²	2.59 (1.45-4.63)	0.0014	3.82 (1.86-7.81)	0.0002
	BSA 0.75 - 1.5 m²	1.57 (0.88-2.82)	0.1262	2.01 (1.00-4.02)	0.0485
	BSA > 1.5 m²	1		1	
Time after transplantation					
	Implantation	1		1	
	6 months	5.28 (2.84-9.82)	<0.0001	5.86 (3.09-11.1)	<0.0001

	12 months	9.48 (4.69-19.2)	<0.0001	10.7 (5.14-22.3)	<0.0001
	24 months	14.1 (7.12-27.9)	<0.0001	16.5 (8.17-33.4)	<0.0001
Prior acute rejection episode					
	No	1			
	Prior AR	1.83 (1.04-3.23)	0.0364		
Pristine kidney at implantation					
	Yes	1			
	No	1.61 (1.02-2.54)	0.0423		
Donor age					
	< 25 years	1		1	
	25 - 35 years	1.87 (1.09-3.20)	0.0232	2.24 (1.17-4.28)	0.0149
	> 35 years	2.46 (1.41-4.27)	0.0014	3.41 (1.81-6.40)	0.0001

*Analyses were performed using the GENMOD procedure with generalized-estimating-equations (GEE).

		Determinants of vascular intimal thickening*			
		Univariate odds ratio	Univariate p-value	Multivariate p-value after backward elimination	Multivariate adjusted odds ratio after backward elimination
Treatment group					
	Steroid-based	1			
	Steroid-free	0.70 (0.38-1.28)	0.2405		
Recipient sex					
	Female	1			
	Male	1.37 (0.69-2.71)	0.3622		
Donor sex					
	Female	1			
	Male	1.36 (0.75-2.47)	0.3134		
Recipient age					
	< 5 years	2.28 (1.16-4.52)	0.0176		
	5 - 12 years	0.90 (0.40-2.01)	0.7961		
	> 12 years	1			
Donor source					
	Living	1			
	Deceased	0.40 (0.22-0.75)	0.0044		
Recipient size					
	BSA < 0.75 m²	2.04 (0.89-4.68)	0.0939		
	BSA 0.75 - 1.5 m²	0.90 (0.42-1.94)	0.7903		
	BSA > 1.5 m²	1			
Time after transplantation					
	Implantation	1		1	
	6 months	8.06 (2.74-23.8)	0.0002	8.33 (2.76-25.2)	0.0002

	12 months	6.14 (2.03-18.6)	0.0013	6.26 (2.03-19.3)	0.0014
	24 months	7.32 (2.44-22.0)	0.0004	7.41 (2.41-22.8)	0.0005
Prior acute rejection episode					
	No	1			
	Prior AR	2.97 (1.54-5.74)	0.0012		
Pristine kidney at implantation					
	Yes	1			
	No	2.77 (1.52-5.08)	0.0009		
Donor age					
	< 25 years	1		1	
	25 - 35 years	2.44 (1.06-5.63)	0.0367	2.50 (1.05-5.93)	0.0383
	> 35 years	3.07 (1.27-7.41)	0.0125	3.18 (1.27-7.99)	0.0136

*Analyses were performed using the GENMOD procedure with generalized-estimating-equations (GEE).

		Determinants of arteriolar hyalinosis*			
		Univariate odds ratio	Univariate p-value	Multivariate p-value after backward elimination	Multivariate adjusted odds ratio after backward elimination
Treatment group					
	Steroid-based	1			
	Steroid-free	1.94 (0.82-4.61)	0.1326		
Recipient sex					
	Female	1			
	Male	0.61 (0.25-1.46)	0.2652		
Donor sex					
	Female	1			
	Male	1.75 (0.71-4.31)	0.2258		
Recipient age					
	< 5 years	1.19 (0.41-3.45)	0.7423		
	5 - 12 years	0.42 (0.12-1.44)	0.1668		
	> 12 years	1			
Donor source					
	Living	1			
	Deceased	0.44 (0.18-1.07)	0.07		
Recipient size					
	BSA < 0.75 m²	0.76 (0.21-2.80)	0.683		
	BSA 0.75 - 1.5 m²	1.08 (0.41-2.81)	0.8795		
	BSA > 1.5 m²	1			
Time after transplantation					
	Implantation	1		1	
	6 months	2.33 (0.73-7.38)	0.1521	2.47 (0.74-8.20)	0.1409

	12 months	2.14 (0.56-8.16)	0.2651	2.18 (0.54-8.80)	0.2737
	24 months	1.91 (0.56-6.47)	0.2979	1.84 (0.51-6.68)	0.3552
Prior acute rejection episode					
	No	1			
	Prior AR	1.60 (0.46-5.60)	0.4622		
Pristine kidney at implantation					
	Yes	1			
	No	1.66 (0.70-3.95)	0.2501		
Donor age					
	< 25 years	1		1	
	25 - 35 years	1.59 (0.37-6.87)	0.5356	1.58 (0.36-6.87)	0.5415
	> 35 years	7.94 (2.32-27.1)	0.0009	8.04 (2.33-27.7)	0.001

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		Determinants of ischemic glomeruli*			
		Univariate odds ratio	Univariate p-value	Multivariate p-value after backward elimination	Multivariate adjusted odds ratio after backward elimination
Treatment group					
	Steroid-based	1			
	Steroid-free	1.22 (0.77-1.93)	0.3994		
Recipient sex					
	Female	1			
	Male	1.50 (0.95-2.36)	0.0792		
Donor sex					
	Female	1			
	Male	0.98 (0.62-1.55)	0.9302		
Recipient age					
	< 5 years	1.87 (1.13-3.09)	0.0147		
	5 - 12 years	1.29 (0.75-2.20)	0.3528		
	> 12 years	1			
Donor source					
	Living	1			
	Deceased	0.59 (0.37-0.93)	0.0245		
Recipient size					
	BSA < 0.75 m²	2.17 (1.15-4.08)	0.0168	2.87 (1.34-6.13)	0.0066
	BSA 0.75 - 1.5 m²	1.41 (0.76-2.60)	0.2793	1.65 (0.79-3.45)	0.1851
	BSA > 1.5 m²	1		1	
Time after transplantation					
	Implantation	1		1	
	6 months	2.35 (1.14-4.86)	0.0212	2.25 (1.05-4.82)	0.0377

	12 months	7.36 (3.64-14.9)	<0.0001	7.25 (3.45-15.3)	<0.0001
	24 months	12.5 (5.77-27.1)	<0.0001	13.2 (5.86-29.5)	<0.0001
Prior acute rejection episode					
	No	1			
	Prior AR	1.95 (1.07-3.54)	0.0283		
Pristine kidney at implantation					
	Yes	1		1	
	No	1.82 (1.16-2.88)	0.0099	1.87 (1.09-3.21)	0.0229
Donor age					
	< 25 years	1			
	25 - 35 years	1.37 (0.81-2.31)	0.2408		
	> 35 years	1.93 (1.08-3.46)	0.0274		

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		Determinants of tubular microcalcifications*			
		Univariate odds ratio	Univariate p-value	Multivariate p-value after backward elimination	Multivariate adjusted odds ratio after backward elimination
Treatment group					
	Steroid-based	1			
	Steroid-free	0.98 (0.49-1.96)	0.9495		
Recipient sex					
	Female	1			
	Male	0.82 (0.41-1.65)	0.5818		
Donor sex					
	Female	1			
	Male	1.45 (0.71-2.97)	0.305		
Recipient age					
	< 5 years	1.85 (0.81-4.19)	0.1426		
	5 - 12 years	1.08 (0.47-2.46)	0.8543		
	> 12 years	1			
Donor source					
	Living	1			
	Deceased	1.93 (0.91-4.11)	0.0876		
Recipient size					
	BSA < 0.75 m²	2.32 (0.79-6.82)	0.1262		
	BSA 0.75 - 1.5 m²	1.49 (0.58-3.78)	0.4049		
	BSA > 1.5 m²	1			
Time after transplantation					
	Implantation	1		1	
	6 months	9.71 (2.32-40.7)	0.0019	8.65 (1.96-38.1)	0.0043

	12 months	13.5 (2.96-61.9)	0.0008	13.1 (2.65-64.8)	0.0016
	24 months	14.9 (3.23-68.8)	0.0005	13.0 (2.67-63.6)	0.0015
Prior acute rejection episode					
	No	1		1	
	Prior AR	3.85 (1.63-9.11)	0.0021	3.28 (1.42-7.60)	0.0054
Pristine kidney at implantation					
	Yes	1			
	No	0.50 (0.26-0.99)	0.0452	0.34 (0.16-0.75)	0.0076
Donor age					
	< 25 years	1			
	25 - 35 years	0.97 (0.46-2.06)	0.9467		
	> 35 years	0.36 (0.15-0.87)	0.0237		

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		Determinants of higher glomerulosclerosis group*			
		Univariate odds ratio	Univariate p-value	Multivariate p-value after backward elimination	Multivariate adjusted odds ratio after backward elimination
Treatment group					
	Steroid-based	1			
	Steroid-free	0.86 (0.51-1.46)	0.5829		
Recipient sex					
	Female	1			
	Male	0.96 (0.57-1.60)	0.8659		
Donor sex					
	Female	1			
	Male	0.74 (0.45-1.22)	0.239		
Recipient age					
	< 5 years	1.75 (1.00-3.09)	0.0516		
	5 - 12 years	1.52 (0.80-2.88)	0.1967		
	> 12 years	1			
Donor source					
	Living	1			
	Deceased	0.51 (0.30-0.85)	0.0097		
Recipient size					
	BSA < 0.75 m²	1.55 (0.76-3.18)	0.2294		
	BSA 0.75 - 1.5 m²	1.30 (0.66-2.54)	0.4467		
	BSA > 1.5 m²	1			
Time after transplantation					
	Implantation	1		1	
	6 months	0.81 (0.43-1.52)	0.5078	0.68 (0.34-1.40)	0.3009

	12 months	1.25 (0.68-2.30)	0.472	1.15 (0.58-2.28)	0.6829
	24 months	3.03 (1.68-5.46)	0.0002	3.30 (1.77-6.18)	0.0002
Prior acute rejection episode					
	No	1			
	Prior AR	1.07 (0.54-2.13)	0.8403		
Pristine kidney at implantation					
	Yes	1		1	
	No	3.35 (2.03-5.56)	<0.0001	3.24 (1.88-5.57)	<0.0001
Donor age					
	< 25 years	1		1	
	25 - 35 years	2.50 (1.32-4.73)	0.005	2.52 (1.32-4.81)	0.0052
	> 35 years	3.21 (1.65-6.24)	0.0006	2.51 (1.23-5.12)	0.011

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		Determinants of higher CADI score*			
		Univariate odds ratio	Univariate p-value	Multivariate p-value after backward elimination	Multivariate adjusted odds ratio after backward elimination
Treatment group					
	Steroid-based	1			
	Steroid-free	0.93 (0.58-1.49)	0.7677		
Recipient sex					
	Female	1			
	Male	1.28 (0.78-2.10)	0.3218		
Donor sex					
	Female	1			
	Male	0.94 (0.59-1.49)	0.7812		
Recipient age					
	< 5 years	2.65 (1.70-4.12)	<0.0001		
	5 - 12 years	1.15 (0.63-2.08)	0.6505		
	> 12 years	1			
Donor source					
	Living	1			
	Deceased	0.59 (0.37-0.94)	0.0269		
Recipient size					
	BSA < 0.75 m²	3.36 (1.93-5.85)	<0.0001	5.44 (2.91-10.1)	<0.0001
	BSA 0.75 - 1.5 m²	1.55 (0.91-2.65)	0.1102	2.07 (1.10-3.89)	0.0236
	BSA > 1.5 m²	1			
Time after transplantation					
	Implantation	1		1	
	6 months	7.43 (4.24-13.0)	<0.0001	7.53 (4.20-13.5)	<0.0001

	12 months	9.78 (5.14-18.6)	<0.0001	10.1 (5.01-20.5)	<0.0001
	24 months	13.9 (7.01-27.6)	<0.0001	14.4 (6.88-29.9)	<0.0001
Prior acute rejection episode					
	No	1		1	
	Prior AR	4.35 (2.68-7.08)	<0.0001	2.48 (1.39-4.41)	0.002
Pristine kidney at implantation					
	Yes	1			
	No	1.99 (1.24-3.20)	0.0046		
Donor age					
	< 25 years	1		1	
	25 - 35 years	1.60 (0.95-2.69)	0.075	1.63 (0.88-3.04)	0.1221
	> 35 years	2.15 (1.19-3.88)	0.0114	3.11 (1.62-5.97)	0.0007

*Analyses were performed using the GENMOD procedure with generalized-estimating-equations (GEE).