

Supplementary Figures

Figure S1

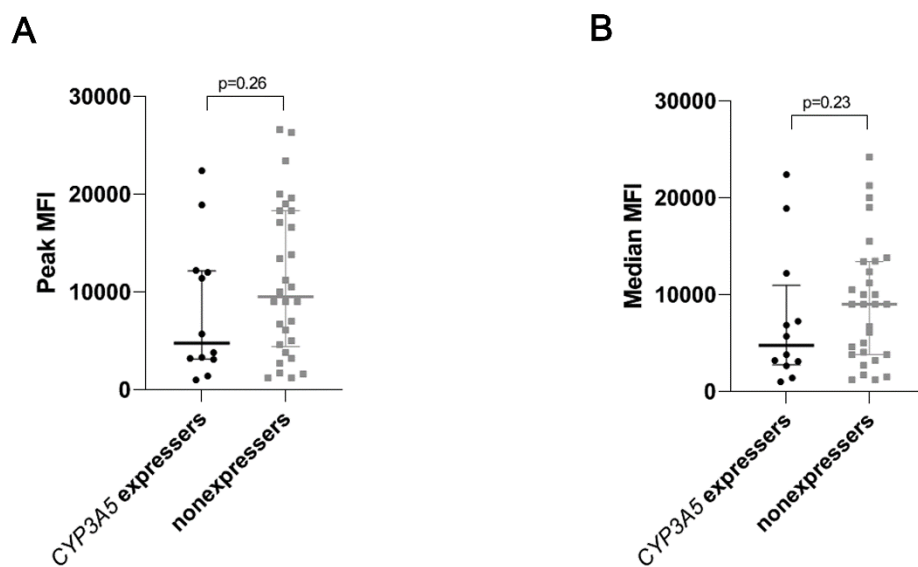
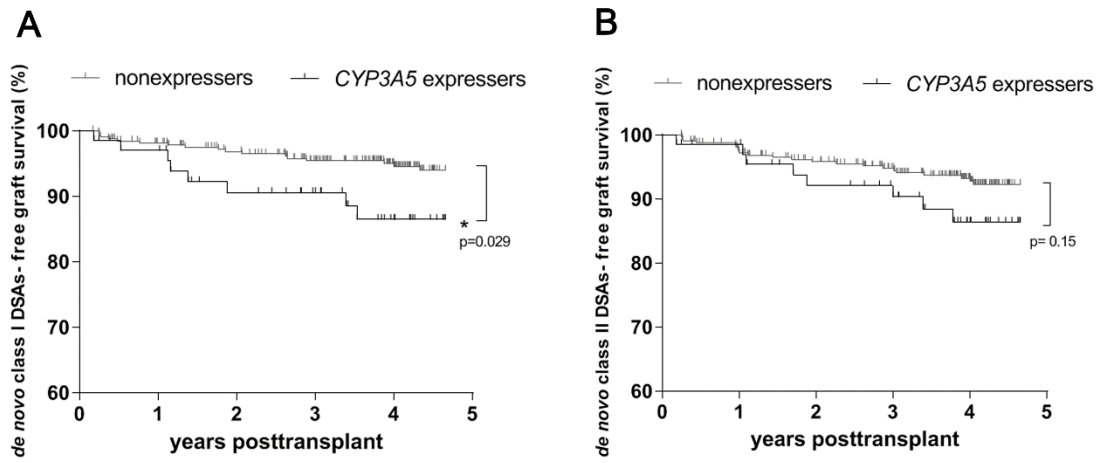


Figure S2



Supplementary Tables

Table S1. Anti-HLA antibody specification of 400 renal allograft recipients.

	All patients n=400
<i>de novo</i> anti-HLA antibodies, n (%)	107 (27)
Class I, n (%)	69 (17)
anti-HLA-A, n (%)	48 (12)
anti-HLA-B, n (%)	58 (15)
anti-HLA-C, n (%)	23 (6)
Class II, n (%)	68 (17)
anti-HLA-DQ, n (%)	32 (8)
anti-HLA-DR, n (%)	43 (11)
anti-HLA-DQA, n (%)	41 (10)
anti-HLA-DP, n (%)	5 (1)
<i>de novo</i> anti HLA DSAs, n (%)	46 (12)
Class I, n (%)	25 (6)
anti-HLA-A, n (%)	16 (4)
anti-HLA-B, n (%)	20 (5)
anti-HLA-C, n (%)	11 (3)
Class II, n (%)	30 (8)
anti-HLA-DQ, n (%)	21 (5)
anti-HLA-DR, n (%)	22 (6)
anti-HLA-DQA, n (%)	27 (7)
anti-HLA-DP, n (%)	2 (0,5)

Anti-HLA, anti-human leukocyte antigen; DSA, donor-specific antibody.

Table S2. Numbers of *CYP3A5* expressers and nonexpressers with tacrolimus trough levels below the target value at various time points during the three years after renal transplant.

	All patients	<i>CYP3A5</i> expressers	nonexpressers	χ^2 square	OR	p value
2 weeks after Tx, (tacrolimus target range 6-8 ng/ml)	75 (20)	21 (33)	54 (17)	0,08	2,33	0,002
1 month after Tx, (tacrolimus target range 6-8 ng/ml)	41 (11)	14 (22)	27 (9)	9,62	2,97	0,001
3 months after Tx, (tacrolimus target range 6-8 ng/ml)	83 (23)	13 (21)	70 (23)	0,33	0,88	0,36
6 months after Tx, (tacrolimus target range 5-7 ng/ml)	66 (19)	13 (22)	53 (18)	0,54	1,29	0,23
12 months after Tx, (tacrolimus target range 5-7 ng/ml)	87 (24)	15 (24)	72 (24)	0,01	1,03	0,46
24 months after Tx, (tacrolimus target range 5-7 ng/ml)	69 (21)	15 (28)	54 (20)	1,81	1,57	0,09
36 months after Tx, (tacrolimus target range 5-7 ng/ml)	69 (22)	10 (18)	59 (22)	0,19	0,85	0,33

OR, odds ratio; Tx, transplant.

Table S3. Results of univariate and multivariate analyses identifying risk factors for development of *de novo* anti-HLA antibodies among 400 patients after renal allograft transplant.

	<i>de novo</i> anti-HLAs-positive n=107	Patients without <i>de novo</i> anti-HLAs n=293	Univariate relative risk (95% CI)	p value	Multivariate relative risk (95% CI)	p value
Women, n (%)	45 (42)	120 (41)	1,03 (0,74-1,44)	0,84		
Previous transplants, n (%)	29 (27)	23 (8)	2,49 (1,79-3,34)	0,0001	2,67 (1,68-4,22)	0,0001
Preformed anti-HLA antibodies, n (%)	61 (57)	90 (31)	2,12 (1,58-3,03)	0,0001	1,86 (1,23-2,83)	0,003
Class I, n (%)	55 (51)	71 (24)	2,30 (1,68-3,15)	0,0001		
Class II, n (%)	36 (34)	35 (12)	2,35 (1,73-3,2)	0,0001		
Preformed anti-HLA DSAs, n (%)	24 (22)	13 (4)	2,84 (2,1-3,84)	0,0001	3,54 (2,17-5,78)	0,0001
MM (A/B), n (%)	90 (84)	242 (83)	1,08 (0,69-1,7)	0,72		
MM (DR), n (%)	75 (70)	211 (72)	0,93 (0,66-1,33)	0,71		
ABO-incompatible transplant, n (%)	9 (8)	22 (8)	1,09 (0,61-1,94)	0,77		
Autoimmune disease as cause of ESRD, n (%)	7 (7)	11 (4)	1,49 (0,81-2,72)	0,23		
<i>CYP3A5</i> variant, n (%)	24 (22)	45 (15)	1,39 (0,96-2,01)	0,1	1,88 (1,19-2,98)	0,007
Deceased donors, n (%)	76 (71)	209 (71)	0,99 (0,69-1,41)	0,95		
Number of female donors, n (%)	52 (49)	134 (46)	1,5 (0,79-1,5)	0,61		

Anti-HLA, anti-human leukocyte antigen; CI, confidence interval; DSA, donor-specific antibody; anti-HLA, anti-human leukocyte antigen; MM, mismatch.

Table S4. Results of multivariate Cox regression analysis for *de novo* class I and class II anti-HLA DSA-free and *de novo* class I and class II anti-HLA antibody-free survival.

Variables	<i>de novo</i> class I anti HLA DSAs		<i>de novo</i> class II anti HLA DSAs	
	Multivariate relative risk (95% CI)	p value	Multivariate relative risk (95% CI)	p value
Previous transplants	3,31 (1,19-9,18)	,022	2,82 (1,12-7,15)	,029
Preformed anti-HLA antibodies Class II	1,29 (0,42-3,98)	,661	1,41 (0,52-3,87)	,499
Preformed anti-HLA DSAs, n (%)	1,77 (0,57-5,46)	,323	0,81 (0,24-2,77)	,732
MM (A/B)	5,99 (0,79-45,38)	,083	3,55 (0,83-15,28)	,088
<i>CYP3A5</i> variant	2,93 (1,24-6,92)	,014	2,0 (0,88-4,55)	,096

Variables	<i>de novo</i> class I anti-HLA antibodies		<i>de novo</i> class II anti-HLA antibodies	
	Multivariate relative risk (95% CI)	p value	Multivariate relative risk (95% CI)	p value
Previous transplants	2,17 (1,23-3,84)	,007	3,62 (2,06-6,38)	,000
Preformed anti-HLA antibodies	2,03 (1,19-3,48)	,010	1,4 (0,81-2,43)	,230
Preformed anti-HLA DSAs	4,65 (2,64-8,2)	,000	1,97 (1,02-3,80)	,044
<i>CYP3A5</i> variant	2,23 (1,28-3,9)	,005	1,75 (0,98-3,14)	,058

Anti-HLA, anti-human leukocyte antigen; CI, confidence interval; DSA, donor-specific antibody; anti-HLA, anti-human leukocyte antigen; MM, mismatch.

Table S5. Results of Cox regression analysis for de novo DSA-free survival adjusted for tacrolimus trough levels at 1 month after transplant.

<i>de novo</i> anti HLA DSAs		
Variables	Multivariate relative risk (95% CI)	p value
Previous transplants	2,85 (1,28-6,34)	,011
Preformed class II anti-HLA antibodies	1,63 (0,7-3,82)	,257
Preformed anti-HLA DSAs, n (%)	1,22 (0,48-3,12)	,683
MM (A/B)	3,01 (0,9-10,07)	,073
<i>CYP3A5</i> variant	1,96 (0,93-4,13)	,075
Patients with tacrolimus trough levels below the target (6-8 ng/ml) 1 month after Tx	0,91 (0,78-1,06)	,227

Anti-HLA, anti-human leukocyte antigen; CI, confidence interval; DSA, donor-specific antibody; anti-HLA, anti-human leukocyte antigen; MM, mismatch.