**Supplemental Table S1. Histological lesions on the last kidney biopsy before graft loss, according to CYP3A5 genotype.**

| | *CYP3A*3/*3* (n=74) | *CYP3A*3/- (n=13) | p-value |
|---|---|---|---|
| Chronic ABMR | 8 (10.8%) | 1 (7.69%) | 1.000 |
| Acute ABMR | 11 (14.9%) | 1 (7.69%) | 0.684 |
| Acute TCMR | 16 (21.6%) | 1 (7.69%) | 0.449 |
| Chronic TCMR | 3 (4.05%) | 0 | 1.000 |
| Borderline rejection | 13 (17.6%) | 0 | 0.202 |
| Acute tubular necrosis | 29 (39.2%) | 6 (46,2%) | 0.868 |
| Pyelonephritis | 4 (5.41%) | 0 | 1.000 |
| Recurence of primary kidney disease | 4 (5.41%) | 2 (15.4%) | 0.218 |
| Tacrolimus chronic nephrotoxicity | 11 (14.9%) | 3 (23.1%) | 0.432 |
| BK virus nephropathy | 8 (10.8%) | 0 | 0.600 |
| Thrombotic microangiopathy | 10 (13.5%) | 5 (38.5%) | 0.043 |
| Donor specific lesions | 34 (45.9%) | 4 (30.8%) | 0.475 |
| *De novo* glomerulonephritis | 0 | 2 (15.4%) | 0.021 |

Abbreviations : ABMR = Antibody Mediated Rejection, TCMR = T cell Mediated Rejection

**Supplemental Table S2. Linear mixed model for Tacrolimus daily dose / body weight (mg/kg/day) according to CYP3A5 expression from 1 year post transplantation.**

|  | Association with Tac daily dose / body weight (baseline effect) | | | Association with Tac daily dose / body weight evolution (slope effect) | | |
|---|---|---|---|---|---|---|
|  | Coefficients | CI95% | p-value | Coefficients | CI95% | p-value |
| Referential value | 0.0656 | (0.0629; 0.0682) | < 0.01 | - 0.0027 | (- 0.0031; - 0.0025) | < 0.01 |
| *CYP3A5 \*1/-* (*versus CYP3A5 \*3/\*3*) | 0.0342 | (0.0280; 0.0404) | < 0.01 | - 0.0006 | (-0.0015; 0.0003) | 0.17 |

Time is expressed as a continuous variable in years.
The mean Tacrolimus daily dose / body weight (mg/kg/day) for the estimated model is calculated as: Tacrolimus daily dose / body weight = 0.0656 + 0.0342\*[*CYP3A5 \*1/-*] + (– 0.0027 – 0.0006\*[*CYP3A5 \*1/-*])\*time (in years) with 1 if *CYP3A5 \*1/-* and 0 otherwise.
Abbreviations: CI95% = Confidence Interval 95%; Tac = Tacrolimus

**Supplemental Table S3. Linear mixed model for Tacrolimus C0 over time according to *CYP3A5* genotype from 1 year post transplantation.**

|  | Association with Tacrolimus C0 (baseline effect) | | | Association with Tacrolimus C0 evolution (slope effect) | | |
|---|---|---|---|---|---|---|
|  | Coefficients | CI95% | p-value | Coefficients | CI95% | p-value |
| Referential value | 8.36 | (8.07; 8.65) | < 0.01 | -1.18 | (-1.32; -1.03) | < 0.01 |
| *CYP3A5 \*1/-* (*versus CYP3A5 \*3/\*3*) | -1.36 | (-2.03 ; -0.69) | < 0.01 | 0.13 | (-0.21 ; 0.48) | 0.46 |

Time is expressed as a continuous variable in years. Square root time is included to account for a changing effect on time. Thus, estimated Tacrolimus C0 evolution over time is for square root time unit. The mean Tacrolimus daily dose / body weight (mg/kg/day) for the estimated model is calculated as: Tacrolimus daily dose / body weight = 8.36 – 1.36\*[*CYP3A5 \*1/-*] + (– 1.18+0.13\*[*CYP3A5 \*1/-*])\*sqr (time) with 1 if *CYP3A5 \*1/-* and 0 otherwise.
Abbreviations: C0 = Tacrolimus blood through concentration, CI95% = Confidence Interval 95%; Tac = Tacrolimus

**Supplemental Table S4. Linear mixed model for C0 / Tacrolimus daily dose estimation over time according to CYP3A5 expression from 1 year post transplantation.**
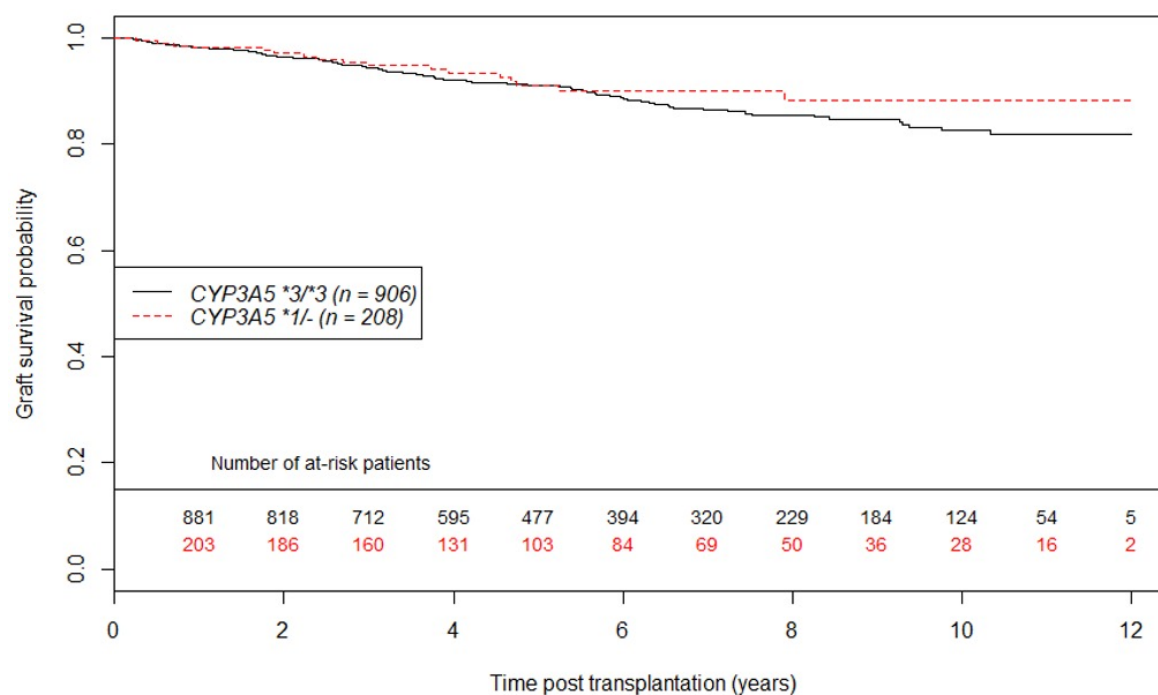
|  | Association with the C0 / daily dose (baseline effect) | | | Association with the C0 / daily dose evolution (slope effect) | | |
|---|---|---|---|---|---|---|
|  | Coefficients | CI95% | p-value | Coefficients | CI95% | p-value |
| Referential value | 2.00 | (1.90; 2.09) | < 0.01 | -0.01 | (-0.03; 0.01) | 0.22 |
| *CYP3A5 \*1/-* (*versus CYP3A5 \*3/\*3*) | - 1.01 | (- 1.23; - 0.78) | < 0.01 | 0.01 | (- 0.04; 0.05) | 0.81 |

Time is expressed as a continuous variable in years. The mean C0 / daily dose for the estimated model is calculated as: C0/daily dose(time) = 2.00 – 1.01\*[*CYP3A5 \*1/-*] + (-0.01 + 0.01\*[*CYP3A5 \*1/-*])\*time with 1 if *CYP3A5 \*1/-* and 0 otherwise. Abbreviations: C0 = Tacrolimus blood through concentration, CI95% = Confidence Interval 95%.

**Supplemental Table S5. Multivariate Cox model for death censored graft survival.**

| | HR | CI95% | p-value |
|---|---|---|---|
| *CYP3A5 *1/- (versus CYP3A5 *3/*3)* | 0.73 | [0.43; 1.23] | 0.23 |
| Recipient age (per 10 years) | 0.99 | [0.80; 1.21] | 0.89 |
| Donor age (per 10 years) | 1.14 | [0.94; 1.38] | 0.17 |
| Retransplantation (yes *versus* no) | 0.99 | [0.58; 1.67] | 0.96 |
| Time spent in dialysis (per 1 year) | 1.05 | [1.02; 1.08] | < 0.01 |
| Donor vital status | | | |
| -    Living donor | Ref. | | |
| -    Non cerebrovascular donor death | 3.62 | [0.80; 16.38] | 0.09 |
| -    Cerebrovascular donor death | 5.36 | [1.18; 24.23] | 0.03 |
| -    Donor after cardiac death | 12.56 | [2.50; 63.13] | < 0.01 |
| Cold ischemia time (per 10 hours) | 1.06 | [0.79; 1.44] | 0.68 |
| Occurrence of BPAR (yes *versus* no) | 4.18 | [2.81; 6.22] | < 0.01 |

Abbreviations: HR = Hazard Ratio, CI95% = Confidence interval 95%, BPAR = Biopsy Proven Acute Rejection. Occurrence of BPAR was a time dependent covariate. 22 observations were deleted due to missingness

**Supplemental Figure S1: Unadjusted curves of death censored graft survival using the Kaplan Meier estimator according to CYP3A5 genotype (n = 1114 patients).**