

Supplementary material**Suppl. Table 1.** Drug monitoring data of kidney recipients at one-year post-transplant

| Variables | TAC5/EVR (80) | TAC10/EVR (96) | TAC10/MPS (93) | p-Value |
|----------------------|------------------------------|-------------------------------|------------------------------|---------|
| Tacrolimus | | | | |
| Concentration, ng/mL | 4.5 [3.7 – 5.8] ^a | 4.7 [3.4 – 6.4] ^a | 5.8 [4.4 – 7.2] ^b | <0.0001 |
| Dose, mg/kg | 3.0 [2.0 – 4.0] ^a | 3.0 [2.0 – 6.0] ^{ab} | 4.0 [3.0 – 6.0] ^b | 0.007 |
| Co/D, ng/mL*mg | 1.53 [0.93 – 2.35] | 1.52 [1.00 – 2.34] | 1.37 [0.98 – 2.13] | 0.939 |
| Everolimus | | | | |
| Concentration, ng/mL | 6.2 [5.1 – 7.5] | 5.6 [4.6 – 6.8] | - | 0.073 |
| Dose, mg/kg | 4.0 [3.0 – 4.0] | 4.0 [3.0 – 4.1] | - | 0.857 |
| Co/D, ng/mL*mg | 1.80 [1.40 – 2.65] | 1.53 [1.15 – 2.40] | - | 0.177 |

Continuous variables are shown as median and interquartile range. Tacrolimus monitoring data were compared by Kruskal-Wallis test followed by Bonferroni's correction for multiple comparisons. Different superscript letters indicate significant differences. Everolimus monitoring data were compared by Mann-Whitney test. Co/Do, adjusted concentration for dose administered.

Suppl. Table 2. Association of gene polymorphisms with high serum creatinine in kidney recipients at one-year post-transplant: Univariable logistic regression analysis

| Polymorphism | Genotype | OR (95%CI) | p-Value |
|------------------------------|----------|--------------------|---------|
| <i>MTOR</i> c.1437T>C | CC | 1.74 (0.96 – 3.15) | 0.067 |
| | CT+TT | Reference | |
| <i>MTOR</i> c.2997C>T | TT | 1.30 (0.73 – 2.30) | 0.371 |
| | TC+CC | Reference | |
| <i>MTOR</i> c.4731G>A | AA | 0.90 (0.50 – 1.62) | 0.726 |
| | AG+GG | Reference | |
| <i>PPP3CA</i> c.249G>A | GG | 0.86 (0.46 – 1.62) | 0.646 |
| | GA+AA | Reference | |
| <i>FKBP1A</i> n.259+24936T>C | TT | 0.94 (0.60 – 1.49) | 0.807 |
| | TC+CC | Reference | |
| <i>FKBP2</i> c.-2110G>T | GG | 1.19 (0.73 – 1.94) | 0.475 |
| | GT+TT | Reference | |
| <i>FOXP3</i> c.-22-902A>G | GG | 1.41 (0.89 – 2.23) | 0.141 |
| | GA+AA | Reference | |
| <i>FOXP3</i> c.-23+2882A>C | CC | 1.75 (1.07 – 2.86) | 0.025 |
| | CA+AA | Reference | |

Analysis of *MTOR* polymorphisms was carried out with data from TAC5/EVR and TAC10/EVR groups. Serum creatinine was categorized in three groups (tertiles). The highest tertile (>1.50 mg/dL) was considered the risk group. OR: odds ratio; CI: Confidence interval.

Suppl. Table 3. Clinical variables associated with high serum creatinine in kidney recipients at one-year post-transplant: Univariable logistic regression analysis

| Independent variables | Risk factor | OR (95%CI) | p-Value |
|-----------------------------|--------------------|--------------------|---------|
| Model 1 | | | |
| Age | Per 1 year | 0.99 (0.97 – 1.01) | 0.530 |
| Weight | Per 1 kg | 1.03 (1.01 – 1.05) | 0.012 |
| Gender | Male | 3.47 (1.87 – 6.46) | 0.0001 |
| Donor type | Deceased | 0.85 (0.47 – 1.56) | 0.602 |
| Time on hemodialysis | Per 1 month | 1.00 (0.99 – 1.01) | 0.509 |
| Delayed graft function time | Per 1 day | 1.02 (0.98 – 1.06) | 0.407 |
| Cold ischemia time | Per 1 h | 0.99 (0.97 – 1.02) | 0.692 |
| Acute rejection | Presence | 3.21 (1.28 – 8.05) | 0.013 |
| Proteinuria | Presence | 1.98 (0.79 – 4.95) | 0.145 |
| CMV | Use of ganciclovir | 1.06 (0.35 – 3.22) | 0.921 |
| Model 2 | | | |
| Age | Per 1 year | 0.99 (0.97 – 1.00) | 0.121 |
| Weight | Per 1 kg | 1.03 (1.01 – 1.05) | 0.002 |
| Gender | Male | 4.00 (2.38 – 6.74) | 0.0001 |
| Donor type | Deceased | 0.81 (0.50 – 1.31) | 0.381 |
| Time on hemodialysis | Per 1 month | 1.00 (0.99 – 1.01) | 0.843 |
| Delayed graft function time | Per 1 day | 1.02 (0.99 – 1.06) | 0.206 |
| Cold ischemia time | Per 1 h | 0.99 (0.97 – 1.02) | 0.612 |
| Acute rejection | Presence | 3.41 (1.63 – 7.10) | 0.001 |
| Proteinuria | Presence | 1.88 (0.86 – 4.12) | 0.112 |
| Therapy group* | Presence | 1.61 (0.99 – 2.62) | 0.055 |
| CMV | Use of ganciclovir | 1.08 (0.58 – 1.99) | 0.808 |

*Model 1: TAC5/EVR and TAC10/EVR groups. Model 2: All therapy groups. Serum creatinine was categorized in three groups (tertiles). The highest tertile (>1.50 mg/dL) was considered the risk group. OR: odds ratio; CI: Confidence interval. *Reference: TAC/EVR therapy group.*

Suppl. Table 4. Variables associated with acute rejection in kidney recipients at one-year post-transplant:
Univariable regression analysis

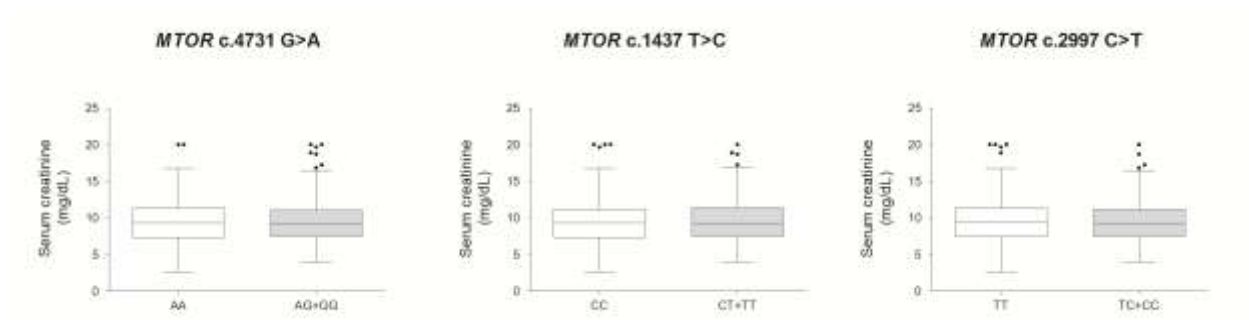
| Independent variables | Risk Factor | OR (95%CI) | p-Value |
|------------------------------|-------------|---------------------|---------|
| Polymorphisms | | | |
| <i>MTOR</i> c.1437T>C | Genotype | | |
| | CC | Reference | |
| | CT+TT | 1.25 (0.51 – 3.09) | 0.609 |
| <i>MTOR</i> c.2997C>T | TT | Reference | |
| | TC+CC | 1.07 (0.45 – 2.55) | 0.859 |
| <i>MTOR</i> c.4731G>A | AA | Reference | |
| | AG+GG | 3.37 (1.10 – 10.30) | 0.037 |
| <i>PPP3CA</i> c.249G>A | GG | Reference | |
| | GA+AA | 0.82 (0.30 – 2.24) | 0.681 |
| <i>FKBP1A</i> n.259+24936T>C | TT | Reference | |
| | TC+CC | 0.95 (0.48 – 1.86) | 0.904 |
| <i>FKBP2</i> c.-2110G>T | GG | Reference | |
| | GT+TT | 1.39 (0.66 – 2.93) | 0.382 |
| <i>FOPX3</i> c.-22-902A>G | GG | Reference | |
| | GA+AA | 1.14 (0.58 – 2.23) | 0.735 |
| <i>FOXP3</i> c.-23+2882A>C | CC | Reference | |
| | CA+AA | 0.88 (0.43 – 1.80) | 0.725 |
| Other variables | | | |
| Model 1 | | | |
| Age | Per 1 year | 0.98 (0.95 – 1.01) | 0.139 |
| Weight | Per 1 kilo | 1.03 (0.99 – 1.06) | 0.074 |
| Donor type | Deceased | 0.74 (0.33 – 1.67) | 0.466 |
| Time on hemodialysis | Per 1 month | 1.00 (0.99 – 1.02) | 0.485 |
| Delayed graft function time | Per 1 day | 1.06 (1.03 – 1.10) | 0.001 |
| Cold ischemia time | Per 1 hour | 1.00 (0.96 – 1.04) | 0.880 |
| Model 2 | | | |
| Age | Per 1 year | 0.98 (0.95 – 1.00) | 0.077 |
| Weight | Per 1 kilo | 1.01 (0.98 – 1.03) | 0.485 |
| Donor type | Deceased | 0.91 (0.45 – 1.88) | 0.807 |
| Time on hemodialysis | Per 1 month | 1.00 (0.99 – 1.01) | 0.932 |
| Delayed graft function time | Per 1 day | 1.11 (1.06 – 1.16) | 0.0001 |
| Cold ischemia time | Per 1 hour | 1.01 (0.97 – 1.04) | 0.712 |

Analysis for *MTOR* polymorphisms was carried out with data from TAC5/EVR and TAC10/EVR groups. Other gene polymorphisms and other variables were analyzed using data from all therapy groups. Model 1: TAC5/EVR and TAC10/EVR groups. Model 2: All therapy groups. OR: odds ratio; CI: Confidence interval.

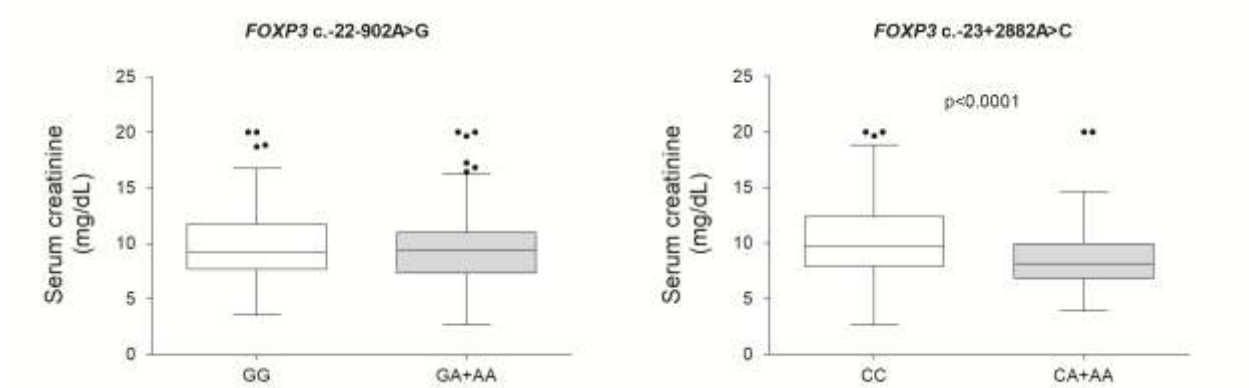
Suppl. Table 5. Variables associated with secondary clinical outcomes in kidney recipients at one-year post-transplant: Univariable logistic regression

| Independent variables | Risk factor | OR (95%CI) | p-Value |
|-------------------------------|--------------------|---------------------|---------|
| Leukopenia | | | |
| <i>FKBP2</i> c.-2110G>T | GG genotype | 3.87 (1.26 – 11.91) | 0.018 |
| Age | Per every 1 year | 1.03 (0.99 – 1.07) | 0.122 |
| Weight | Per every 1 kg | 0.97 (0.93 – 1.01) | 0.113 |
| Gender | Male | 0.92 (0.30 – 2.82) | 0.878 |
| Therapy group* | TAC+MPS | 3.66 (1.19 – 11.28) | 0.024 |
| CMV | Use of ganciclovir | 9.68 (3.08 – 30.38) | 0.0001 |
| Constipation | | | |
| <i>FKBP1A</i> n.259+24936T>C | TC+CC genotype | 2.40 (1.08 – 5.37) | 0.033 |
| Age | Per every 1 year | 1.01 (0.99 – 1.04) | 0.425 |
| Weight | Per every 1 kg | 1.00 (0.97 – 1.03) | 0.986 |
| Gender | Male | 2.15 (0.90 – 5.14) | 0.087 |
| Therapy group* | TAC+MPS | 1.59 (0.77 – 3.30) | 0.213 |
| Epigastric pain | | | |
| <i>FOXP3</i> c.-22-902A>G | GA+AA genotype | 2.15 (1.01 – 4.56) | 0.047 |
| Age | Per every 1 year | 1.01 (0.98 – 1.04) | 0.428 |
| Weight | Per every 1 kg | 1.01 (0.98 – 1.04) | 0.468 |
| Gender | Male | 0.83 (0.38 – 1.83) | 0.648 |
| Therapy group* | TAC+MPS | 1.69 (0.81 – 3.53) | 0.164 |
| Nausea and/or vomiting | | | |
| <i>FOXP3</i> c.-23+2882A>C | CA+AA genotype | 2.38 (1.05 – 5.38) | 0.038 |
| Age | Per every 1 year | 1.03 (1.00 – 1.06) | 0.038 |
| Weight | Per every 1 kg | 1.01 (0.98 – 1.04) | 0.587 |
| Gender | Male | 2.12 (0.94 – 4.78) | 0.071 |
| Therapy group* | TAC+MPS | 1.00 (0.43 – 2.35) | 0.996 |

*Reference: TAC+EVR therapy group. OR: odds ratio; CI: confidence interval; CMV: cytomegalovirus.



SUPPL. FIGURE 1. Influence of *MTOR* polymorphisms on pre-transplant serum creatinine levels in kidney recipients. Data are shown as box plots and interquartile range and compared by Mann-Whitney test. P>0.05.



SUPPL. FIGURE 2. Influence of *FOXP3* polymorphisms on pre-transplant serum creatinine levels in kidney recipients. Data are shown as box plots and interquartile range and compared by Mann-Whitney test.