

Table S1. a) Univariate and b) multivariate associations of Banff biopsy scores and c) Banff biopsy scores and donor-derived cell-free DNA on eGFR over time excluding ABO-incompatible recipients and recipients with BK nephropathy (n=169).

a)

| <b>Predictor</b>                               | <b>Coefficient<br/>(ml/min/1.73 m<sup>2</sup>/month; 95% CI)</b> | <b>p<br/>value</b> |
|------------------------------------------------|------------------------------------------------------------------|--------------------|
| <b>Recipient characteristics</b>               |                                                                  |                    |
| <b>Age at dd-cfDNA assessment (continuous)</b> |                                                                  |                    |
| Coefficient: $\Delta$ eGFR/month               | -0.8 (-1.8 to 0.2) <sup>a</sup>                                  | 0.11               |
| Age x months interaction                       | 0.01 (-0.006 to 0.03) <sup>b</sup>                               | 0.17               |
| <b>Gender (male vs. female)</b>                |                                                                  |                    |
| Reference (female): $\Delta$ eGFR/month        | -0.3 (-0.7 to 0.2) <sup>a</sup>                                  | 0.22               |
| Gender x months interaction                    | 0.2 (-0.3 to 0.8) <sup>b</sup>                                   | 0.42               |
| <b>Donor type (deceased vs. living donor)</b>  |                                                                  |                    |
| Reference (living donor): $\Delta$ eGFR/month  | -0.2 (-0.7 to 0.3) <sup>a</sup>                                  | 0.37               |
| Donor type x months interaction                | 0.1 (-0.5 to 0.7) <sup>b</sup>                                   | 0.66               |
| <b>Presence of DSA (yes vs. no)</b>            |                                                                  |                    |
| Reference (no DSA): $\Delta$ eGFR/month        | -0.04 (-0.4 to 0.3) <sup>a</sup>                                 | 0.84               |
| DSA x months interaction                       | -0.3 (-0.8 to 0.3) <sup>b</sup>                                  | 0.38               |
|                                                |                                                                  |                    |
| <b>Banff Scores</b>                            |                                                                  |                    |

|                                                     |                                   |      |
|-----------------------------------------------------|-----------------------------------|------|
| <b>cg=3 vs. cg&lt;3</b>                             |                                   |      |
| Reference (cg<3): $\Delta$ eGFR/month               | -0.05 (-0.3 to 0.2) <sup>a</sup>  | 0.74 |
| cg x months interaction                             | -1.3 (-2.4 to -0.2) <sup>b</sup>  | 0.02 |
| <b>ci+ct<math>\geq</math>3 vs. ci+ct&lt;3</b>       |                                   |      |
| Reference (ci+ct<3): $\Delta$ eGFR/month            | 0.02 (-0.3 to 0.3) <sup>a</sup>   | 0.89 |
| ci+ct x months interaction                          | -0.6 (-1.2 to -0.03) <sup>b</sup> | 0.06 |
| <b>g+ptc<math>\geq</math>2 vs. g+ptc&lt;2</b>       |                                   |      |
| Reference (g+ptc<2) $\Delta$ eGFR/month             | 0.01 (-0.3 to 0.4) <sup>a</sup>   | 0.96 |
| g+ptc x months interaction                          | -0.3 (-0.9 to 0.2) <sup>b</sup>   | 0.22 |
| <b>i+t<math>\geq</math>2 vs. i+t&lt;2</b>           |                                   |      |
| Reference (i+t<2): $\Delta$ eGFR/month              | 0.05 (-0.3 to 0.4) <sup>a</sup>   | 0.77 |
| i+t x months interaction                            | -0.4 (-1.0 to 0.1) <sup>b</sup>   | 0.13 |
| <b>i-IFTA=3 vs. i-IFTA&lt;3</b>                     |                                   |      |
| Reference (i-IFTA<3): $\Delta$ eGFR/month           | -0.01 (-0.3 to 0.3) <sup>a</sup>  | 0.96 |
| i-IFTA x months interaction                         | -0.4 (-1.0 to 0.2) <sup>b</sup>   | 0.20 |
| <b>v<math>\geq</math>1 vs. v&lt;1</b>               |                                   |      |
| Reference (v<1): $\Delta$ eGFR/month                | -0.1 (-0.4 to 0.2) <sup>a</sup>   | 0.48 |
| v x months interaction                              | -0.4 (-1.5 to 0.6) <sup>b</sup>   | 0.42 |
|                                                     |                                   |      |
| <b>Donor-derived cell-free DNA percentage</b>       |                                   |      |
| <b>dd-cfDNA (Quartiles 3-4 vs. 1-2)<sup>c</sup></b> |                                   |      |
| Reference (quartiles 1-2): $\Delta$ eGFR/month      | 0.1 (-0.3 to 0.5) <sup>a</sup>    | 0.63 |
| dd-cfDNA x months interaction                       | -0.4 (-1.0 to 0.1) <sup>b</sup>   | 0.12 |

<sup>a</sup>Reference coefficient ( $\Delta$  eGFR/month)

<sup>b</sup>Interaction terms are interpreted as the difference in eGFR slope between the reference and comparator groups.  $\Delta$  eGFR/month for the comparator group equals the sum of the coefficients for the reference group and the interaction.

<sup>c</sup>dd-cfDNA range: Quartiles 1-2: 0.15%-0.71%; Quartiles 3-4: 0.72%-12%

b)

| <b>Predictor</b>                                               | <b>Coefficient<br/>(95% CI)</b> | <b>p<br/>value</b> |
|----------------------------------------------------------------|---------------------------------|--------------------|
| $\Delta$ eGFR/month (ml/min/1.73 m <sup>2</sup> /month)        | 0.1 (-0.2 to 0.4)               | 0.57               |
| <b>Banff Scores</b>                                            |                                 |                    |
| cg=3 vs. cg<3 (ml/min/1.73 m <sup>2</sup> )                    | -9.2 (-22.2 to 3.9)             | 0.17               |
| cg x months interaction (ml/min/1.73 m <sup>2</sup> /month)    | -1.2 (-2.3 to -0.2)             | 0.03               |
| ci+ct $\geq$ 3 vs. ci+ct<3 (ml/min/1.73 m <sup>2</sup> )       | -10.2 (-17.3 to -3.1)           | 0.005              |
| ci+ct x months interaction (ml/min/1.73 m <sup>2</sup> /month) | -0.5 (-1.1 to 0.1)              | 0.08               |

c)

| <b>Predictor</b>                                                                             | <b>Coefficient<br/>(95% CI)</b> | <b>p<br/>value</b> |
|----------------------------------------------------------------------------------------------|---------------------------------|--------------------|
| $\Delta$ eGFR/month (ml/min/1.73 m <sup>2</sup> /month)                                      | 0.3 (-0.1 to 0.7)               | 0.17               |
| <b>Banff Scores</b>                                                                          |                                 |                    |
| cg=3 vs. cg<3 (ml/min/1.73 m <sup>2</sup> )                                                  | -15.0 (-27.7 to -2.3)           | 0.02               |
| cg x months interaction (ml/min/1.73 m <sup>2</sup> /month)                                  | -1.1 (-2.2 to -0.01)            | 0.05               |
| ci+ct $\geq$ 3 vs. ci+ct<3 (ml/min/1.73 m <sup>2</sup> )                                     | -7.7 (-14.5 to -0.8)            | 0.03               |
| ci+ct x months interaction (ml/min/1.73 m <sup>2</sup> /month)                               | -0.6 (-1.2 to 0.01)             | 0.05               |
| <b>Donor-derived cell-free DNA percentage</b>                                                |                                 |                    |
| Quartiles 3-4 vs. 1-2* (ml/min/1.73 m <sup>2</sup> )                                         | 13.2 (7.2 to 19.3)              | <0.001             |
| dd-cfDNA (quartiles 3-4 vs. 1-2) x months interaction<br>(ml/min/1.73 m <sup>2</sup> /month) | -0.4 (-0.9 to 0.2)              | 0.16               |

\* dd-cfDNA range: Quartiles 1-2: 0.15%-0.71%; Quartiles 3-4: 0.72%-12%

Table S2. Comparison of model fit between nested models excluding ABO-incompatible recipients and recipients with BK nephropathy (n=169). A lower AIC and BIC indicates better model fit.

|                       | Likelihood-ratio test           |    |         | AIC   | BIC   |
|-----------------------|---------------------------------|----|---------|-------|-------|
|                       | Likelihood Ratio Test Statistic | df | p-value |       |       |
| Model 1 (table S1b)*  | 18.5                            | 2  | <0.001  | 17640 | 17698 |
| Model 2 (table S1c)** |                                 |    |         | 17625 | 17695 |

\* Model 1:  $eGFR = \alpha + \beta_1(cg^{\dagger}) + \beta_2(months) + \beta_3(cg^{\dagger} \times months) + \beta_4(ci+ct^{\ddagger}) + \beta_5[(ci+ct^{\ddagger}) \times (months)]$

\*\* Model 2:  $eGFR = \alpha + \beta_1(cg^{\dagger}) + \beta_2(months) + \beta_3(cg^{\dagger} \times months) + \beta_4(ci+ct^{\ddagger}) + \beta_5[(ci+ct^{\ddagger}) \times (months)] + \beta_6(dd-cfDNA) + \beta_7(dd-cfDNA \times months)$

<sup>†</sup>  $cg=3$  vs.  $cg<3$

<sup>‡</sup>  $ci+ct \geq 3$  vs.  $ci+ct < 3$