

Improved Kidney Allograft Function after Early Conversion of Fast IR-Tac Metabolizers to LCP-Tac

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Table S1. Immunosuppression.

| | fast metabolizers n=58 | slow metabolizers n=22 | p-value |
|--|---------------------------|---------------------------|---------------------|
| prednisolone dose after 1 month | 17.5 (5 - 25) | 15 (5 - 50) | 0.680 ^a |
| mycophenolate after 1 month | | | |
| mycophenolate mofetil, n (%) | 30 (51.7%) | 13 (59.1%) | 0.621 ^b |
| mycophenolate sodium, n (%) | 28 (48.3%) | 9 (40.9%) | |
| mycophenolate mofetil dose (mg) | 1000 (500 - 2000) | 1000 (500 - 2000) | 0.932 ^a |
| mycophenolate sodium dose (mg) | 1440 (720 - 1440) | 1080 (720 - 1440) | 0.213 ^a |
| Tac doses (mg) | | | |
| IR-Tac M1 | 12 (5 - 20) | 7 (4 - 12) | <0.001 ^a |
| before switch (IR-Tac) | 10.25 (3 - 18) | 6.75 (1.5 - 17) | <0.001 ^a |
| D10 LCP-T | 7 (1.5 - 14) | 3.5 (1.8 - 11) | <0.001 ^a |
| M1 LCP-T | 6 (1.5 - 13.5) | 3 (1.5 - 11) | <0.001 ^a |
| M3 LCP-T | 4.75 (1.5 - 12) | 3 (1 - 8) | 0.002 ^a |
| M6 LCP-T | 4 (1.5 - 12) | 2.5 (0.75 - 5) | 0.001 ^a |
| M9 LCP-T | 4 (1.5 - 11) | 2.5 (1 - 6) | 0.001 ^a |
| M12 LCP-T | 3.63 (1.5 - 11) | 2.25 (1 - 5) | 0.001 ^a |
| M24 LCP-T | 3.38 (1 - 9) | 2.13 (0.75 - 5.5) | 0.008 ^a |
| M36 LCP-T | 3 (1 - 8.5) | 2 (0.75 - 3.5) | 0.016 ^a |
| Tac trough levels (ng/mL) | | | |
| IR-Tac M1 | 6.8 (2.4 - 15.9) | 8.7 (6.8 - 13.5) | <0.001 ^a |
| before switch (IR-Tac) | 6.3 (2.4 - 12.3) | 7.5 (3.9 - 13.5) | 0.065 ^a |
| D10 LCP-T | 7.2 (1.6 - 14.7) | 6.3 (4.1 - 9.9) | 0.026 ^a |
| M1 LCP-T | 7.6 (1.5 - 19.5) | 6.2 (3.7 - 12.9) | 0.041 ^a |
| M3 LCP-T | 7.3 (3.8 - 18.1) | 6.7 (4.9 - 9.9) | 0.311 ^a |
| M6 LCP-T | 7.0 (2.7 - 11.4) | 6.2 (4.0 - 10.4) | 0.043 ^a |
| M9 LCP-T | 6.5 (3.4 - 10.7) | 6.3 (4.2 - 9.2) | 0.992 ^a |
| M12 LCP-T | 6.2 (3.5 - 10.3) | 6.05 (3.8 - 8.3) | 0.224 ^a |
| M24 LCP-T | 6.2 (4.0 - 10.7) | 6.2 (2.1 - 9.4) | 0.254 ^a |
| M36 LCP-T | 5.5 (4.1 - 8.9) | 5.40 (4.0 - 8.7) | 0.698 ^a |
| Tac C/D ratio (ng/mL·1/mg) | | | |
| IR-Tac M1 | 0.64 (0.24 - 1.01) | 1.25 (1.08 - 3.38) | <0.001 ^a |
| before switch (IR-Tac) | 0.66 (0.24 - 2.10) | 1.15 (0.32 - 3.60) | 0.001 ^a |
| D10 LCP-T | 1.08 (0.33 - 4.90) | 1.91 (0.40 - 4.06) | 0.002 ^a |
| M1 LCP-T | 1.24 (0.21 - 6.93) | 2.23 (0.55 - 3.47) | 0.010 ^a |
| M3 LCP-T | 1.52 (0.55 - 4.93) | 2.33 (0.94 - 6.60) | 0.004 ^a |
| M6 LCP-T | 1.58 (0.39 - 5.93) | 2.65 (1.06 - 7.07) | 0.007 ^a |

| | | | |
|------------|--------------------|--------------------|---------------------|
| M9 LCP-T | 1.63 (0.40 - 5.07) | 3.23 (1.23 - 6.30) | <0.001 ^a |
| M12 LCPT-T | 1.74 (0.42 - 5.43) | 2.75 (1.08 - 5.90) | 0.007 ^a |
| M24 LCP-T | 1.81 (0.64 - 5.40) | 2.58 (0.96 - 6.27) | 0.083 ^a |
| M36 LCP-T | 1.85 (0.69 - 5.80) | 2.65 (1.32 - 5.73) | 0.026 ^a |

Data presented as median (25% quantile-75% quantile), or absolute and relative frequencies.
Abbreviations: Tac, tacrolimus; C/D, concentration to dose; two-sided p-values from ^a Mann-Whitney U test or ^b Fisher's exact test.

Table S2. Model-based estimates of eGFR.

| | | Estimate | Lower 95% confidence limit | Upper 95% confidence limit | p-value |
|---|-------------------------------|----------|----------------------------|----------------------------|---------|
| Difference of metabolism group fast vs slow combined over all time points | | 3.55 | -4.50 | -11.60 | 0.382 |
| Effect of time combined over both metabolism groups | | | | | 0.003 |
| Interaction term of metabolism groups*time points | | | | | 0.146 |
| Least square mean differences between fast and slow metabolizer by time points (combination of main and interaction effects of tacrolimus metabolism group and time points) | | | | | |
| Before switch | fast vs slow | -0.72 | -9.20 | 7.76 | 0.866 |
| at D10 | fast vs slow | 3.43 | -6.02 | 12.88 | 0.473 |
| at M1 | fast vs slow | 5.27 | -3.38 | 13.92 | 0.229 |
| at M3 | fast vs slow | 5.28 | -2.71 | 13.27 | 0.192 |
| at M6 | fast vs slow | 4.82 | -3.24 | 12.87 | 0.237 |
| at M9 | fast vs slow | 3.98 | -4.10 | 12.06 | 0.330 |
| at M12 | fast vs slow | 3.91 | -4.51 | 12.33 | 0.358 |
| at M24 | fast vs slow | 2.51 | -7.29 | 12.31 | 0.611 |
| at M36 | fast vs slow | 3.51 | -5.91 | 12.94 | 0.460 |
| Least square means of the mean change between the time points (Δ) by metabolism group (combination of main and interaction effects of tacrolimus metabolism group and time points) | | | | | |
| fast metabolizers | Δ D10 vs before switch | 4.23 | 2.11 | 6.34 | <0.001 |
| | Δ M1 vs before switch | 6.98 | 4.84 | 9.11 | <0.001 |
| | Δ M3 vs before switch | 6.69 | 4.32 | 9.05 | <.0001 |
| | Δ M6 vs before switch | 7.62 | 5.05 | 10.19 | <.0001 |
| | Δ M9 vs before switch | 7.38 | 4.82 | 9.94 | <.0001 |
| | Δ M12 vs before switch | 6.05 | 3.24 | 8.87 | <.0001 |
| | Δ M24 vs before switch | 6.52 | 3.17 | 9.88 | <0.001 |
| | Δ M36 vs before switch | 6.60 | 2.67 | 10.55 | 0.001 |

| | | | | | |
|-------------------|-------------------------------|------|-------|------|-------|
| slow metabolizers | Δ D10 vs before switch | 0.08 | -2.85 | 3.01 | 0.966 |
| | Δ M1 vs before switch | 0.97 | -1.94 | 3.92 | 0.505 |
| | Δ M3 vs before switch | 0.69 | -4.18 | 5.55 | 0.780 |
| | Δ M6 vs before switch | 2.08 | -2.40 | 6.56 | 0.358 |
| | Δ M9 vs before switch | 2.68 | -2.32 | 7.88 | 0.290 |
| | Δ M12 vs before switch | 1.42 | -4.51 | 7.36 | 0.635 |
| | Δ M24 vs before switch | 3.29 | -3.08 | 9.66 | 0.307 |

Least square mean differences in the change between time points (Δ) compared between metabolism groups (combination of main and interaction effects of tacrolimus metabolism group and time points)

| | | | | | |
|-------------------------------|--------------|-------|-------|------|-------|
| Δ D10 vs before switch | fast vs slow | 4.15 | 0.54 | 7.76 | 0.025 |
| Δ M1 vs D10 | fast vs slow | 1.84 | -1.39 | 5.07 | 0.259 |
| Δ M3 vs M1 | fast vs slow | 0.01 | -3.95 | 3.97 | 0.996 |
| Δ M6 vs M3 | fast vs slow | -0.46 | -3.76 | 2.84 | 0.781 |
| Δ M9 vs M6 | fast vs slow | -0.84 | -3.49 | 1.81 | 0.531 |
| Δ M12 vs M9 | fast vs slow | -0.07 | -2.72 | 2.58 | 0.959 |
| Δ M24 vs M12 | fast vs slow | 1.40 | -5.34 | 2.54 | 0.482 |
| Δ M36 vs M24 | fast vs slow | 1.00 | -2.72 | 4.73 | 0.593 |

Results of the linear mixed model. Selected parameter estimates and least square means for estimated glomerular filtration rate (eGFR) (mL/min/1.73m²) are shown. Main effects of metabolism groups and time points and the interaction term were included as influencing factors. P-values are from Wald tests. Repeated measurements for each patient were modelled using SAS PROC MIXED by fitting a marginal linear mixed model with an unstructured variance-covariance matrix for the residuals with patient as subject and the order given by time. The empirical sandwich covariance estimator was applied. D10, day 10 after switch; M1-M36, month 1 – month 36 after switch.