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Multiple regression analysis of factors associated with neutropenia in steroid-free adult renal transplant recipients taking tacrolimus and mycophenolate in three different study periods during the first year post-transplant

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PURPOSE: Frequent occurrence of neutropenia during the first year after engraftment is evident in renal transplant recipients while on mycophenolate (MPA) and tacrolimus (TAC). The purpose of this clinical study was to test the hypothesis that overexposure of MPA/TAC and/or inadequate renal function recovery may be potential causes of neutropenia in steroid-free kidney transplant patients.

METHODS: Age, absolute neutrophil count (ANC), glomerular filtration rate (GFR), MPA daily dose (g), TAC daily dose (mg), C1-C2-C4 MPA levels (mg/L), and C0-C2TAC levels (lg/L) were collected prospectively within 20–40 days (period 1), 4–7 months (period 2), and 11–13 months (period 3) post transplant (n=6–17). Validated limited sampling strategies (Ther Drug Monit; 33:50–55, 2011) were used to estimate MPA and TAC exposure. Simple and multiple linear regression analyses between dose-normalized MPA/TAC exposure, GFR, and ANC were conducted (SigmaStat, v3.5).

RESULTS: Mean characteristics (baseline age 56 years) across 3 study periods: ANC (3–5 9 103 cells/lL), MPA dose (1–2 g/D), TAC dose (5–9 mg/D), limited sampling strategy-predicted dose-normalized MPA exposures (22–36 mg 9 hour/L/g), and limited sampling strategy-predicted dose-normalized TAC exposures (22–29 lg 9 hour/L/mg). Multiple regression analysis incorporating MPA/TAC exposure, GFR, and ANC indicated that only MPA exposure predicted ANC ($p<0.05$) in period 1 (n=17), whereas trends toward significance were observed for periods 2 and 3 (n=6–12). Linear regression revealed inverse associations ($p<0.05$) between MPA exposure and ANC within all 3 periods ($R2=0.35$, 0.36, and 0.47) and across the 3 visits, but no such associations were observed for TAC exposure and GFR.

CONCLUSION: To our knowledge, this is the first study to examine associations between MPA/TAC exposure, renal function, and neutropenia in steroid-free kidney transplant recipients. Our novel findings suggest a significant association between MPA, but not TAC exposure or GFR, with ANC throughout all 3 study periods. Patient enrollment is currently ongoing.