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COVID-19 Vaccination Response in Kidney Transplant Recipients With and Without Mycophenolate Mofetil: Follow-up of a Randomized Controlled Trial



To the Editor: Antimetabolite therapy is considered a risk factor for poor response to COVID-19 vaccination.^{1,2} We have performed a randomized controlled trial in immunologically low-risk kidney transplant recipients comparing tacrolimus (TAC) and mycophenolate mofetil (MMF) to TAC monotherapy (TACmono) (EudraCT nr.: 2014-001372-66).

Antibody-based immune responses to COVID-19 vaccination (mRNA-1273 or BNT162b2) were investigated as part of the RECOVAC study (EudraCT nr.: 2021-001520-18). Four to eight weeks after the second vaccination we measured IgG antibodies using the Sanquin anti-SARS-CoV-2 receptor binding domain IgG enzyme-linked immunosorbent assay.³ Patients were classified as nonresponders (≤ 50 binding antibody unit [BAU/ml]), low responders (50–300 BAU/ml), and responders (>300 BAU/ml) for wild-type SARS-CoV-2.⁴

Between 2015 and 2018, 79 recipients were randomized to TAC/MMF ($n = 41$) or TACmono ($n = 38$), 6 months post-transplantation, after discontinuing steroids. At the outbreak of the COVID-19 pandemic in early 2020, 67 patients were alive with a functioning graft. Antibody response could be established in 27 patients: 10 were excluded from the analyses because of symptomatic COVID-19 infection and 1 because of a positive nucleocapsid test result, possibly from an asymptomatic infection. The rest was excluded because of ChAdOx1-S, age >80 years, or lack of informed consent.

In the 27 included patients without prior COVID-19 infection (13 TAC/MMF, 14 TACmono), antibody

SARS-CoV-2 serological vaccination response

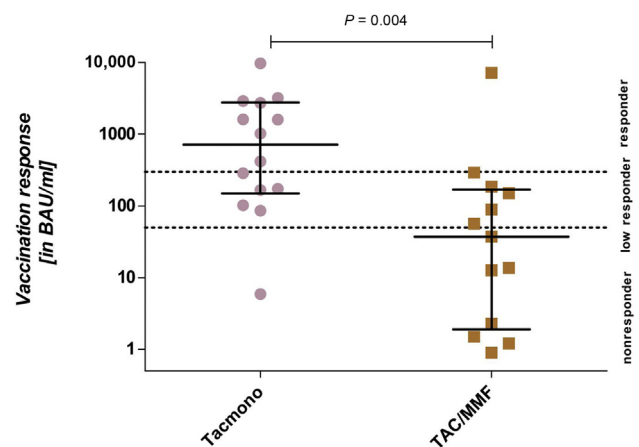


Figure 1. SARS-CoV-2 serologic vaccination response in TACmono versus TAC/MMF 4 to 8 weeks after vaccination. BAU, binding antibody unit; TACmono, tacrolimus monotherapy; TAC/MMF, tacrolimus and mycophenolate mofetil therapy.

responses were measured after mRNA-1273 ($n = 25$) or BNT162b2 ($n = 2$) vaccination. With mean age 64 (43–75) years, median time after transplantation 4.2 (3.0–6.5) years, estimated glomerular filtration rate 53 (36–105) ml/min per 1.73 m², TAC trough levels 6.6 (± 0.3) $\mu\text{g/l}$ in both groups, and MMF dose 1000 mg daily (range 500–2000) in TAC/MMF (Supplementary Table S1). Median SARS-CoV-2 spike S1-specific IgG antibody levels were 37.3 BAU/ml in TAC/MMF (5 non, 7 low, 1 responder) and 715.6 BAU/ml in TACmono (1 non, 6 low, 7 responders, $P = 0.004$; Figure 1). Antibody levels of >1000 BAU/ml, as a presumed threshold for protection against Omicron (B.1.1.529), were reached in 1 of 13 TAC/MMF and 7 of 14 TACmono patients ($P = 0.03$).

In this controlled study, MMF on top of TAC severely hampered serologic response to SARS-CoV-2 vaccination.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Baseline characteristics of recipients before receiving SARS-CoV-2 vaccination. #: normally distributed *: not normally distributed TACmono: tacrolimus monotherapy n: number BMI: body mass index eGFR: estimated glomerular filtration rate TAC:

Tacrolimus MMF: Mycophenolate mofetil IQR: Inter-quartile range.

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