MO186 **THIRD COVID-19 VACCINE DOSE MAXIMIZES ANTIBODY TITER IN KIDNEY TRANSPLANT RECIPIENTS**

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BACKGROUND AND AIMS: COVID-19 infection in solid organ transplant recipients (SOT) is associated with increased morbidity and mortality due to comorbidities and immunosuppression state (Chaudhry ZS et al, 2020). Although vaccines represent the greatest hope to control COVID-19 pandemic, several studies showed the low immunogenicity of a two-dose mRNA COVID-19 vaccine regimen in SOT as compared with general population (Boyarsky BJ et al, 2021). Based on this evidence, on September 2021, the Italian Medicine Agency (AIFA) authorized a third vaccine administration as additional primary dose to immunocompromised patients. The aim of this study is to evaluate the seroconversion rate after the third dose of BNT162b2 (Pfizer-BioNTech) SARS-CoV-2 mRNA vaccine in kidney transplant recipients (KTRs) and to investigate the baseline factors associated with the absence of the antibody response.

METHOD: we performed a prospective and observational study on a monocentric cohort of 329 consecutive Caucasian KTRs given three doses of the BNT162b2 COVID-19 vaccine. Key exclusion criteria were a previous history of COVID-19 infection and transplantation or having underwent chemotherapy treatment within the last year. Antibody response against the spike protein was tested on blood sample collected before the administration of vaccine (T_0), at 15 and 90 days after the second dose (T_2 and T_3, respectively) and one month after the third dose (T_5). The level of antibodies was assessed using the Roche Elecsys anti–SARS-CoV-2 S enzyme immunoassay (positive cut-off $\geq$ 0.8 U/mL). A total of 22 patients were excluded from the analysis because categorized as SARS-CoV-2-pre-immunized according to the antibodies' baseline status (T_0) above the positivity cut-off.

The Local Ethics Committees approved the study protocol and written informed consent was obtained before enrolment.

RESULTS: The study population of 307 KTRs was 57.10 $\pm$ 13.10 years, with a predominance of male sex (64.2%). Median time from transplantation to vaccine was 10 [IQR 5–17] years. Blood analysis at baseline revealed mean eGFR assessed by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to be 56.95 $\pm$ 23.04 mL/min/1.73 m^2.

The standard immunosuppressive regimen consisted of glucocorticoids in all patients, calcineurin inhibitors (88.6% of patients), antimetabolites (73.3% of patients) and mTOR inhibitors (in 15.6% of patients). The first two doses were administered 21 days apart, and the third dose was administrated 172 $\pm$ 4 days after the second dose.

In our cohort, 43.3% patients (133/307) responded to the vaccine at T_2. The proportion of responders increased to 68.4% (186/272) at T_3 (median antibody level: 5.2 [0.40–74.07]). One month after the third dose, a positive antibody titer was detected in 251 of 307 patients (81.8%) (median antibody titre: 1137.50 [9.32–4189.75]). The response curve starting at T_2 and increasing at T_3 makes apparent that there is a distinctive kinetic of humoral response in immunocompromised patients compared to immunocompetent individuals (Walsh EE *et al.*, 2020). A multivariate analysis showed that the negative response to the third primary dose was associated with antimetabolite immunosuppressants ($P = .001$), lower estimated glomerular filtration rate ($P < .001$) and female sex ($P = .04$) (Figure 1). No serious adverse events were reported. Neither *de novo* DSAs nor change in proteinuria were reported after vaccination.

The limitation of this study is the absence of assays for cellular immune response.

CONCLUSION: Although the exact threshold of antibody titer for protection against SARS-CoV-2 infection remains unclear, the ability of the additional mRNA COVID-19 vaccine dose to increase both immune response (Figure 2A) and the prevalence of seroconversion rate (Figure 2B) associated with the acceptable safety profile supports its use after an initial 2-dose mRNA COVID-19 primary vaccine series in immunocompromised patients.

	Anti-SARS-CoV2 positive patients	Anti-SARS-CoV2 negative patients	Univariate OR (95% IC)	p-value	Multivariate OR (95% IC)	p-value
Age	56.45 (±13.37)	60.05(±11.50)	0.978 (0.955-1.001)	0.06		
Sex Female (ref.) Male	 82 (74.5%) 169 (85.5%)	 28 (25.5%) 28 (14.2)	 2.061 (1.146-3.705)	**0.016**	1.941 (1.017-3.702)	**0.044**
BMI	25.40 (±3.71)	25.01 (±3.51)	1.030 (0.946-1.122)	0.496		
T2D (yes)	27 (73%)	10 (27%)	0.551 (0.247-1.228)	0.145		
eGFR (CKD-EPI)	59.03(±22.91)	47.00 (±21.21)	1.024 (1.008-1.041)	**0.004**	1.029 (1.013-1.046)	**<0.001**
Time from Tx (year) median, IQR	7 (4-12)	10 (5-18)	1.021 (0.990-1.052)	0.190		
Donor type -Living -DBD (ref.)	 25 (83.3%) 220 (81.8%)	 5 (16.7%) 49 (18.2%)	 1.114 (0.406-3.054)	0.834		
Immunosuppression maintenance therapy Includes antimetabolite[a] Does not include antimetabolite[b] (ref.)	 175 (77.8%) 71 (94.7%)	 50 (22.2%) 4 (5.3%)	 0.197 (0.069-0.566)	**0.003**	0.161 (0.055-0.477)	**0.001**

Abbreviations: T2D, type 2 diabetes; eGFR, estimated Glomerular Filtration Rate (Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation).
[a]Includes mycophenolate mofetil, mycophenolic acid, or azathioprine.
[b]Includes corticosteroids, tacrolimus, cyclosporine, sirolimus, everolimus.

FIGURE 1: Univariate and multivariate analysis of factors associated with vaccine response one month after third dose of SARS-CoV-2 mRNA vaccine.

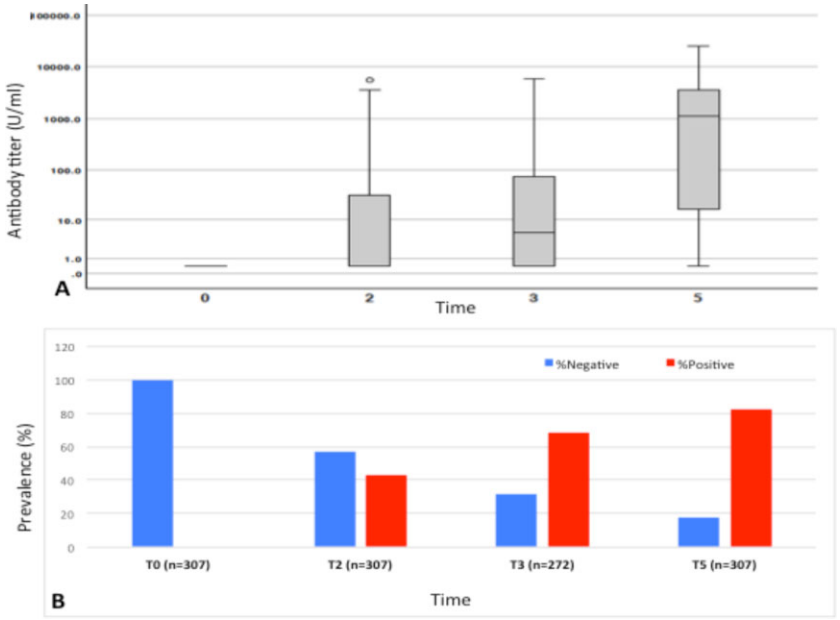

FIGURE 2: Antibody Response. Panel A shows the anti-SARS-CoV-2 antibody titers at different timepoints T0, T2, T3 and T5. Panel B shows prevalence of responders and noresponders at different timepoints T0, T2, T3 and T5.

MO187 **HEALTHCARE COSTS BASED ON RISK OF PROGRESSION IN PATIENTS WITH CHRONIC KIDNEY DISEASE**

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BACKGROUND AND AIMS: Nephrologists follow patients with chronic kidney disease (CKD) stage G3 and G4 as a homogeneous group with the assumption that everyone had similar rates of progression with scheduled visits and lab investigations based on the stage of the disease. We now recognize that not all patients progress at similar rates to kidney failure and treatment and follow-up needs vary. The Kidney Failure Risk Equation (KFRE) identifies patients at different risks of progression to kidney failure (low, medium and high risk) in each stage of the disease. Previous studies had looked at resource utilization of patients based on the stage of the CKD. The purpose of our analysis was to examine resource utilization and associated costs based on the risk of progression by KFRE in the setting of a universal healthcare system.

METHOD: We conducted a retrospective cohort study of adults with CKD G3 and G4 enrolled in multidisciplinary CKD clinics in the province of Saskatchewan, Canada. Data was collected from January 2004 through December 2012 and patients were followed for 5 years. The predicted risk of kidney failure for each patient was calculated using the 8-variable KFRE. The equation used clinical and routine laboratory data, to stratify patients into three risk categories (low, medium and high risk) of progression. We compared the number and cost of hospital admissions, physician visits and prescription drugs by risk within G3 and G4. Negative binomial regression and generalized linear model were used to compare healthcare utilization and cost between the groups respectively ($\alpha = 0.05$).

RESULTS: A total of 1003 adults with CKD G3 and G4 were included in the study. In patients with stage G3 CKD, 311 (59%), 150 (28%) and 68 (13%) were in low, medium and high-risk categories, respectively. Amongst patients with CKD stage G4, 275 (58%), 86 (18%) and 113 (24%) were in similar categories respectively. The cost of hospital admissions, physician visits and drug dispensations in stage G4 high risk in comparison to low risk over the 5-year study period was CAD $89 265 versus $48 374 ($P = .008$), $23 423 versus $11 231 ($P < .001$) and $21 853 versus $16 757 ($P = .01$), respectively. In stage G3, the cost of hospital admissions was CAD $55 944 versus $36 740 ($P = 0.10$), physician visits $13 414 versus $10 370 ($P = .08$) and prescription drugs $20 394 versus $14 902 ($P = .02$) in high-risk patients in comparison to low-risk patients (Figure 1).

CONCLUSION: In patients followed in multidisciplinary clinics with CKD stages G3 and G4, the cost of hospital admissions, physician visits and prescription drugs were higher in high-risk patients compared to patients in low-risk category. In our study, the KFRE, designed to predict the risk of progression to dialysis in patients with CKD, also assisted in identifying patients with higher health resource utilization and healthcare costs compared to those with lower health resource use. We additionally suggest that patients who are in medium and high-risk categories be followed in multidisciplinary clinics rather than individual physician offices to delay the trajectory of decline to kidney failure.