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Delayed Humoral Response After 2 Doses of the BNT162b2 Vaccine in a Belgian Kidney Transplant Cohort

Hélène Georgery, MD,^{1*} Arnaud Devresse, MD, PhD,^{1,2*} Imane Saad Albichr, PharmD,^{3*}

Sophie Lucas, PhD,⁴ Jean-Cyr Yombi, MD,^{2,5} Leila Belkhir, PhD,^{2,5} Julien De Greef, MD,^{2,5}

Anais Scohy, PharmD,³ Benoit Kabamba, MD,^{2,3} Eric Goffin, MD,^{1,2} Nada Kanaan, MD^{1,2}

¹ Department of Nephrology, Cliniques Universitaires Saint-Luc, Brussels, Belgium.

² Institut de Recherche Expérimentale et Clinique, Université Catholique de Louvain, Brussels, Belgium.

³ Department of Microbiology, Cliniques Universitaires Saint-Luc, Brussels, Belgium.

⁴ de Duve Institute, Université Catholique de Louvain, Brussels, Belgium

⁵ Department of Internal Medicine and Infectious Disease, Cliniques Universitaires Saint-Luc, Brussels, Belgium.

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All authors discussed and reviewed the manuscript.

*These authors contributed equally to this study.

Correspondence: Arnaud Devresse MD, PhD, Department of Nephrology, Cliniques Universitaires Saint-Luc, Brussels, Belgium. E-mail: arnaud.devresse@gmail.com

Abbreviations page:

Ab, antibody

KTRs, kidney transplant recipients

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We previously published disappointing results regarding the humoral response 28 days after the second dose of the BNT162b2 (Pfizer) vaccine in kidney transplant recipients (KTRs).¹ The present paper reports the serological response rate 90 days after the second injection using an immunoassay detecting antibody (Ab) against the spike protein receptor-binding domain (RBD) (Elecsys anti-SARS-CoV-2, Roche Diagnostics GmbH, Mannheim, Germany - positive threshold ≥ 0.8 U/mL-upper limit of detection 250 U/mL). This work received IRB approval.

Eighty-two patients were included. None had history of COVID-19 infection and all tested negative for anti-SARS-CoV-2 nucleocapsid Ab. The median age was 60 (range 18-84) years; 58 % were male. The median time since transplantation was 113 (range 8-439) months. Fifty percent were treated with an association of tacrolimus, mycophenolate and steroids.

The humoral response rates and mean anti-RBD Ab titers were 50 % vs 70.7 % ($p=0.010$) and 45.2 (95% CI 27.7-62.8) U/mL vs 66.3 (95% CI 45.9-86.7) U/mL ($p<0.001$), at day 28 and day 90, respectively (Figure 1A and B). Forty-six percent ($n=38$) of KTRs showed increased anti-RBD Ab titers at day 90 compared to day 28. These patients had similar baseline characteristics than KTRs whom Ab titers remained stable or decreased at day 90. Seventeen of 41 patients (41%) who had no humoral response at day 28 mounted a serological response at day 90. Overall, 24 patients (29%) did not have any serological response following vaccination. The characteristics of these patients did not differ from those who showed a serological response.

These results suggest that some KTRs show delayed kinetics of anti-RBD Ab after 2 doses of the mRNA BNT162b2 vaccine, contrasting with what has been observed in the general population in whom the peak of humoral immunity appears earlier.² Indeed, Shrotry et al demonstrated in a cohort of 552 SARS-CoV-2 naïve individuals an anti-spike Ab peak between 21-41 days after the second dose of the BNT162b2 or ChAdOx1 vaccine, followed

by a significant decrease.² We might hypothesize to explain the delayed humoral response in our population of KTRs, that immunosuppressive drugs decrease the activation and proliferation of CD4 T helper cells, leading to delayed interactions between T and B cells in lymph nodes.

Recent evidence emerged from the literature regarding the efficacy of a third dose of mRNA vaccine in KTRs.³⁻⁵ Notably, a recently published placebo-controlled randomized trial including 120 KTRs demonstrated that a booster third dose of the mRNA-1273 vaccine given 2 months after the second dose was associated with higher rates of seroconversion, anti-RBD Ab titers and virus neutralization 1 month after injection compared to placebo.⁵ Interestingly, in line with our findings, the authors found that a subgroup of patients who received placebo showed mild increases in Ab titers.⁵

Our study adds interesting findings pointing out that some KTRs might naturally develop a delayed humoral response after 2 doses of mRNA vaccine. Still, Ab titers reached 3 months after the second injection in our cohort remained weak, justifying a third dose vaccine injection to promote humoral response.

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Figure legend

Figure 1. Evolution of anti-RBD Ab response rate (A) and titers (B) between day 28 and day 90, after the second dose of vaccine. Statistic comparisons between humoral response rates (A) was performed using Fisher's exact test. Ab, antibody; RBD, receptor-binding domain.

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Figure 1

