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Poor Anti-SARS-CoV-2 Humoral and T-cell Responses After 2 Injections of mRNA Vaccine in Kidney Transplant Recipients Treated with Belatacept

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Abbreviations Page

EliSpot: enzyme-linked immunospot assay

IQR: interquartile range

KTRs: kidney transplant recipients

KT: kidney transplantation

mTOR: mammalian target of rapamycin

RBD: receptor binding domain

S: spike

SFU: spot forming unit

Data about COVID-19 vaccine in the general population provided an excellent profile of immunogenicity strong antibody response following the second dose of mRNA-1273 or BNT162b2 vaccines,[1] associated to a potent T-cell immune response.[2]

Kidney transplant recipients(KTRs) exhibit lower immunogenicity to vaccines. A recent study reported a poor immune response after the first dose of mRNA anti-SARS-CoV2 vaccine in KTRs treated with calcineurin-inhibitors.[3] In abatacept(CTLA4-Ig)-treated patients, vaccination against influenza/H1N1 was associated with poor antibody response.[4] This could be related to the inhibition of the crosstalk between B and T cells by the CTLA4, leading to impaired germinal center formation and improper antibody response.

We aimed to assess the humoral and T-cell postvaccinal responses in 101 belatacept-treated KTRs including 54 (53.5%) at Necker Hospital (Paris, France) and 47 (46.5%) at Rangueil Hospital (Toulouse, France).

We included 101 patients (68 men(67.3%), median age:64 years[53–73] treated with belatacept. Median time between KT and vaccination was 59 months, [29-104]. Belatacept was associated to mycophenolic acid(n=79, 78.2%), mammalian target of rapamycin (mTOR) inhibitors(n=12, 11.9%), tacrolimus(n=8, 7.9%), azathioprine(n=2, 2.0%), and steroids(n=97, 96.0%). No patient had a history of COVID-19 infection.

Two injections of 30-µg doses of BNT162b2 mRNA COVID-19 Vaccine(Pfizer-BioNTech) were administered intramuscularly 28 days apart. Vaccine and belatacept injections were performed the same day in Necker's patients and 15 days apart in Toulouse's patients. Anti-spike antibodies were assessed 28 and 60 days after the first vaccine dose using SARS-CoV-2 IgG II Quant antibody test (Abbott) in Necker and serum total SARS-CoV-2 antibodies ELISA kit (Beijing Wantai Biological Pharmacy Ent Co.,Ltd,China) in Toulouse according to the manufacturer's instructions. Both tests display a high specificity (>99%) and sensitivity (respectively 97% and 90% for WANTAI and Abbott tests).[5]

To analyze T cell responses, enzyme-linked immunospot assay (EliSpot) measuring interferon-γ produced by specific SARS-CoV-2 T-cells were performed, at days 28 and 60. Freshly isolated peripheral blood mononuclear cells were stimulated using individual 15-mers 11-aa overlapping peptide pools derived from a peptide scan through SARS-CoV-2 Spike glycoprotein (S1, S2) (JPT-Peptide-Technologies). Results were expressed as spot forming unit(SFU)/10^6 CD3+ T-cell. A positive response was defined by a S1 reactivity>20 spots.

Twenty-eight days after the first injection, 2/101 patients(2.0%) developed anti-spike antibodies. Among the 35/101 patients(34.7%) with serology testing 1 month after the second dose, 2 patients(5.7%) developed anti-spike antibodies (Figure 1A). The timing between vaccination and belatacept injection didn't impact the seroconversion rate.

A specific T-cell response for the SARS-CoV-2 S1 pool of peptides was observed in 2/40 patients(5.0%) on day 28, and in 7/23 patients(30.4%) 1 month after the second injection (Figure 1B).

This is the first study assessing humoral and T-cell vaccinal responses to mRNA anti-SARS-CoV2 vaccine in KTRs treated with belatacept. Seroconversion occurred in very few patients, and T-cell response in less than one-third of patients.

The seroconversion rate at day 28 (2%) was lower than the one recently reported in a cohort of KTRs given calcineurin-inhibitors (17%).[3] Hence, while waiting for new strategies to improve the immunogenicity of anti-SARS-CoV2 vaccine, such as the use of higher antigen doses or a third booster dose, or to test the efficacy of other approved vaccines, KTRs, especially those receiving belatacept should maintain enhanced barrier measures. Vaccination of household members could also confer an indirect protection to KTRs.

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Figure 1. Humoral and T-cell responses following anti-SARS-CoV2 mRNA vaccine in KTRs treated with belatacept. (A). Anti SARS-CoV-2 IgG on days 0, 28 and 60 after vaccine injection. 2.0% of patients had a positive IgG response on Day 28 and 5.7% on Day 60 after vaccine injection. (B). Specific anti-spike T-cell response occurred in 2/40 (5%) patients on Day 28 and in 7/23 (30.4%) patients on Day 60. (S: spike protein, SFU: spot forming unit)

Figure 1