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Anti-SARS-CoV-2 T-cell Responses After mRNA Vaccination in Belatacept Treated Renal Transplant Patients

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Dear Editor,

We read with interest the recent letter by Dr. Chavarot and colleagues on the humoral and T-cell responses after 2 injections of mRNA vaccine in kidney transplant recipients.[1] The authors reported a low sero-conversion rate at days 60 and a T-cell response in only 30.4% of the patients measured. Importantly, the T-cell response was measured by IFNγ-EliSpot after stimulation with overlapping peptide pools for SARS-CoV-2 spike protein. We would like to further discuss the determination of the T-cell response as it has important implications for the interpretation of the findings.

The safety and efficacy of mRNA vaccines has been demonstrated in numerous clinical studies and in most of these studies, vaccine-specific T-cell responses were reported.[2-4] In these studies, next to IFNγ EliSpot, T-cells were detected in addition by flow cytometry to characterize the cytokine profile. Sahin and colleagues found in a Phase I/II study that BNT161b1 elicited a strong Th1 response.[3] In most of the experimental groups, IL-2 producing T-cells dominated over IFNγ producing T-cells or even $IFN\gamma^{+}IL\text{-}2^{+}$ T-cells. A similar observation was made in a phase I/II trial on BNT162b2 as reported in preprint by Sahin and colleagues.[4] In a Phase I study on the mRNA-1273 vaccine, Anderson and colleagues demonstrated that vaccine-specific T-helper-cell responses measured on day 43 were of the Th1 type.[2] However, the IL-2 response by T-helper-cells was greater than the IFNγ response but lower than the TNFα response.[2] This effect was consistent over 2 different age groups ranging from 56-70 years of age and ≥71 years of age. Thus, vaccine-specific T-cell responses are not restricted to IFNγ producing Th1 cells.

We would like to point out that the lack of T-cell response reported by Dr. Chavarot and colleagues may not give a comprehensive information on the overall T-cell response to vaccination in renal transplant patients as an IFNγ EliSpot was the only read-out.[1] IL-2 or TNFα single positive T-helper-cells are not detected in this assay but usually evolve after vaccination in healthy persons. Thus, renal transplant patients may well harbor vaccine-specific T-cell immunity upon vaccination. Additionally, it remains unclear whether the impaired Th1-

response is a mainly belatacept dependent effect as suggested by the authors. From our point of view this is not exclusively related to the inhibition of costimulation but to the high grade immunosuppressive regimen after kidney transplantation.

In summary, the measurement of vaccine-specific T-cell responses is complex and a comprehensive characterization of vaccine-specific T-cell responses is necessary to draw conclusions on the immunogenicity of BNT162b2 in renal transplant patients. Nevertheless, the present study provides substantial evidence that vaccine responses in kidney transplant patients should be monitored and individualized vaccination strategies might be needed in this vulnerable cohort.

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