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LETTER TO THE EDITOR

COVID-19: impact of vaccination in myeloma patients

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Dear Editor,

The worldwide COVID-19 pandemic represents an unprecedented crisis that affects the entire medical community and appears to be a devastating infection in patients with hematological disorders, including myeloma (MM) [1–3]. Vaccination is therefore crucial in this population [4]. Seroconversion after COVID-19 has been shown to be lower in MM patients compared to the general population. The same is expected after vaccination, as different studies have already reported a lower antibody response after anti-SARS-CoV-2 vaccination in this group [5–8].

We investigated the impact of anti-SARS-CoV-2 vaccination in patients with MM or related disorders, excluding MGUS. Immunization was assessed after two shots of either a mRNA (Pfizer®/Moderna®) or a viral vector (Astra Zeneca®) vaccine, using the Elecsys® immunoassay performed on cobas®8000 (Roche Diagnostics®) that measures anti-SARS-CoV-2 antibodies including IgG.

From March 2020 to September 2021, we determined the serological status at day 30 (median 36, range 1–148), of the first 164 patients with plasma cell dyscrasias that completed vaccination. Among them, 114 were affected by MM, 26 by asymptomatic MM, 8 by MGRS, 16 by AL amyloidosis.

The characteristics of our cohort were as followed: median age of 69 (range 35–89), median IgG level of 700 mg/dL (range 80–1840), median CD4/CD8 levels of 530/µL (range 58–1668), and 398/µL (range 33–4556), respectively (Fig. 1).

One hundred fifty patients (92%) developed regular antibodies confirmed by the presence of the receptor-binding domain of the spike protein (RBD) antibodies, while 23 (14%) presented nucleocapsid protein (N) antibodies, suggesting a previous contact with the virus. Among these, 12 had a history of a positive RT-PCR nasopharyngeal swab and 11 were fortuitously found to be positive in the absence of any clinical manifestation (Fig. 1).

Thirteen patients failed to develop any immunization; all had received immunosuppressive therapies (renal transplantation in 1, long-term corticosteroids in 2, cyclophosphamide in 4, anti-CD20 monoclonal antibodies in 4, both in 2) or multiple lines of therapies in 1. We failed to identify any link with immunoparesis or CD4/CD8 levels. As well, there was no correlation between RBD antibody and CD4 levels. All patients tested after the third dose develop immunization except those exposed to anti-CD20 therapies in the previous 12 months. Only one patient underwent an interferon-gamma-release assay testing that was negative.

Nowadays, with an 8-month median follow up after vaccination, if only 5 patients experienced a mild form of COVID-19 during the Delta-variant wave, more patients ($n=12$) are tested positive with the emergence of the omicron variant, but there were no significant clinical manifestations, hospitalizations, or deaths.

In conclusion, SARS-CoV-2 vaccination provided an adequate coverage in our MM population during the delta wave since only five patients developed a mild infection after vaccination. Seroconversion was however clearly affected by the anti-MM treatment. With the appearance of the omicron variant, we observed an upsurge of cases, even of benign evolution, which questions this protection. Whether non-responding patients will eventually develop T cell protection against COVID-19 remains also to be answered, as well as the positivity cutoff that measures neutralizing antibodies, the optimal vaccination schedule, particularly in the context of immunodeficiency, and diverse anti-MM therapies.

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Fig. 1 Patients characteristics and results

Table 1. Population characteristics	
Age, median (years)	69 (35-89)
IgG, median (mg/dL)	700 (80-1840)
CD4, median (/µL)	530 (58-1668)
CD8, median (/µL)	398 (33-4556)

Population (n = 164)		
Anti-RBD antibodies, n (%)	150 (92 %)	
Anti-N antibodies, n (%) RT-PCR nasopharyngal swab, n (%)	23 (14,1 %) 12 (7 %)	
	Treated	**Untreated**
Anti-RBD antibodies - median (U/mL)	111 (0-250)	250 (3.49-250)
IgG levels - median (mg/dL)	435 (200-1090)	885 (80-1790)
	Anti-RBD positive	**Anti-RBD negative**
IgG levels - median (mg/dL)	720 (80-1840)	502 (160-1070)
CD4 levels - median (/µL)	529 (101-1668)	569 (58-894)
	Anti-N positive	**Anti-N negative**
Anti-RBD antibodies - mean (U/mL)	226 (97-250)	125 (0-250)

Author contribution E.H., F.D., A.V.M., and M.C.V. analyzed the data.
E.H., F.D., and M.C.V. wrote the manuscript.
F.D., A.H., S.B., and M.C.V. collected the data and obtained the consent of each patient.
All authors approved the final manuscript.

Declarations

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate Informed consent was obtained from all individual patients included in the study.

Competing interests The authors declare no competing interests.

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