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serum of 126 patients who had undergone alloHCT between 1996 and 2021. Vaccination regimens included homologous vaccination with AstraZeneca ChAdOx1 (AZ, n=9), mRNA vaccines (Pfizer-BioNTech BNT162b2 (PB) or Moderna mRNA-1273 (M), n=107) or heterologous vaccination (AZ followed by PB or M, n=10). Patients on immunosuppression (IS, n=28, 22%) were grouped according to the number of systemic drugs applied. Patients with positive anti-N were excluded from the analysis, as these were assumed to have been exposed to active SARS-CoV2 infection.

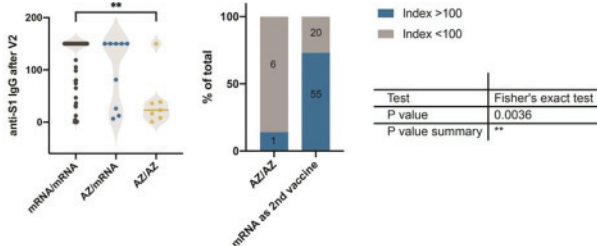


Fig. 1. Left: median anti-S1 IgG index ≥ 150 (PB) vs. 23.15 (AZ), $p = 0.001$, Mann Whitney U test after 2nd vaccination (V2). Right: fraction of patients off IS with index >100 (blue) or <100 (gray) after tandem AZ vaccination (AZ/AZ) or with mRNA vaccine during second vaccination.

Results: Among the total cohort of 126 patients, 83% had a detectable immune response after two vaccinations (anti-S1 IgG index ≥ 1 , SARS-CoV-2 Total Assay). Among the 82 patients without systemic IS, the main determinant of the anti-S1 level was the type of vaccine, with mRNA vaccines showing significantly higher index levels compared to AZ (Fig. 1). While almost no anti-S1 response was observed as soon as more than one systemic IS drug was administered, we found that 68% and 40% of patients off IS and on only one systemic drug, respectively, showed a strong vaccination response (index >100). There was no association between anti-S1 IgG index and time from alloHCT, leukocyte, lymphocyte, CD4, CD8, B cell or NK cell numbers. Exacerbation or aggravation of cGVHD was observed in 5% of all patients and in 18% of those who were on IS for treatment of cGVHD.

Conclusion: Strong anti-S1 immune responses can be elicited with current SARS-CoV2 vaccines in the vast majority of alloHCT recipients off immunosuppression. The likelihood of a sufficient response decreases with the number of immunosuppressive drugs employed. Tandem mRNA-based vaccinations or combination strategies consisting of vector first followed by mRNA appear to be preferable over tandem vector vaccinations. The considerable number of patients in which vaccination induced exacerbation of cGVHD warrants the search for biomarkers to help decide on whether to vaccinate patients with a history of cGVHD against SARS-Cov2.

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Vaccination Against Sars-Cov-2 Induces Robust Humoral Immune Response in Patients with Previous Hematologic Stem Cell Transplantation

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Introduction: Efficacy mRNA SARS-CoV-2 vaccines was demonstrated in healthy population but immunization rate in hematopoietic stem cell transplantation (HSCT) patients is not well known.

Objective: The objective of this study is to evaluate the serologic response to the 1273 SARS-CoV-2 (Moderna) vaccination in HSCT patients.

Methods: A prospective single center study was conducted. Autologous HSCT (Auto-HSCT) and allogeneic HSCT (Allo-HSCT) patients were included, and all were vaccinated with 1273 SARS-CoV-2 vaccine. Blood samples were taken before and after the second dose of the vaccine to assess antibodies titers against SARS-CoV-2. Patients were interrogated to adverse events (AE). Univariate logistic regression model was performed to estimate risk factors. The data analyses were carried out using R statistical software.

Results: One hundred twenty patients were included: 74 Allo-HSCT and 54 Auto-HSCT. 83.8% developed immunization against SARS-CoV-2, no significant difference between type of

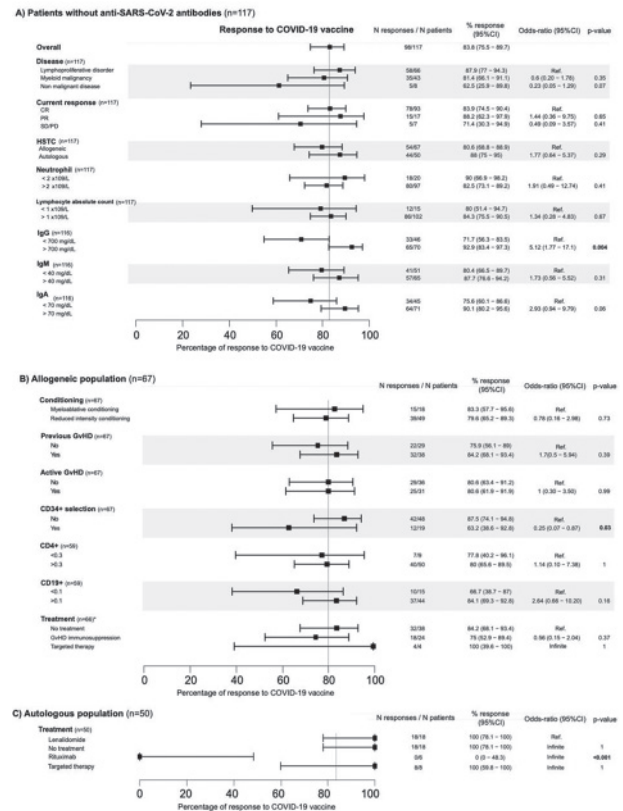


Figure 1.- Variables conferring risk for a reduced immunization rate to SARS-CoV-2 vaccination as defined by the ORR. (A): evaluation of baseline characteristics of the whole population without anti-SARS-CoV-2 antibodies. (B) evaluation of characteristics that only apply to the allogeneic stem cell transplant population without SARS-CoV-2 antibodies. (C) the graph shows the impact of the different treatments in patients that have received an autologous stem cell transplant.

transplant. A univariate analysis (Figure 1) identified as risk factors of lack of response: in all the population, basal levels of IgG < 700 mg/dL (71.7% vs 92.9%, $p=0.004$); in Auto-HSCT, have received rituximab (0% vs 100%, $p<0.001$); and in Allo-HSCT, have undergone an ex-vivo CD34+ positive selection HSCT (63.2% vs 87.5%, $p=0.03$). A quantitative analysis showed higher titers of antibodies against spike protein of SARS-CoV-2 in those patients under lenalidomide, without evidence of difference in those patients under immunosuppressant therapy (Figure 2A and 2B). Those patients ($n=11$) who had antibodies before the vaccination showed increased levels after the

vaccine (Figure 2C). The most common AE was local pain (88%), and no patient was admitted because of an AE.

Conclusion: In our cohort of HSTC patients, mRNA-1273 vaccine (Moderna) was effective and safe, so prioritizing this specific population should be recommended.

Low levels of immunoglobulins and, particularly, treatment with rituximab were associated with an inferior humoral response, and it would be advisable to individualize the vaccination in these patients.

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Humoral Immunogenicity of Sars-Cov-2 Vaccination in the First Year after Hematopoietic Cell Transplant or Chimeric Antigen Receptor T Cell Therapy: A CIBMTR and BMT CTN Study

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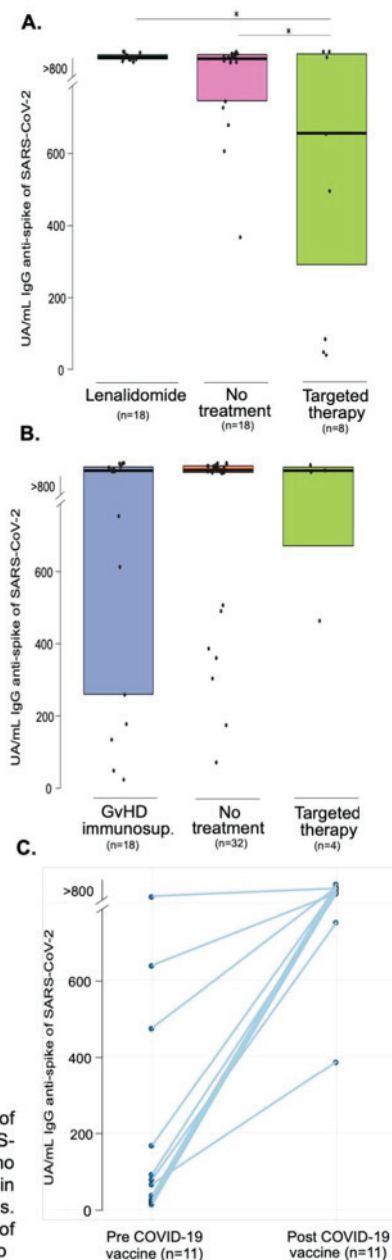


Figure 2.- Titers of antibodies against SARS-CoV-2 in patients who respond to the vaccine in three different settings. Panel A shows titers of antibodies in patients who

underwent an Auto-HSCT and were under treatment with other agents at the moment of the vaccine; panel B, shows titers of antibodies in Allo-HSCT patients according to the GVHD immunosuppressive therapy. Boxes and vertical bars denote interquartile range and median area under the curve, respectively. Panel C, represents the titers of antibodies of those patients who had COVID-19 before vaccination and their antibody levels after vaccination.

Background: Immunogenicity of SARS-CoV-2 vaccines in recipients of HCT or CAR-T therapy remains ill-defined, particularly within the first year after cell therapy. Impaired antibody responses to the vaccines are likely; further, optimal timing for vaccination and predictors of immunogenicity are poorly understood.

Methods: In an ongoing prospective, multi-center, observational study, patients within 1 year of HCT or CAR-T therapy who underwent SARS-CoV-2 vaccination, provide blood within