Predictors of Humoral Response to SARS-CoV-2 Vaccination after Hematopoietic Cell Transplantation and CAR T Cell Therapy

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Running title: Response to SARS-CoV-2 Vaccination after Cellular Therapies

Word count: 4051

Conflict of interest statement:

RT, DK, JY, LM, SD, SMD, LVR, MP, ED, MAP, CDB, GP, and MK report no conflicts of interest.

SV is on the advisory board for Immunai and has received consulting fees from ADC therapeutics.

DJC reports research support from Genentech and NexImmune, outside the submitted work.

IP serves as a Data and Safety Monitoring Board for ExcellThera and has received research funding from Merck.

MAP reports honoraria from Abbvie, Astellas, Bristol-Myers Squibb, Celgene, Equillium, Incyte, Karyopharm, Kite/Gilead, Merck, Miltenyi Biotec, MorphoSys, Novartis, Nektar Therapeutics, Omeros, OrcaBio, Takeda, and VcetvBio AG, Vor Biopharma. He serves on DSMBs for Cidara Therapeutics, Medigene, Sellas Life Sciences, and Servier, and the scientific advisory board of NexImmune. He has ownership interests in NexImmune and Omeros. He has received research support for clinical trials from Incyte, Kite/Gilead, Miltenyi Biotec, and Novartis.

GLS reports research funding from Janssen and Amgen outside the submitted work.

Copyright 2021 by American Association for Cancer Research.
Financial Disclosures: This research was supported in part by National Institutes of Health award number P01 CA23766 and NIH/NCI Cancer Center Support Grant P30CA008748. This study was also supported by The Society of Memorial Sloan Kettering (DJC), National Institutes of Health/National Cancer Institute 5K08CA248966-02 (DAK), Leukemia and Lymphoma Society (SAV), Pershing Square Sohn Cancer Research Alliance (SAV), and Conrad Hilton Foundation (SAV).

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors thank Theodore and Laura Hromadka for their support.
Abstract

Cellular therapies including allogeneic and autologous hematopoietic cell transplant (allo-HCT, auto-HCT) and chimeric antigen receptor T cell therapy (CAR T) render patients severely immunocompromised for extended periods post-therapy, and data on responses to COVID-19 vaccines are limited. We analyzed anti-SARS-CoV-2 spike IgG antibody (spike Ab) titers and neutralizing Ab among 217 recipients of cellular treatments (allo-HCT, n=149, auto HCT n=61, and CAR T n=7). At 3 months after vaccination, 188 patients (87%) had positive spike Ab levels and 139 (77%) had positive neutralization activity, compared to 100% for both in 54 concurrent healthy controls. Time from cellular therapy to vaccination and immune recovery post-cellular therapy were associated with response. Vaccination against COVID-19 is an important component of post-cellular therapy care, and predictors of quantitative and qualitative response are critical in informing clinical decisions about optimal timing of vaccines and the requirement for booster doses.
Identifying predictors of response to vaccination against SARS-CoV-2 in patients following cellular therapy is critical to managing this highly vulnerable patient population. To date, this is the most comprehensive study evaluating quantitative and qualitative responses to vaccination, providing parameters most predictive of response and potentially informing booster vaccination strategies.
Introduction

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a pandemic by the WHO in March 2020. Cancer patients with hematologic malignancies, chronic lymphopenia, and/or corticosteroid use are at increased risk for hospitalization, severe respiratory illness, and increased mortality (1-4). Based on observed outcomes in the early part of the pandemic, factors including presence of lung infiltrates at presentation and neutropenia were identified as predictors for poor outcomes in recipients of cellular therapies for hematologic malignancies (5). Later, a multicenter data from the Center of International Blood and Marrow Transplant Research (CIBMTR) reported that 27% of allogeneic hematopoietic cell transplantation (allo-HCT) recipients and 20% of autologous hematopoietic cell transplantation (auto-HCT) recipients with COVID-19 manifested moderate severity illness, while severe disease was reported in 15% and 13%, respectively, with an overall mortality of 21% (6). Our group has also reported the negative indirect effects of the pandemic on patients undergoing cellular therapies from delays in treatment leading to progression of disease and mortality (7).

Effective immunization is vital for protecting cellular therapy recipients from COVID-19 and to mitigate spreading of the pandemic. There are currently two mRNA vaccines against SARS-CoV-2 approved under an Emergency Use Authorization protocol (EUA) in the United States, BNT162b2 (Pfizer-BioNTech) (8) and mRNA-1273 (Moderna) (9), administered as two-dose series separated by 21 days (Pfizer-BioNTech) or 28 days (Moderna). Both mRNA vaccines are highly effective in healthy individuals, with >90% prevention of severe disease and mortality. However, among patients with malignancies (10,11) and recipients of solid organ transplantation (12-14) emerging data suggest lower vaccine efficacy compared to the healthy population. Data for patients undergoing cellular therapies are sparse, with small studies reporting attenuated humoral and/or cellular immune responses (15-17).

We therefore aimed to assess immune responses to mRNA COVID-19 vaccines among patients who underwent cellular therapies at our center, with the goal of identifying predictors of response, determining the ideal timing for vaccination, and to identify patients at high risk for non-protective immune responses who might benefit from additional doses (‘boosters’) of vaccines.

Results

Recipients of cellular therapy have lower vaccine responses than healthy donors.

Between 12/22/2020 and 2/28/2021, 217 patients who were vaccinated against SARS-CoV-2 participated in this prospective observational study. Patient characteristics are summarized in Table 1. Patients were vaccinated as early as 2 months post cellular treatment (day 63), with a median time between treatment and first dose of vaccine of 1,007 days (IQR 488-1761, 2.75 years). All patients received mRNA vaccines according to the recommended doses and timing, including 70% received the BNT162b2 (Pfizer-BioNTech) vaccine and 30% the mRNA-1273 (Moderna) vaccine. Fifty-two patients (23.9%) met our institutional immune recovery criteria for initiation of inactivated vaccines after transplant (CD4+ T cell count >200 cells/μL, CD19+ B cell count >50

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cells/μL, IgG>500 mg/dl and PHA mitogen proliferation >40%), and 151 patients (64.9%) initiated or completed standard post-transplant vaccinations prior to receiving a COVID-19 vaccine. As of August 1, 2021, none of the 217 vaccinated patients were diagnosed with COVID-19 disease after vaccination. At 1 month after the first vaccine dose, 39 (18%) patients were tested for response. Twenty-four (61%) had a positive spike Ab defined as >50 AU/ml (median: 479.75 AU/ml, IQR 170.4-3,658.8), and 15 (38.5%) had positive neutralization activity defined as >30% (median: 57.3%, IQR 37.8-89.6%). At 3 months after the first vaccine, 188 patients (87%) had a positive spike Ab (median: 5,379 AU/mL, IQR 451-15,750), and 139 (77%) had a positive neutralization Ab assay (median: 93%, IQR 36-96%). A higher spike antibody titer was associated with higher neutralization activity, and neutralization activity was absent for spike Ab levels <250 AU/mL (Figure 1A).

Fifteen patients (7%) had a documented COVID-19 infection or presence of N antibodies to SARS-CoV-2 prior to vaccination. Among these, 7 had spike Ab level > 50 AU/mL and neutralization Ab >30% detected prior to vaccination. Two patients with COVID-19 disease prior to their cellular treatment did not mount a measurable response to the vaccines given after treatment, while the remaining 13 generated very high spike Ab levels (25,000 AU/mL in 12/13 patients).

Sixty-nine healthy volunteers participated as a control group. The median age was 31 years (range: 22-67) with 78% female and 13% having COVID-19 disease prior to vaccination. Fifty-eight (84%) and 11 (16%) received the BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccine according to the recommended doses and timing, respectively. The response rates among the HC group were significantly higher. Fifty-nine were assessed for response at 1 month after the first vaccination and 100% had a positive spike Ab (median: 886.2, IQR 502.3-2240) and 93.2% had neutralizing Ab (median:63.6%, IQR 51- 78). At 3 months, 100% had spike Ab (median: 7720, IQR 3885-9746) and neutralizing Ab (median: 96%, IQR 94- 96) (Figure 1B, Table 2).

Time from cellular therapy to vaccination correlated with humoral response

Sixty-seven percent of patients vaccinated in the first 12 months post-cellular therapy mounted a spike Ab response, compared to 89% of patients vaccinated between 12-24 months, 91% of patients vaccinated between 24-36 months, and 93% of patients vaccinated after 36 months post cellular treatment, p=0.001 (Supplemental Table 1). Four patients were vaccinated before day 100 post cellular treatment, of whom only 1 had a positive spike Ab level of 1,016.6 and detected neutralizing Ab. An additional 12 patients were vaccinated between day 100-180 and 6 mounted spike Ab (median: 409.4, IQR: 123.4-5091.7), with only 2 having detectable neutralizing Abs.

There were no statistically significant associations between the likelihood to respond to the vaccine and other variables including gender, age, underlying hematologic malignancy, prior COVID-19 infection, treatment with IVIG and type of mRNA COVID-19 vaccine.

Immune recovery post cellular therapy is associated with vaccine response

B cells and helper CD4 T cells are the primary drivers of vaccine responses in germinal centers. We therefore profiled immune subsets in the peripheral blood, responses to
mitogen stimulus, and IgG levels as measures of immune reconstitution in our patient population. These factors have previously been identified to predict vaccine responses to influenza, pneumococcus, and shingles (18)(19), but their role in predicting response to mRNA-based vaccinations remains ill-defined. Immune function as assessed by CD4 or CD19 counts, mitogen proliferation response, and IgG levels each associated strongly with response to vaccine both for spike Ab and neutralizing Abs (Supplemental Table 1).

Patients meeting all the criteria defined above were significantly more likely to respond to vaccination both by titer and percent neutralization. Among patients who did not meet criteria at time of vaccination, 37 (71%) had a positive spike Ab compared to 58 (98%) of patients who met criteria, p<0.001, and 26 (60%) of patients who did not meet all criteria at time of vaccination had detectable neutralizing Ab compared to 47 (90%) of patients who met criteria, p= 0.001 (Figure 1C, Supplemental Table 1).

In a multivariate analysis (MVA) including type of cellular treatment (auto and allo-HCT), time from transplant to vaccination, CD4 count, CD19 count, mitogen level, and IgG, CD19 (OR 1.49, p <0.001), mitogen levels (OR 1.31, p=0.002) and IgG (OR 1.13, p= 0.034) remained independently associated with mounting a spike Ab response (Supplemental Table 2).

Response to vaccine varied between different types of cellular treatments

One hundred and forty-nine patients who underwent allo-HCT were vaccinated between days 63 and 5,186 (median 1,109, IQR:571-2,040) post therapy. Of the 25 on whom samples were available at one month after vaccination, 17 (68%) mounted a spike Ab response (median: 739.2, IQR 219.5-3051.3) and in 11/21 (52%) had >30% neutralizing Ab (median: 57.29, IQR 36.6-85.2%). At 3 months post vaccination, all patients were tested for spike Ab with 89% mounting a response (median: 5,019.8, IQR 635.4-15,914.5), and of the 122 who had neutralizing Ab tested, 78% were higher than the positive threshold (median: 90%, IQR 41.7-96.3). This was significantly lower compared to HC (p=0.024 and 0.025 for the spike Ab and neutralizing Ab, respectively) (Table 2).

In allo-HCT recipients, the response rates were 79% for patients vaccinated in the first year (early allo-HCT), 89% for those vaccinated between 1-3 years post allo-HCT (mid allo-HCT), and 92% for those >3 years post allo-HCT (late allo-HCT), though this association was not statistically significant p=0.282. Titers were significantly lower among patients vaccinated in the first-year post-transplant (p=0.019) (Table 3). Among 7 patients vaccinated within the first 6 months post-transplant, 3 had a positive spike Ab and in one patient neutralizing Ab were detected. In comparison to HC, patients who were vaccinated >36 months post allo-HCT had an Ab response comparable to HC, while patients who were vaccinated in the first year and between 1-3 years post-transplant had significantly lower responses (p=<0.001 and p=0.027 respectively) (Table 2).

Immune function assessed by CD4, CD19, and IgG levels was available in 102 (68%) patients and strongly associated with response to vaccine both for spike Ab and neutralizing Abs. The median spike Ab levels for patients with CD4 count <200 cell/uL and >200 cell/uL were 422.6 (IQR 13.2-2247.2) and 6,651.7 (IQR 1,258-2,0281.6), respectively with 71% vs 93% having a positive Ab (p=0.016). Only 56% patients with CD4 <200 cell/uL had detected neutralizing Ab, (median: 53.7 %, IQR 2-93.3), vs 85% of patients with CD4 >200 cell/uL,(median: 95.5%, IQR 64.6-96.4), p value=0.019 (Table
3). Among patients whose CD19 count was <50 cell/μL and >50 cell/μL at time of vaccination, 46% vs 94% had a positive spike Ab with medians of 27.5 (IQR: 5.2-373.2) and 6,425.7, (IQR: 1,258.2-2,0281.6) respectively (p value<0.001). Only 20% of patients with CD19<50 cell/μL had detected neutralizing Ab, (median: 0, IQR: 0-20.7) compared to 87% patients with CD19 >50 cell/μL (median 95.5%, IQR: 67.4-96.3), p<0.001 (Table 3). Among patients whose IgG level was <500 mg/dL and >500 mg/dl at time of vaccination, 78% vs 95% had a positive spike Ab with medians of 1,156.5 (IQR 373.4-24,333.3) vs 6,538.7 (IQR 1,257.1-20,457.2), p value=0.038, while 67% patients with IgG level <500 mg/dL had detected neutralizing Ab (median 49.3%, IQR: 12.9-96) compared to 85% with IgG level >500, (median 94.7%, IQR: 66.7-96.3), p=0.133 (Table 3). Lastly, a significant difference in response to COVID-19 vaccine was seen among patients who met all criteria to initiate vaccinations compared to the those who did not (p =0.002) (Table 3).

Forty-six allo-HCT patients (31%) were on immunosuppressive treatments (ruxolitinib, cyclosporine or tacrolimus) at time of vaccination, either for treatment of or as prophylaxis against GVHD and 14% were on oral steroids (all were on low dose, <0.5 mg/kg) for various indications. Treatments with immunosuppressive medications did not appear to decrease the likelihood of spike Ab response; but these patients were less likely to produce neutralizing Ab. Steroid use was associated with both lower spike Ab and neutralizing Ab response rates, with 67% of patients treated with steroids having positive spike Ab and 44% a neutralizing Ab detected compared to 93%, p=0.002 and 84%, p=0.001 among patients not treated with corticosteroids, respectively (Table 3).

In a MVA in patients who underwent an allo-HCT including CD4 count, CD19 count, IgG, and steroid use, CD19 (OR 1.53, p <0.001) and IgG levels (OR 1.15, p =0.023) were associated with mounting a spike Ab response (Supplemental Table 2).

Sixty-one patients who underwent auto-HCT were vaccinated between days 79 and 3,784 (median 774 days, IQR 245-1,367) post therapy. Thirteen patients had samples available at one month after first vaccination with 7(54%) mounting spike Ab responses (median: 202.3, IQR 109.3-296) and in 4/11 (36%) neutralizing Ab were detected (median: 46.3%, IQR 36.13-85.8). At 3 months post vaccination, all patients tested for spike Ab, and 87% mounted a response (median: 2,260.1 IQR 419.4-10,598.8) and 80% had >30% neutralizing Ab (median: 79.8% IQR 33.9-96). This was significantly lower compared to HC p<0.001 and 0.002 for the spike Ab and neutralizing Ab, respectively (Table 2).

Patients vaccinated in the first year after auto-HCT (early auto) had significantly lower response rates for both the spike Ab (p value=0.001) and neutralizing Ab (p=0.025) compared to patients vaccinated after the first year post-transplant (Table 3). Compared to HC, patients who were vaccinated early (p<0.001) or late after an auto-HCT (p=0.009) had a significantly lower response (Table 2).

Immune function assessed by CD4, CD19, mitogen and IgG levels were available for 29 (47%) of the patients, and among these patients, only CD19 levels were associated with spike Ab response but not with neutralizing Ab response (Table 3).

Forty-three patients (71%) were on active treatment at time of vaccination:

Immunomodulatory drugs (IMiDs: lenalidomide and pomalidomide) in 20 patients (33%),
and daratumumab in 12 (20%). Single agents IMiDs were used mostly as maintenance
treatment. While response rates were not different between patients on treatments with
either IMiDs or daratumumab compared to patients not on treatment, a significantly
lower level of spike Ab (p=0.045) but not neutralizing Abs (p= 0.119) was noted among
patients treated with daratumumab (spike Ab median 513AU/mL, IQR 226.6-1486.9, and
neutralizing Ab median 59%, IQR 8.8-81.4) vs those not on treatment (median 3,297
IQR 655-19,499, and median 80.5% IQR 44.8-96.3, respectively).

Seven patients who underwent CAR-T therapy were included in this analysis. The
patients were vaccinated between days 66-825 (median 218, IQR:123-720). Response
at 1 months was assessed in one patient and the patient did not mount a response. At 3
months, only 2/7 (28.5%) patients had a positive spike Ab response with levels of
3,281UA/ml and 16,067 UA/ml. Immune function data was available on 6 patients with a
median CD4, CD19, mitogen and IgG levels of 247 cell/uL, 0 cell/uL,59 %, and 710
mg/dl.

Assessing different cutoffs for the anti-SARS-CoV-2 spike IgG response

A cutoff of 50 AU/mL was defined by the manufacturer as positive. Because the
adequate titer threshold for predicting for neutralization capacity in vitro or clinically
preventing disease is unknown, we evaluated for predictors of higher spike Ab titers.
This analysis highlights that association between higher levels of spike Ab and the
presence of neutralizing Ab as demonstrated in figure 1A. Immune function at the time of
vaccination remained a significant predictor regardless of cutoff (Supplemental Table 3).

Discussion

In this largest analysis to date of humoral responses to anti-SARS-CoV-2 mRNA
vaccines among recipients of cellular therapies, we demonstrate overall high response
rates to mRNA vaccines, but with significant variability among the different cellular
treatments based on immune reconstitution status. Transplant patients and patients after
CAR T cell therapy had inferior responses to the vaccines compared to healthy controls,
confirming the potential overall vulnerability of this population and the need to consider
booster vaccination strategies.

Time from cellular therapy to vaccination was a strong predictor of response with less
robust responses seen in patients vaccinated within the first-year post transplant. Yet, it
is important to note that among patients vaccinated within the first year, the response
rate among the allo-HCT was 79% and among the auto-HCT 65%. Our cohort included
16 patients vaccinated within the first 6 months post-transplant, a group where the spike
Ab responses are particularly low, with 1 responder among 4 vaccinated in the first 100
334 days and 6 of 12 among those vaccinated between days 100-180. Since time post -
transplant likely serves as a surrogate marker of immune recovery, our data suggest the
use of more reliable predictors (particularly CD19 and IgG levels) to guide timing of
vaccination and in patients with a good immune recovery vaccination should be offered
as early as 3 months post cellular therapy.

Considering the immunosuppressive nature of cellular treatments, routine post-
transplant vaccinations are often recommended based on immune recovery and time
from transplant (18-20). However, in January 2021, ASH-ASTCT advised that SARS-
CoV-2 vaccines be offered as early as 3 months following HCT or CAR T cell therapies (https://www.hematology.org/covid-19/ash-astct-covid-19-vaccination-for-hct-and-car-t-cell-recipient). We therefore applied the standard criteria to initiate vaccination, and found that among patients who underwent allo-HCT immune recovery was strongly associated with response to vaccination while for patients post auto-HCT, who routinely initiate vaccination at 1 year after transplant regardless of immune function status, only CD19 levels were associated with response. This is in agreement with findings reported by Greenberg et al (21) in a non-transplant hematologic malignancies cohort, indicating a lower response to the vaccine among patients treated with B cells directed therapies. Additionally, In a cohort of 80 patients post cellular therapies, Ram et al (16) observed an association between higher CD19 levels and humoral response to the vaccine, while a higher CD4+CD8+ ratio was associated with a cellular response. In another recent publication evaluating patients post cellular therapies, Dhakal et al (22) reported on a cohort of 130 patients and did not find a statistically significant association between immune recovery. The small sample size of this study likely limited the ability to observe the differences noted in our analysis. Our detailed analysis thus provides more granular information on immune recovery predictors to SARS-CoV-2 vaccination and highlights the differences between patients post allo-HCT, auto-HCT, and CAR T cell therapies.

In this analysis, the positive cutoffs were 50.0 AU/mL for the SARS-CoV-2 IgG spike and 30% for the surrogate virus neutralization assay as determined by the manufacturer. However, a positive neutralization assay was not detected in any case with a SARS-CoV-2 IgG spike level lower than 250 AU/mL, and there was a strong correlation between the two tests, with higher levels of SARS-CoV-2 IgG Spike correlating with higher neutralization capacity, as demonstrated when we applied higher levels of cutoffs for the SARS-CoV-2 IgG Spike protein. These findings suggest that there was a group of patients who mounted a serologic response but remain vulnerable to SARS-CoV-2 infection in the absence of neutralizing Ab capacity. Identifying the threshold that provides protection post-vaccination against SARS-CoV-2 remains a challenge also in the healthy population (23). Because post-vaccination antibody response assessment with neutralizing assay is not readily available and established cutoffs for clinical protection are unknown, we strongly recommend that patients post cellular treatments continue to use masks and practice social distancing as additional protective measures against emerging variants.

Optimizing humoral response in patients with low Ab titers or lack of serological response, or revaccination of those who received COVID-19 vaccine before cellular therapy is an area of ongoing investigation. To date, only a few studies have reported responses after a third mRNA dose and mostly among non-cancer immunocompromised patients. Werbel et al (12) reported a cohort of 30 solid organ transplant patients who had suboptimal response to the first 2 doses of mRNA vaccines. Among patients who received a third dose of vaccine, a 40% response rate was observed (100% among patients with low positive titers after initial vaccination, and only 25% among patients who had no response to the initial vaccine). Among another group of solid organ transplant patients in France (24) who received 3 doses of Pfizer-BioNTech COVID-19 (BNT162b2) vaccine, there was a 44% response rate among patients who had no response to the first two doses of the vaccine. While the mRNA vaccines have high safety profiles among healthy individuals, the potential for worsening already present graft-versus-host disease and new cytopenias are lingering safety concerns for cellular therapy patients (16,25). Most recently, the Center for Disease Control (CDC)
recommended a booster vaccine dose to Immunocompromised patients (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html). and this will likely be extended to the general population in light of evidence of increased number of infections also among vaccinated healthy individuals (26). Our data suggests that an approach based on immune function can be a useful practical guide for a third dose administration and particularly to identify those who are less likely to respond.

One limitation of this study is that all patients received mRNA-based vaccines and therefore our findings may not apply to other types of vaccines. This analysis was also limited to early post-vaccination assessment (3 months) and follow-up analysis over time in this patient population is warranted. Although the largest study to date, the number of eligible individuals early post cellular therapy treatment was small, and we particularly had a small cohort of patients post CAR T therapy. Due to the heterogenous nature of the cohort, it was not possible to examine the effects of other potential clinical predictors on vaccine induced antibody levels. Additionally, our control cohort was not a matched control and the age and gender of the HC were significantly younger than the patient’s population. Lastly, with data supporting a critical role of cellular immunity against SARS-CoV-2 infection(27),(28) incorporating detailed analysis of cellular immunity response in patients post-stem cell transplant and CAR T therapies undergoing vaccination is of high importance.

In summary, our study demonstrates high response rates to anti-SARS-CoV-2 mRNA vaccines among patients post-cellular therapy, while highlighting the variability in degree of response based on immune reconstitution at that time. Moreover, this analysis underscores the importance of qualitative assessment provided by the neutralization assay, as many patients meeting thresholds for spike Ab titers did not have adequate neutralizing capacity. Since this is unlikely to be clinically available, our study provides guidance on anti-spike antibody levels that are likely to correlate with an adequate neutralization antibody response.

Methods

Study design

This observational study included adult patients who underwent cellular therapies including autologous and allogeneic HCT and chimeric antigen receptor T cell therapy (CAR T) at Memorial Sloan Kettering Cancer Center (MSKCC) between October 2001 and November 2021 and remain under active follow up. Patients were included in this study if they received the anti-SARS-CoV-2 vaccine between 12/22/2020 and 2/28/2021. Spike Ab antibody titers and circulating neutralizing antibodies were prospectively measured at 1 and 3 months after the 1st dose of vaccination. CD4 T cell counts, CD19 B cell counts, PHA mitogen proliferation responses, and IgG levels were collected in a subset of patients to assess immune recovery prior to vaccination. Patient demographics and clinical characteristics were retrospectively collected from the electronic medical record and institutional databases. Additionally, 69 healthy individual controls (HC) who were vaccinated over the same time period at our center were recruited and served as a healthy control group. The study was conducted through the Division of Hematologic Malignancies at MSKCC in accordance with the Declaration of Helsinki guidelines. Informed consent was waived under a retrospective research protocol.
(protocol 20-390) approved by the Institutional Review and Privacy Board of Memorial Hospital/MSKCC.

**Antibodies assays**

**Anti-SARS-CoV-2 spike IgG assay**

The SARS-CoV-2 IgG spike antibodies were measured using the AdviseDx SARS-CoV-2 IgG II assay on the Architect i2000 analyzer using chemiluminescent microsphere immunoassay (CMIA) technology. The resulting chemiluminescent reaction, measured as a relative light unit (RLU), was compared with a cutoff value of 50.0 AU/ml, defined during calibration of the instrument.

**Surrogate Virus Neutralization Assay**

The SARS-CoV-2 Surrogate Virus Neutralization Test (sVNT) Kit (Genescript) measured circulating neutralizing antibodies against SARS-CoV-2 that block the interaction between the RBD of the viral spike glycoprotein with the ACE2 cell surface receptor. The absorbance of the sample is inversely dependent on the titer of the anti-SARS-CoV-2 neutralizing antibodies. Percent inhibition was calculated per manufacturer’s instructions with a positive cutoff value of 30% and validated with a panel of confirmed COVID-19 patient and healthy control sera.

**Statistics**

Descriptive statistics for patient-, disease-, and transplantation-related variables as well as laboratory variables were reported using frequency and percentages for categorical variables and medians and interquartile ranges (IQRs) for continuous variables.

Wilcoxon rank-sum tests compared the levels of anti-SARS-CoV-2 spike IgG and neutralizing antibodies between healthy donors and recipients of cellular therapies, both overall and separated by the type and timing of the cellular therapy.

Fisher’s exact tests or chi-square tests, as appropriate, assessed the association between various factors and response to COVID-19 vaccine. Variables evaluated included: age at time of vaccination (dichotomized as <60 years, 60-70 years and ≥70 years), sex (male vs female), disease groups (Acute Leukemia, MDS and MPN, Chronic Leukemia, MM and amyloid, Low grade lymphoma, High grade lymphoma and HD, T cell lymphoma and other: AA, Systemic Mastocytosis and BPDCN), time from cellular therapy to first vaccination dose (<12 month, 12-24 months, 24-36 months and >36 months) as well as time from treatment to first vaccination dose within the subgroups of cellular treatments (Auto-HCT, Allo-HCT and CAR T cell therapies), prior COVID infection, type of mRNA vaccine, use of immunosuppressive therapies among the Allo-HCT patients only, disease directed treatment among the auto-HCT only (Imids, monoclonal Ab or other), as well as laboratory variables including CD4 count, CD19 count, IgG levels and mitogen levels prior to vaccinations. CD4, CD19, IgG and mitogen proliferation response levels were dichotomized based on ≥200, ≥50, ≥500, and ≥40, respectively as clinical thresholds used to define criteria for immunization. A p value of less than 0.05 was considered statistically significant.
Acknowledgments

We thank the patients and healthy volunteers for participating in the trial. We also thank the nurses, advanced practice providers, research staff, and physicians of the Laboratory Medicine, and Bone Marrow Transplant services.
References:


Undetectable SARS-CoV-2-Specific IgG. *Emerg Infect Dis* 2021;27(1) doi 10.3201/2701.203772.
Tables Legends:

Table 1: Patient Characteristics
Table 2: Comparisons between patients post allo-HCT and auto-HCT to HC
Table 3: Allo- and Auto-HCT response characteristics
Legend for figure 1

Panel 1A: Scatter plot of anti-SARS-CoV-2 spike IgG antibody titers and neutralizing antibodies. The red lines denote the thresholds for positive assays (Anti-SARS-CoV-2, 50 AU/mL, neutralization antibodies: 30% inhibition). The 3 groups of Allo-HCT (yellow), Auto-HCT (green) and CAR T cell therapy (blue) are represented in this graph.

Panel 1B: Antibody responses to COVID-19 vaccines according to type of cellular therapy and timing post treatment. Anti-SARS-CoV-2 spike IgG and neutralizing antibody titers were measured at 3 months after initial COVID-19 vaccination and summarized using scatter plots with median and interquartile range. (Left panel) Plots comparing anti-SARS-CoV-2 spike IgG categorized according to time for cellular treatment and type of cellular treatment (orange- Auto HCT, blue- Allo-HCT, red- CAR T) compared with healthy controls (HC; gray dots) Green dashed line denotes the threshold for a positive result (50.0 AU/mL). (Right panel) Circulating neutralizing antibodies against SARS-CoV-2 were assessed at 3 months after initial COVID-19 vaccination. Plots comparing neutralizing antibodies categorized according to time for cellular treatment and type of cellular treatment (orange- Auto HCT, blue- Allo-HCT, red- IEC) compared with healthy controls (HC; gray dots) Green dashed line denotes the threshold for a positive result (30% inhibition). *P<0.05, **P<0.01, ***P<0.001
Early Allo= First year, Mid Allo=1-3 years, Late Allo>3 years, Early Auto=First year, Late Auto>1 year Number of patients is reported for spike Ab (S) and neutralizing Ab (N) for each group: HD (S:63/N25), early auto (S:20/N15), late auto (S:41/N37), early allo (S:19/N14), mid allo (S:55/N49), late allo (S:75/N61), CAR (S:7/N2).

Panel 1C: Antibody responses to COVID-19 vaccines according to immune recovery. Anti-SARS-CoV-2 spike IgG and neutralizing antibody titers were measured at 3 months after initial COVID-19 vaccination and summarized using scatter plots with median and interquartile range. (Left panel) Plots comparing anti-SARS-CoV-2 spike IgG among patients meeting immune recovery post treatment (green) vs patients not meeting criteria (red). Green dashed line denotes the threshold for a positive result (50.0 AU/mL). (Right panel) Circulating neutralizing antibodies against SARS-CoV-2 were assessed at 3 months after initial COVID-19 vaccination. Plots comparing neutralizing antibodies among patients meeting immune recovery post treatment (green) vs patients not meeting criteria (red). Green dashed line denotes the threshold for a positive result (30% inhibition). **P<0.01, ***P<0.001
Pos= meeting all criteria, i.e CD4+ T cell count>200 cells/μL, CD19+ B cell count>50 cells/μL, IgG>500 mg/dl and PHA mitogen proliferation >40%
Neg S:52/N43, Pos S:52/N52
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<thead>
<tr>
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<td>Gender, male</td>
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<td>Disease Group</td>
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<tr>
<td>Acute Leukemia</td>
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<td>MDS and MPN</td>
<td>41</td>
<td>18.8%</td>
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<tr>
<td>Chronic Leukemia</td>
<td>8</td>
<td>3.6%</td>
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<tr>
<td>MM and amyloid</td>
<td>40</td>
<td>18.4%</td>
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<td>Low grade lymphoma</td>
<td>8</td>
<td>3.6%</td>
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<tr>
<td>High grade lymphoma and HD</td>
<td>35</td>
<td>16.1%</td>
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<tr>
<td>T cell lymphoma</td>
<td>6</td>
<td>2.7%</td>
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<tr>
<td>Other: AA, Systemic Mastocytosis, BPDCN</td>
<td>4</td>
<td>1.8%</td>
</tr>
<tr>
<td>Time from cellular therapy to COVID vaccine, median days (range)</td>
<td>1007 (63-7026)</td>
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<tr>
<td>2-12 months</td>
<td>42</td>
<td>19.3%</td>
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<tr>
<td>12-24 months</td>
<td>45</td>
<td>20.7%</td>
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<tr>
<td>24-36 months</td>
<td>32</td>
<td>14.7%</td>
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<tr>
<td>&gt;36 months</td>
<td>98</td>
<td>45.2%</td>
</tr>
<tr>
<td>Time groups per type of cellular therapy</td>
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<td></td>
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<tr>
<td>Early Allo</td>
<td>19</td>
<td>8.7%</td>
</tr>
<tr>
<td>Mid Allo</td>
<td>55</td>
<td>25.3%</td>
</tr>
<tr>
<td>Late Allo</td>
<td>75</td>
<td>34.6%</td>
</tr>
<tr>
<td>Early Auto</td>
<td>20</td>
<td>9.2%</td>
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<tr>
<td>Late Auto</td>
<td>41</td>
<td>18.9%</td>
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<tr>
<td>CAR</td>
<td>7</td>
<td>3.2%</td>
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<tr>
<td>Prior COVID-19 Infection</td>
<td>15</td>
<td>6.9%</td>
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<tr>
<td>Type of COVID vaccine</td>
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<tr>
<td>BNT162b2 (Pfizer-BioNTech)</td>
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<td>70%</td>
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<tr>
<td>mRNA-127(Moderna)</td>
<td>65</td>
<td>30%</td>
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<tr>
<td>Re-immunization with primary inactivated series prior to COVID vaccine</td>
<td>141</td>
<td>64.9%</td>
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<tr>
<td>Treatments prior to COVID vaccine</td>
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<tr>
<td>Immune suppression with Tacrolimus/cyclosporine or Ruxolitinib (among Allo-HCT only)</td>
<td>46</td>
<td>30.8%</td>
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<tr>
<td>On Steroids (among Allo-HCT only)</td>
<td>21</td>
<td>14%</td>
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<tr>
<td>Daratumumab (among Auto-HCT only)</td>
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<td>19.6%</td>
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<tr>
<td>IMiDs (among Auto-HCT only)</td>
<td>20</td>
<td>32.7%</td>
</tr>
<tr>
<td>Chemotherapy (other)</td>
<td>11</td>
<td>5%</td>
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</table>

Abbreviations: Early Allo= <1 year, Mid Allo=1-3 years, Late Allo>3 years, Early Auto=<1 year, Late Auto>1 year, MDS= Myelodysplastic Syndrome, MPN= Myeloproliferative Neoplasms, MM= Multiple Myeloma, HD=Hodgkin Disease, AA= Aplastic Anemia, BPDCN= Blastic Plasmacytoid Dendritic cell Neoplasm
<table>
<thead>
<tr>
<th>Table 2: Comparisons between patients post allo-HCT and auto-HCT to HC</th>
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<tr>
<td><strong>Anti-SARS-CoV-2 spike IgG Median (IQR)</strong></td>
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<td>---------------------------------------------------------------</td>
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<td>Healthy (N=54) 7720 (3885-9746)</td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

Abbreviations: Allo = Allogeneic. HCT = hematopoietic cell transplant. Early Allo= <1 year, Mid Allo=1-3 years, Late Allo>3 years, Early Auto=<1 year, Late Auto>1 year
### Table 3: Allo- and Auto- HCT response characteristics

#### Allogeneic HCT

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<tr>
<th>Variable</th>
<th>Group</th>
<th>N</th>
<th>Median (IQR)</th>
<th>&lt; 50</th>
<th>&gt; 50</th>
<th>P-value</th>
<th>N</th>
<th>Median (IQR)</th>
<th>&lt; 30</th>
<th>&gt; 30</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Time groups per type of cellular treatment</td>
<td>Early Allo</td>
<td>19</td>
<td>445.6 (112.3-5728.2)</td>
<td>4 (21%)</td>
<td>15 (79%)</td>
<td>0.282</td>
<td>14</td>
<td>74.9 (12.3-95.7)</td>
<td>5 (36%)</td>
<td>9 (64%)</td>
<td>0.341</td>
</tr>
<tr>
<td></td>
<td>Mid Allo</td>
<td>55</td>
<td>3409.3 (683.8-20901.2)</td>
<td>6 (11%)</td>
<td>49 (89%)</td>
<td></td>
<td>49</td>
<td>88.5 (46.5-96.3)</td>
<td>10 (20%)</td>
<td>39 (80%)</td>
<td></td>
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<tr>
<td></td>
<td>Late Allo</td>
<td>75</td>
<td>6786.6 (1833.5-17535.7)</td>
<td>6 (8%)</td>
<td>69 (92%)</td>
<td></td>
<td>61</td>
<td>94.6 (60.3-96.3)</td>
<td>11 (18%)</td>
<td>50 (82%)</td>
<td></td>
</tr>
<tr>
<td>CD4 Count</td>
<td>&lt;200</td>
<td>21</td>
<td>422.6 (13.2-2247.2)</td>
<td>6 (29%)</td>
<td>15 (71%)</td>
<td>0.016</td>
<td>16</td>
<td>53.7 (2-93.3)</td>
<td>7 (44%)</td>
<td>9 (56%)</td>
<td>0.019</td>
</tr>
<tr>
<td></td>
<td>≥200</td>
<td>81</td>
<td>6651.7 (1258-20281.6)</td>
<td>6 (7%)</td>
<td>75 (93%)</td>
<td></td>
<td>71</td>
<td>95.5 (64.6-96.4)</td>
<td>11 (15%)</td>
<td>60 (85%)</td>
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<tr>
<td>CD19 Count</td>
<td>&lt;50</td>
<td>13</td>
<td>27.5 (5.2-373.2)</td>
<td>7 (54%)</td>
<td>6 (46%)</td>
<td>&lt;0.001</td>
<td>10</td>
<td>0 (0-20.7)</td>
<td>8 (80%)</td>
<td>2 (20%)</td>
<td>&lt;0.001</td>
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<tr>
<td></td>
<td>≥50</td>
<td>89</td>
<td>6425.7 (1258-20281.6)</td>
<td>5 (6%)</td>
<td>84 (94%)</td>
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<td>77</td>
<td>95.5 (67.4-96.3)</td>
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<td>67 (87%)</td>
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<td>IgG level</td>
<td>&lt;500</td>
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<td>1156.5 (373.4-24333.3)</td>
<td>4 (22%)</td>
<td>14 (78%)</td>
<td>0.038</td>
<td>15</td>
<td>49.3 (12.9-96)</td>
<td>5 (33%)</td>
<td>10 (67%)</td>
<td>0.133</td>
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<tr>
<td></td>
<td>≥500</td>
<td>78</td>
<td>6538.7 (1257.1-20457.2)</td>
<td>4 (5%)</td>
<td>74 (95%)</td>
<td></td>
<td>68</td>
<td>94.7 (66.7-96.3)</td>
<td>10 (15%)</td>
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<td>All immune criteria for vaccination met prior to COVID vaccine</td>
<td>Not met</td>
<td>35</td>
<td>916.5 (115.8-19124)</td>
<td>7 (20%)</td>
<td>28 (80%)</td>
<td>0.002</td>
<td>29</td>
<td>61 (7.5-96.2)</td>
<td>11 (38%)</td>
<td>18 (62%)</td>
<td>0.002</td>
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<tr>
<td></td>
<td>Met</td>
<td>48</td>
<td>7638 (2322.9-20340.1)</td>
<td>0 (0%)</td>
<td>48 (100%)</td>
<td></td>
<td>43</td>
<td>95.7 (87.5-96.4)</td>
<td>3 (7%)</td>
<td>40 (93%)</td>
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<tr>
<td>Immune suppression with Tacrolimus/cyclosporine or Ruxolitinib</td>
<td>Yes</td>
<td>46</td>
<td>4430.4 (319-15835.9)</td>
<td>5 (11%)</td>
<td>41 (89%)</td>
<td>&gt;0.99</td>
<td>40</td>
<td>89.3 (18.1-96.1)</td>
<td>13 (32%)</td>
<td>27 (68%)</td>
<td>0.036</td>
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<td>No</td>
<td>103</td>
<td>5019.8 (936.8-17529.2)</td>
<td>11 (11%)</td>
<td>92 (89%)</td>
<td></td>
<td>84</td>
<td>94.6 (56.6-96.3)</td>
<td>13 (15%)</td>
<td>71 (85%)</td>
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<tr>
<td>Steroids</td>
<td>Yes</td>
<td>21</td>
<td>543.9 (16.1-5786.1)</td>
<td>7 (33%)</td>
<td>14 (67%)</td>
<td>0.002</td>
<td>16</td>
<td>21 (0-74)</td>
<td>9 (56%)</td>
<td>7 (44%)</td>
<td>0.001</td>
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<td></td>
<td>No</td>
<td>128</td>
<td>5960.4 (952-20340.1)</td>
<td>9 (7%)</td>
<td>119 (93%)</td>
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<td>108</td>
<td>95.1 (56.6-96.4)</td>
<td>17 (16%)</td>
<td>91 (84%)</td>
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#### Autologous HCT

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<th>Variable</th>
<th>Group</th>
<th>N</th>
<th>Median (IQR)</th>
<th>&lt; 50</th>
<th>&gt; 50</th>
<th>P-value</th>
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<th>Median (IQR)</th>
<th>&lt; 30</th>
<th>&gt; 30</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Time groups per type of cellular treatment</td>
<td>Early Auto</td>
<td>20</td>
<td>718 (16.1-6300.1)</td>
<td>7 (35%)</td>
<td>13 (65%)</td>
<td>0.001</td>
<td>15</td>
<td>44.8 (80-83.2)</td>
<td>7 (47%)</td>
<td>8 (53%)</td>
<td>0.025</td>
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<td>Late Auto</td>
<td>41</td>
<td>2512.3 (673-10598.8)</td>
<td>1 (2%)</td>
<td>40 (98%)</td>
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<td>37</td>
<td>85.9 (52.3-96.3)</td>
<td>5 (14%)</td>
<td>32 (86%)</td>
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<td>CD4 Count</td>
<td>&lt;200</td>
<td>6</td>
<td>242 (35.4-407.9)</td>
<td>2 (33%)</td>
<td>4 (67%)</td>
<td>0.612</td>
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<td>30.1 (12.8-53.5)</td>
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<td>2 (50%)</td>
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<td>≥200</td>
<td>23</td>
<td>2390.8 (407-9879.6)</td>
<td>5 (22%)</td>
<td>18 (78%)</td>
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<td>19</td>
<td>80.5 (15.6-96.4)</td>
<td>5 (26%)</td>
<td>14 (74%)</td>
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<td>CD19 Count</td>
<td>&lt;50</td>
<td>9</td>
<td>10.5 (4.4-419.4)</td>
<td>6 (67%)</td>
<td>3 (33%)</td>
<td>0.001</td>
<td>6</td>
<td>15.6 (0-41.4)</td>
<td>3 (30%)</td>
<td>5 (30%)</td>
<td>0.318</td>
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<td>≥50</td>
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<td>3123.9 (901.1-9520.1)</td>
<td>1 (5%)</td>
<td>19 (95%)</td>
<td></td>
<td>17</td>
<td>80.5 (41.6-96.3)</td>
<td>4 (24%)</td>
<td>13 (76%)</td>
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<tr>
<td>IgG level</td>
<td>&lt;500</td>
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<td>487 (28.4-1143.3)</td>
<td>4 (29%)</td>
<td>10 (71%)</td>
<td>0.091</td>
<td>12</td>
<td>59.2 (1.8-79.1)</td>
<td>4 (33%)</td>
<td>8 (67%)</td>
<td>0.433</td>
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<td>2645.4 (584.9-10405.8)</td>
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<td>32 (91%)</td>
<td></td>
<td>30</td>
<td>79.4 (46-95.1)</td>
<td>6 (20%)</td>
<td>24 (80%)</td>
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<tr>
<td>All immune criteria for vaccination met prior to COVID vaccine</td>
<td>Not met</td>
<td>13</td>
<td>554.5 (21.2-2390.8)</td>
<td>4 (31%)</td>
<td>9 (69%)</td>
<td>0.327</td>
<td>19</td>
<td>44.8 (18.1-82.9)</td>
<td>3 (27%)</td>
<td>8 (73%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td></td>
<td>Met</td>
<td>11</td>
<td>3602.3 (1403.2-8277.5)</td>
<td>1 (9%)</td>
<td>10 (91%)</td>
<td></td>
<td>19</td>
<td>86.6 (53.8-96.3)</td>
<td>2 (22%)</td>
<td>7 (78%)</td>
<td>0.317</td>
</tr>
</tbody>
</table>

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| Daratumumab | | | | | | | |
|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| No          | 41          | 2757.1 (419.4-21010.8) | 6 (15%) | 35 (85%) | 33 | 85.9 (51.5-96.5) | 6 (18%) | 27 (82%) |
| Yes         | 12          | 513 (226.6-1486.9) | 1 (8%) | 11 (92%) | >0.99 | 11 | 59 (8.9-81.4) | 4 (36%) | 7 (64%) | 0.253 |
| No          | 49          | 3292.7 (655-19499) | 7 (14%) | 42 (86%) | 41 | 80.5 (44.8-96.3) | 8 (20%) | 33 (80%) |
Figure 1

1A

1B

Anti-SARS-CoV-2 spike IgG

1C

Anti-SARS-CoV-2 spike IgG (immune reconstitution status)

Neutralizing antibody (immune reconstitution status)

Neutralizing antibody

*** ** * ns ns

% inhibition

Neg Pos

% inhibition
Predictors of Humoral Response to SARS-CoV-2 Vaccination after Hematopoietic Cell Transplantation and CAR T Cell Therapy

Roni Tamari, Ioannis Politikos, David A Knorr, et al.

Blood Cancer Discov  Published OnlineFirst September 13, 2021.

Updated version  Access the most recent version of this article at: doi: 10.1158/2643-3230.BCD-21-0142

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