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Letter

Efficacy of a third SARS-CoV-2 mRNA vaccine dose among hematopoietic cell transplantation, CAR T cell, and BiTE recipients

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Hematopoietic cell transplantation (HCT) and cellular therapy (CT) recipients have poor outcomes after developing COVID-19 (Spanjaart et al., 2021, Meir et al., 2021). HCT and/or CT recipients also have blunted responses to SARS-CoV-2 vaccines (Dhakal et al., 2021). Several groups, including ours, have indicated a response rate of 50%–80% among HCT recipients and 20%–30% among chimeric antigen receptor (CAR) T cell recipients (Dhakal et al., 2021, Meir et al., 2021, Abid and Abid, 2021). The general population has demonstrated sustained and durable immune responses to an additional mRNA vaccine dose ("booster") to counteract the waning immunity to the primary vaccination series (Nemet, Kliker, Lustig, Zuckerman, Erster, Cohen, Kreiss, Alroy-Preis, Regev-Yochay, Mendelson, Mandelboim, 2022). It remains unknown whether HCT and/or CT recipients respond to the additional primary or booster dose and/or seroconvert after booster.

We examined serological responses to the third vaccine dose among those HCT (both allogeneic HCT [alloHCT] and autologous HCT [autoHCT]), CAR T cell, and bispecific T cell engager (BiTE) recipients who had not seroconverted after the primary series with an mRNA-based (BNT162b2 [Pfizer-BioNTech] or mRNA1273 [Moderna]) vaccine. We included patients who had not seroconverted after the primary series (no response per the assay cutoff described below), had received a booster, and had serological response examined after the primary series as well as after the booster. Patients were required to have at least 28 days between the second dose and the booster and 14 days to antibody titer testing after receiving the booster. Patients with SARS-CoV-2 antibody testing within 2 weeks of the booster or COVID-19 infection any time prior to the booster dose were excluded from the analysis.

The AdviseDx SARS-CoV-2 IgG II assay was used to detect immunoglobulin G (IgG) antibodies (Ab) directed against the receptor-binding domain (RBD) of the SARS-CoV-2 S1 subunit of the spike protein, and the assay was performed on Abbott's ARCHITECT i2000SR System. This semiquantitative assay has consistently been correlated with neutralizing immunity. The cutoff value is 50 AU/mL, with < 50 AU/mL values reported as negative and a maximum value of 50,000 AU/mL. Patient-, disease-, and treatment characteristics were compared based on vaccine response by using Wilcoxon's rank-sum for continuous variables and Fisher's exact test for the categorical variables. A p value < 0.05 at two-sided testing was considered significant. The study was approved by the Medical College of Wisconsin Institutional Review Board, and informed consents were obtained from the patients.

A total of 75 patients (alloHCT, n = 30; autoHCT, n = 26; CAR-T, n = 10; BiTE, n = 9) did not seroconvert after their primary vaccination series with an mRNA-based vaccine (Table S1). Among these, 44 (59%) developed protective antibodies after the booster. The seroconversion rates were 63%, 58%, 40%, and 67% among autoHCT, alloHCT, CAR-T, and BiTE recipients, respectively. Median age among seroconverters with booster was older than among non-seroconverters (70 [31–77] versus 66 [35–81]; p = 0.04). Although there were no significant differences in seroconversion rates between males and females, the antibody titers were significantly lower in males compared to females (p = 0.046). Also, corticosteroid usage was significantly lower among seroconverters than non-seroconverters (41% versus 59%; p = 0.04) and the antibody titers were significantly lower among corticosteroid recipients (p = 0.012) (Figure S1). No significant differences were noted in the three vaccine strategies (BNT162b2, mRNA1273, and mix-and-match).

We found no significant differences in seroconversion based on age, interval between immunotherapy and vaccination, corticosteroid usage, active graft versus host disease (in alloHCT), immunosuppression status (including active immunosuppressant use), disease relapse prior to booster, absolute lymphocyte count (ALC), or CD4, CD8, or IgG levels. Among autoHCT recipients, the response to the booster in patients with multiple myeloma (MM) was significantly superior compared to the response in patients with lymphoma (80% versus 30%; p = 0.01).

Three other studies so far have reported the efficacy of a third vaccine dose exclusively in alloHCT recipients. Redjoul et al. (2021) showed that a third dose of BNT162b2 mRNA vaccine led to a significant increase in anti-SARS-CoV-2 IgG antibodies (from 737 AU/mL to 11,099 AU/mL; p = 0.00069) in 42

alloHCT recipients. Maillard et al. (2022) showed that 41% of patients (29/70) developed a detectable response after the third dose after not responding to the first two doses. Canti et al. (2022) showed that 87% of alloHCT recipients (33/38) seroconverted after three vaccine doses and that there were strong correlations between Abs against RBD and neutralizing Ab titers.

Continued blunted humoral responses even after the booster among CAR T recipients are concerning and are in alignment with other reported literature. Our systematic review reported antibody responses in 40 CAR-T recipients from five studies and demonstrated a pooled response rate of only 30% (Abid and Abid, 2021). Bange et al. (2021) showed that patients with T cell depletion have the highest risk of death independent of cancer subtype or presence of B cell responses. In contrast, patients with hematologic malignancies and higher $CD8^+$ T cell numbers have higher detectable SARS-CoV-2-specific T cell responses and improved survival. These findings provide insight into why severely lymphodepleted CAR T recipients, independent of their remission status, may have high mortality. Given that the COVID-19-attributable mortality rate in the European Bone Marrow Transplant (EBMT) registry study was 41% (Spanjaart et al., 2021), and continued blunted humoral responses despite one and two additional vaccine doses demonstrated in a recent study (Sesques et al., 2022), the results of our analysis, showing at least partial success in seroconversion with booster among CAR T recipients, are encouraging.

Several factors, indigenous to CAR T recipients, may account for consistently blunted vaccine responses, including pre-existing, profound immunosuppression. Heavily pretreated status, often including prior HCT, lymphodepletion chemotherapy, bridging chemotherapy, prolonged B cell aplasia, preceding on-target off-tumor toxicities such as cytokine release syndrome, and immune effector cell-associated neurotoxicity syndrome requiring corticosteroids and tocilizumab may contribute to blunted vaccine responses (Meir et al., 2021, Abid, 2022).

Given the lack of data in this regard, a substantial seroconversion rate to the booster vaccine dose among BiTE recipients is encouraging. This finding aligns with other recent studies that demonstrate a superior response to primary vaccine series among recipients of BCMA-targeted CAR T compared to those directed against CD19 (Abid and Abid, 2021). This is also likely a function of the underlying disease. Our results are congruent with other data which show that patients with myeloma respond better to mRNA vaccines than do patients with lymphoma (Meir et al., 2021, Van Oekelen et al., 2021).

Besides the retrospective design, limitations of our study include the lack of a concurrent control group without HCT and/or CT and BiTE. Other limitations include the lack of serial assessment of humoral response at various time points, robust immune reconstitution data, B cell numbers, and T cell responses. Further, no conclusion may be drawn from our results in terms of protection against clinical breakthrough infection—especially of the B.1.1.529 (omicron) variant of SARS-CoV-2. Although our study did not sequence the viral genome to the variant level, eight patients received a booster either after or on November 26, 2021, when the World Health Organization (WHO) named omicron as a variant of concern. However, emerging data have demonstrated the importance of a third BNT162b2 vaccine dose and have shown higher neutralization efficiency (by a factor of 100) against omicron after the third dose than after the second dose (Nemet, Kliker, Lustig, Zuckerman, Erster, Cohen, Kreiss, Alroy-Preis, Regev-Yochay, Mendelson, Mandelboim, 2022), including in patients with cancer (Zeng, Evans, Chakravarthy, Qu, Reisinger, Song, Rubinstein, Shields, Li, Liu, 2022).

Overall, our findings can guide patients and physicians, particularly in the setting of emerging highly transmissible variants of concern. Vaccination remains the cornerstone in protecting vulnerable HCT and/or CT patients against COVID-19, and these results strongly support the role of the booster and/or third vaccine dose and pave the way for larger prospective studies. Other novel strategies, such as the use of monoclonal antibodies that have demonstrated efficacy against the omicron variant, either authorized for preexposure prophylaxis or to prevent severe COVID-19, may be utilized earlier in this immunocompromised patient cohort. Although the results of prospective vaccine studies such as CIBMTR study SC21-07/BMT-CTN 2101 are awaited, other mitigation approaches, including vaccination of close contacts, social distancing, and masks, should be continued for the foreseeable future.

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.ccell.2022.02.010.

DECLARATION OF INTERESTS

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REFERENCES

Abid, M.B. (2022). Early immunomodulators with CAR T-cell immunotherapy in the COVID-19 era. Lancet Oncol. *23*, 16–18.

Abid, M.A., and Abid, M.B. (2021). SARS-CoV-2 vaccine response in CAR T-cell therapy recipients: A systematic review and preliminary observations. Hematol. Oncol.

Bange, E.M., Han, N.A., Wileyto, P., Kim, J.Y., Gouma, S., Robinson, J., Greenplate, A.R., Hwee, M.A., Porterfield, F., Owoyemi, O., et al. (2021). $CD8^+$ T cells contribute to survival in patients with COVID-19 and hematologic cancer. Nat. Med. *27*, 1280–1289.

Canti, L., Ariën, K.K., Desombere, I., Humblet-Baron, S., Pannus, P., Heyndrickx, L., Henry, A., Servais, S., Willems, E., Ehx, G., et al. (2022).

Antibody response against SARS-CoV-2 Delta and Omicron variants after third-dose BNT162b2 vaccination in allo-HCT recipients. Cancer Cell, S1535-6108(22)00057-5.

Dhakal, B., Abedin, S., Fenske, T., Chhabra, S., Ledeboer, N., Hari, P., and Hamadani, M. (2021). Response to SARS-CoV-2 vaccination in patients after hematopoietic cell transplantation and CAR T-cell therapy. Blood *138*, 1278–1281.

Maillard, A., Redjoul, R., Klemencie, M., Labussière Wallet, H., Le Bourgeois, A., D'Aveni, M., Huynh, A., Berceanu, A., Marchand, T., Chantepie, S., et al. (2022). Antibody response after 2 and 3 doses of SARS-CoV-2 mRNA vaccine in allogeneic hematopoietic cell transplant recipients. Blood *139*, 134–137.

Meir, J., Abid, M.A., and Abid, M.B. (2021). State of the CAR-T: Risk of Infections with Chimeric Antigen Receptor T-Cell Therapy and Determinants of SARS-CoV-2 Vaccine Responses. Transplant Cell Ther *27*, 973–987.

Nemet, I., Kliker, L., Lustig, Y., Zuckerman, N., Erster, O., Cohen, C., Kreiss, Y., Alroy-Preis, S., Regev-Yochay, G., Mendelson, E., and Mandelboim, M. (2022). Third BNT162b2 Vaccination Neutralization of SARS-CoV-2 Omicron Infection. N. Engl. J. Med. *386*, 492–494.

Redjoul, R., Le Bouter, A., Parinet, V., Fourati, S., and Maury, S. (2021). Antibody response after third BNT162b2 dose in recipients of allogeneic HSCT. Lancet Haematol. *8*, e681–e683.

Sesques, P., Bachy, E., Ferrant, E., Safar, V., Gossez, M., Morfin-Sherpa, F., Venet, F., and Ader, F. (2022). Immune response to three doses of mRNA SARS-CoV-2 vaccines in CD19-targeted chimeric antigen receptor T cell immunotherapy recipients. Cancer Cell *40*, S1535-6108(22)00012-5.

Spanjaart, A.M., Ljungman, P., de La Camara, R., Tridello, G., Ortiz-Maldonado, V., Urbano-Ispizua, A., Barba, P., Kwon, M., Caballero, D., Sesques, P., et al. (2021). Poor outcome of patients with COVID-19 after CAR T-cell therapy for B-cell malignancies: results of a multicenter study on behalf of the European Society for Blood and Marrow Transplantation (EBMT) Infectious Diseases Working Party and the European Hematology Association (EHA) Lymphoma Group. Leukemia *35*, 3585–3588.

Van Oekelen, O., Gleason, C.R., Agte, S., Srivastava, K., Beach, K.F., Aleman, A., Kappes, K., Mouhieddine, T.H., Wang, B., Chari, A., et al.; PVI/Seronet team (2021). Highly variable SARS-CoV-2 spike antibody responses to two doses of COVID-19 RNA vaccination in patients with multiple myeloma. Cancer Cell *39*, 1028–1030.

Zeng, C., Evans, J.P., Chakravarthy, K., Qu, P., Reisinger, S., Song, N.J., Rubinstein, M.P., Shields, P.G., Li, Z., and Liu, S.L. (2022). COVID-19 mRNA booster vaccines elicit strong protection against SARS-CoV-2 Omicron variant in patients with cancer. Cancer Cell *40*, 117–119.

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Supplemental information

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Table S1. Patient-, disease- and vaccine characteristics of immunotherapy recipients by booster response among initial non-seroconverters.

Table S1: Patient-, disease- and vaccine characteristics of immunotherapy recipients by booster response among initial non-seroconverters			
All patients (n=75)	**Vaccine response** [1]		***P*** [2]
	Seroconversion to booster dose (N=44, 59%)	**No seroconversion to booster dose** (N=31, 41%)	
Characteristics			
Median age, y (range)	70 (31-77)	66 (35-81)	**.041**
Gender • Male, n (%) • Female, n (%)	 27 (53%) 17 (71%)	 24 (47%) 7 (29%)	.14
Interval between HCT/CT & vaccination • <12 months • ≥12 months	 19 (56%) 25 (61%)	 15 (44%) 16 (39%)	.66
Median interval between 2nd dose and booster, days (range)	172 (28-296)	165 (93-223)	.35
Median interval between booster and humoral response assessment, days (range)	58 (14-140)	47 (18-127)	.83
Corticosteroid use at the time of booster	9 (41%)	13 (59%)	**.04**
Median IgG level (range) / uL < booster	436 (40-1320)	401 (223-1185)	.63
Median ALC level (range) / uL < booster	0.88 (0.20-4.48)	0.82 (0.04-8.42)	.96
HCT/CT type • AlloHCT • AutoHCT • CAR T • Myeloma BiTE	 15 (58%) 19 (63%) 4 (40%) 6 (67%)	 11 (42%) 11 (37%) 6 (60%) 3 (33%)	.60
Vaccine type -BNT162b2 x 3 (n=43) -mRNA1273 x 3 (n=23) -Heterologous mRNA vaccines (n=9) • Primary BNT162b2 series → mRNA1273 booster (n=6) • Primary mRNA1273 series → BNT162b2 booster (n=3)	 27 (63%) 13 (57%) 4 (44%) 3 (50%) 1 (33%)	 16 (37%) 10 (43%) 5 (56%) 3 (50%) 2 (67%)	.59
Subset of AutoHCT (n=30)			
All patients	**19 (63%)**	**11 (37%)**	N/A
Median age, y (range)	67 (48-77)	62 (54-71)	0.14
Interval between auto-HCT & vaccination • <12 months • ≥12 months	 5 (62%) 14 (64%)	 3 (38%) 8 (36%)	.90
Auto-HCT indication • Lymphoma • Myeloma	 3 (30%) 16 (80%)	 7 (70%) 4 (20%)	**.01**

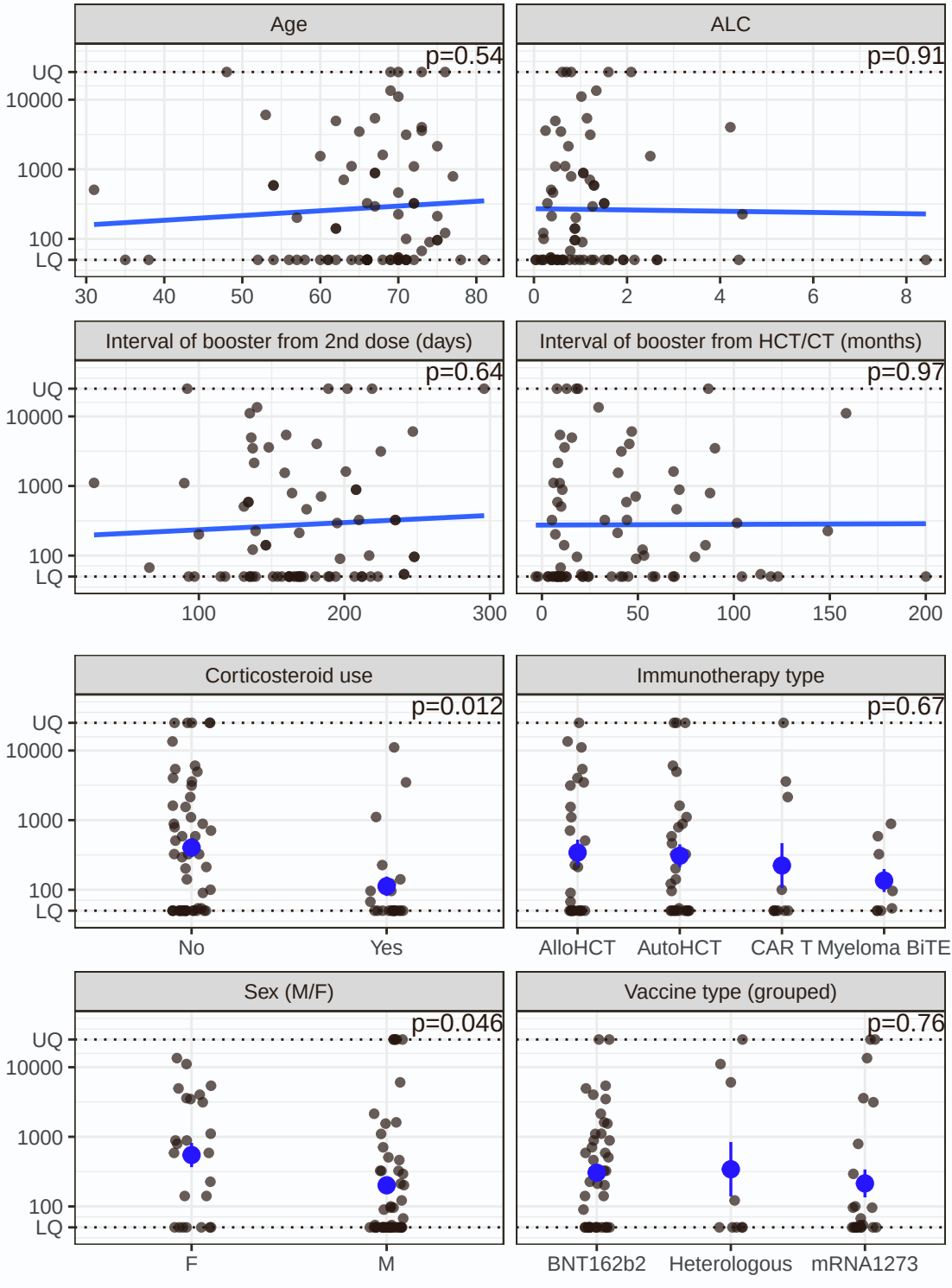
Disease relapse prior to booster	11 (73%)	4 (27%)	.26
Corticosteroid use at the time of booster	3 (43%)	4 (57%)	.37
Median IgG level (range) / uL < booster	436 (40-1320)	236 (223-562)	.36
Median ALC level (range) / uL < booster	0.80 (0.20-1.51)	0.60 (0.04-8.42)	.47
Subset of AlloHCT (n=26)			
All patients	**15 (58%)**	**11 (42%)**	N/A
Median age, y (range)	70 (31-75)	66 (38-78)	0.18
Interval between allo-HCT & vaccination • <12 months • ≥12 months	 5 (50%) 10 (62%)	 5 (50%) 6 (38%)	.69
IST status • Off IST • Ongoing IST drugs*	 3 (50%) 12 (60%)	 3 (50%) 8 (40%)	.90
Active GVHD at the time of booster **	11 (55%)	9 (45%)	.89
Disease relapse prior to booster	8 (62%)	5 (38%)	.69
Corticosteroid use at the time of booster	4 (44%)	5 (66%)	.42
Median IgG level (range) / uL < booster	549 (82-751)	439 (236-592)	.61
Median ALC level (range) / uL < booster	1.1 (0.4-4.5)	1.1 (0.4-2.6)	.82
Median CD4 count (range) /uL < booster	182 (101-265)	176 (76-684)	.90
Median CD8 count (range) /uL < booster	170 (51-289)	348 (84-1795)	.33
Subset of CAR T recipients (n=10)			
All patients	**4 (40%)**	**6 (60%)**	N/A
Median age, y (range)	72 (70-75)	68 (35-81)	0.26
CAR T target antigen • BCMA (n=1) • CD19 (n=2) • CD19.20 (n=7)	 1 (100%) 0 3 (43%)	 0 2 (100%) 4 (57%)	.47
Disease relapse prior to booster	4 (57%)	3 (43%)	.20
Corticosteroid use at the time of booster	0	2 (100%)	.47
Median IgG level (range) / uL < booster	482 (337-628)	503 (350-1185)	.80
Median ALC level (range) / uL < booster	0.5 (0.2-2.1)	1.6 (0.2-4.4)	.41
Median CD4 count (range) /uL < booster	74 (73-109)	1352 (405-3470)	.10
Median CD8 count (range) /uL < booster	144 (85-203)	1007 (616-1053)	.20
Subset of MM BiTE recipients (n=9)			
All patients	**6 (67%)**	**3 (33%)**	N/A
Median age, y (range)	68 (54-75)	70 (66-71)	.99
BiTE construct • BCMA (n=7) • GPRC5D (n=2)	 5 (71%) 1 (50%)	 2 (29%) 1 (50%)	.99
Disease relapse prior to booster	4 (67%)	2 (33%)	.99
Corticosteroid use at the time of booster	2 (50%)	2 (50%)	.52
Median IgG level (range) / uL < booster	405 (40-563)	401 (225-562)	.99
Median ALC level (range) / uL < booster	1.0 (0.36-1.51)	0.5 (0.04-1.92)	.70

Abbreviations: HCT, Hematopoietic cell transplantation; CT, Cellular therapy; ALC, absolute lymphocyte count; IgG, immunoglobulin G; GVHD, graft-versus-host disease; IST, immunosuppressive therapy; N/A, not applicable; CAR T, chimeric antigen receptor T-cells; BCMA, B-cell maturation antigen; BiTE, bispecific T-cell engager; GPRC5D, G Protein-Coupled Receptor Class C Group 5 Member D.

[1] Median (Range); n (%)
[2] Wilcoxon rank sum exact test; Fisher's exact test.

* IST in vaccine responders (n = 12) and non-responders (n = 8) [agents included ruxolitinib, sirolimus, everolimus, tacrolimus, cyclosporin, mycophenolate moefetil, prednisone, ibrutinib, either alone or in combination with other agents].
** Active acute or chronic GVHD defined as either active signs or symptoms of GVHD or ongoing IST drugs used to treat GVHD. Ongoing use of GVHD prophylaxis in the absence of signs or symptoms of GVHD was not considered active GVHD. Group off IST consisted of patients off all systemic medications to treat or prevent GVHD for ≥2 weeks.

Figure S1. Humoral immune responses to mRNA-based SARS-CoV-2 vaccine booster in a cohort of HCT, CAR T cell and BiTE recipients. The AdviseDx SARS-CoV-2 IgG II assay was used to detect immunoglobulin G (IgG) antibodies directed against the receptor-binding domain of SARS-CoV-2 S1 subunit of the spike (S) protein and was performed on Abbott's ARCHITECT i2000SR System. The cutoff value was 50 AU/mL, with <50 AU/ml values reported as negative (LQ – lower limit of quantification) and a maximum value of 25,000 AU/mL (UQ – upper limit of quantification). Titer values were truncated to the quantification limits, and log-transformed. The relationship with continuous covariates was summarized with a linear regression line and corresponding p-value. For categorical predictors, the blue dot showed the mean with standard error of the mean (SEM) error bars, and the p-values were from the analysis of variance (ANOVA). In the panel labeled "corticosteroid use," the anti-S IgG titers were significantly lower among corticosteroid recipients as compared to those who did not receive corticosteroids (p=0.012). Similarly, in the panel labeled "sex (M/F)," the anti-S IgG titers were significantly lower among males as compared to females (p=0.046). There were no statistically significant differences in the quantitative IgG titers by age, absolute lymphocyte count (ALC), intervals between immunotherapy and vaccine booster, and between second dose and booster, immunotherapy type (HCT/CT), and vaccine strategies.


Age
p=0.54
ALC
p=0.91
Interval of booster from 2nd dose (days)
p=0.64
Interval of booster from HCT/CT (months)
p=0.97
Corticosteroid use
p=0.012
Immunotherapy type
p=0.67
Sex (M/F)
p=0.046
Vaccine type (grouped)
p=0.76
UQ
10000
1000
100
LQ
No
Yes
AlloHCT
AutoHCT
CAR T
Myeloma BiTE
F
M
BNT162b2
Heterologous
mRNA1273