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Supplemental information

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

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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**

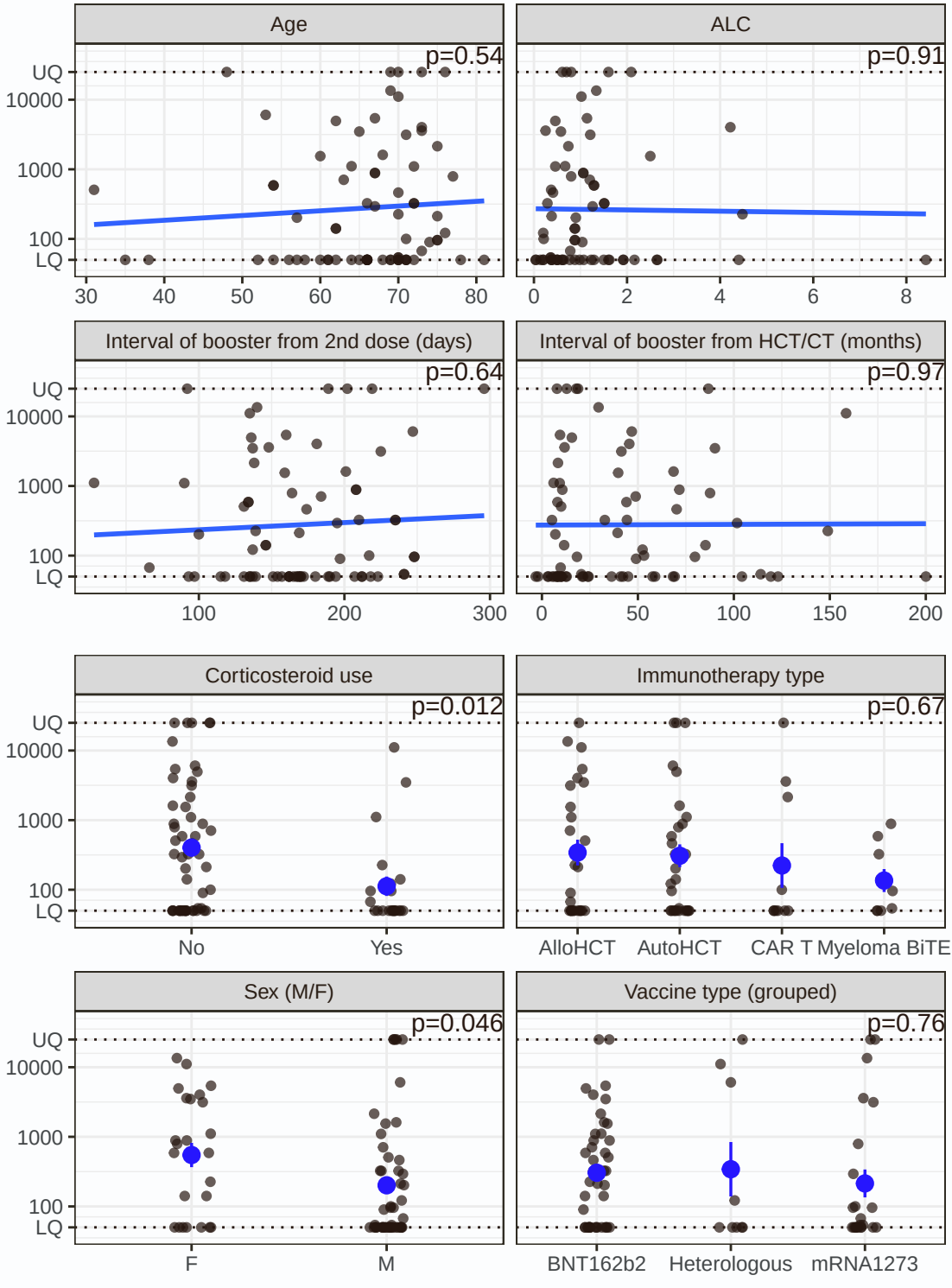
Disease relapse prior to booster	11 (73%)	4 (27%)	.26
Corticosteroid use at the time of booster	3 (43%)	4 (57%)	.37
Median IgG level (range) / uL < booster	436 (40-1320)	236 (223-562)	.36
Median ALC level (range) / uL < booster	0.80 (0.20-1.51)	0.60 (0.04-8.42)	.47
Subset of AlloHCT (n=26)			
All patients	**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