Letters

RESEARCH LETTER

Antibody Response to COVID-19 Vaccination in Adults With Hematologic Malignant Disease

The effectiveness of COVID-19 vaccination remains unknown in patients with hematologic malignant disease who have an impaired humoral immunity from both treatment and disease. Phase 3 registration studies of COVID-19 vaccines excluded patients with immunosuppression or immunosuppressive therapies.[1,2] Despite this, professional organizations suggest vaccination, or even its prioritization, for patients with cancer.[3] As the US Centers for Disease Control loosens pandemic-related precautions for vaccinated people, a better understanding of the vaccine response among patients with hematologic malignant disease is critical.

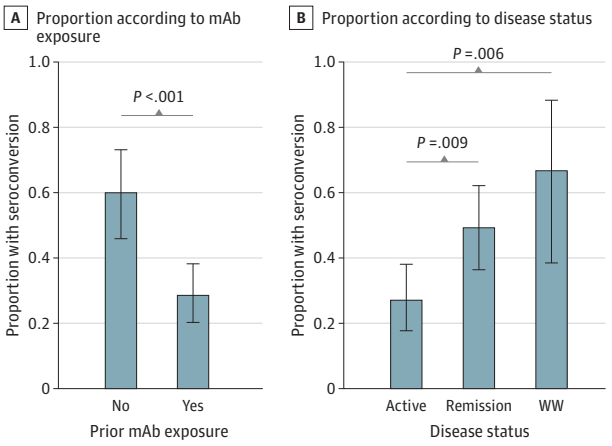
Methods | We conducted a retrospective study of adults with hematologic malignant disease who were vaccinated with 1 of 3 COVID-19 vaccines authorized by the US Food and Drug Administration between February and April of 2021. Eligible patients were identified by a search in the institutional electronic medical record. The study was approved by the institutional review board at Rhode Island Hospital, which waived written informed consent because data collected were part of standard care. Anti-COVID-19 antibodies were assessed with the qualitative SARS-CoV-2 Total Antibody Test (IgG or IgM against receptor binding domain [RBD], Wondfo USA), SARS-CoV-2 IgG (IgG against nucleocapsid protein, Abbott), the semiquantitative Abbott AdviseDx SARS-CoV-2 IgG II (IgG against RBD), and Abbott AdviseDx SARS-CoV-2 IgM (IgM against spike protein).[4] Binary variables were compared using

Table. Patient Characteristics Associated With Seroconversion

Variable	No. (%)			Unadjusted *P* value
	All patients	Post-vaccination seroconversion	No seroconversion	
No.	160	63	97	
Age, median (IQR)	72 (65-79)	71 (64-79)	73 (66-79)	.60
Sex				.33
Female	74 (47)	26 (41)	48 (49)	
Male	86 (54)	37 (59)	49 (51)	
Disease				.37
Indolent B-cell lymphoma	34 (21)	12 (19)	22 (23)	
Aggressive B-cell lymphoma	58 (36)	19 (30)	39 (40)	
Plasma cell disorder	24 (15)	14 (22)	10 (10)	
Other lymphoma	15 (9)	6 (10)	9 (9)	
Myeloid cancer	10 (6)	5 (8)	5 (5)	
CLL	19 (12)	7 (11)	12 (12)	
Disease status				.002
Active	82 (51)	22 (35)	60 (62)	
In remission	63 (39)	31 (49)	32 (33)	
Watchful waiting/never treated	15 (9)	10 (16)	5 (5)	
Monoclonal antibody exposure	105 (66)	30 (48)	75 (77)	<.001
White blood cell count in 10^9/L, median (IQR)	5.8 (4.4-8)	6.3 (4.7-9)	5.5 (4.2-7.6)	.15
Lymphocyte count in 10^9/L, median (IQR)	1.1 (1.1-1.7)	1.5 (1-1.9)	0.8 (0.5-1.3)	<.001
COVID-19 vaccine				.004
Pfizer-BioNTech	96 (60)	32 (52)	64 (66)	
Moderna	50 (31)	28 (45)	22 (23)	
Johnson & Johnson	11 (7)	1 (2)	10 (10)	
Undetermined	2 (1)	1 (2)	1 (1)	
Weeks from first vaccine to test, median (IQR)	8 (6-11)	9 (7.3-11.7)	7 (5.4-9.9)	.03
Months from last treatment to vaccine, median (IQR)	0 (0-12)	8 (0-25.4)	0 (0-3.9)	.005
>12 mo from last treatment	32 (25)	22 (59)	10 (12)	<.001

Abbreviations: CLL, chronic lymphocytic leukemia; IQR, interquartile range.

Figure. Proportion of Vaccinated Patients With Hematologic Cancers Who Attain Postvaccination Seroconversion on the Qualitative IgG/IgM Assay



A, Prior monoclonal antibody exposure. B, Active disease, remission, or watchful waiting (WW) status at the time of vaccination; error bars indicate exact binomial 95% CIs.

Fisher exact tests, and continuous variables using rank-sum tests; *P* values were adjusted for multiple testing (5 hypotheses) using Bonferroni correction, using $P < .01$ as an indicator of statistical significance.

Results | We examined response to COVID-19 vaccines in 160 patients with hematologic cancers; median (IQR) age was 72 (65-79) years and 86 (54%) were male (**Table**). One hundred and five (66%) patients had received a B-cell–depleting monoclonal antibody, most commonly rituximab (n = 85), daratumumab (n = 9), obinutuzumab (n = −7), or bispecific CD3/CD20 antibodies (n = 12). Sixty-three patients (39%, binomial exact 95% confidence interval [CI], 32%-47%) demonstrated seroconversion as evidenced by a positive SARS-CoV-2 total antibody assay. For the quantitative IgG assay (n = 47), patients with a negative qualitative assay result had median anti-COVID-19 IgG quantity of 8 AU/mL (interquartile range [IQR], 0.1-50.0 AU/mL), whereas those with a positive qualitative assay result had median 4289 AU/mL (IQR, 2661-12 586 AU/mL). Response to COVID-19 vaccine by the qualitative assay was significantly less frequent (30 of 105 [29%]) among patients previously exposed to B-cell/plasma cell-depleting monoclonal antibodies (risk difference [RD], 31%; 95% CI, 16%-47%; $P < .001$; **Figure**, A). It was significantly less frequent for patients with active malignant disease (22 of 88 [27%]) compared with those in remission after treatment (31 of 63 [49%]; RD, 22%; 95% CI, 7%-38%; $P = .009$) or those under watchful waiting without any receipt of cancer therapy (67%; RD, 40%; 95 CI, 14%-66%; $P = .006$, Figure B). Longer time from last chemotherapy administration to vaccination was associated with increased rates of seroconversion (median 8.4 vs 0 months, $P = .005$). Among patients who completed chemotherapy longer than 12 months before vaccination (n = 32), 69% showed seroconversion, compared with 24% among those who were vaccinated within 12 months of last treatment (n = 97). The quantitative antibody response to the COVID-19 vaccine was also lower among patients with exposure to B-cell/plasma cell-depleting antibodies (median IgG: 20.7 AU/mL and 489 AU/mL among those with or without antibody exposure, respectively; median IgM S/C index: 0.055 and 0.16, respectively) and those with active malignant disease (median IgG: 28 AU/mL, 1911 AU/mL, and 1950 AU/mL for those with active malignant disease, in remission after treatment, or under watchful waiting, respectively; median IgM signal-to-cutoff [S/C] ratio index: 0.03, 0.12, and 0.16, respectively). Three patients developed COVID-19 infections after vaccination (with no detectable post-vaccination antibodies) with 1 death.

Discussion | Prior studies demonstrate a nearly 100% rate of seroconversion in healthy participants receiving mRNA or adenovirus-based vaccines against COVID-19.[5,6] This study is limited by its retrospective design and possible selection bias of patients who underwent clinical testing for postvaccination seroconversion. The qualitative test for anti-COVID-19 antibodies does not inform about T-cell-based immunity and has not been correlated with clinical outcomes related to potential COVID-19 infection. However, our findings raise a concern that patients with hematologic cancers, particularly those receiving B-cell–depleting immunotherapy, may not gain adequate protection from vaccination, and as observed in our cohort, may still develop a potentially fatal infection. These patients may benefit from ongoing protective measures, including masks, social distancing, and screening. Consideration should be made to prioritizing vaccination for family members and caregivers to protect the patients themselves. With possible infection, we recommend testing regardless of vaccination status, and treatment with COVID-19–specific monoclonal antibody therapy.

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Accepted for Publication: July 12, 2021.

Published Online: August 11, 2021. doi:10.1001/jamaoncol.2021.4381

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Supervision: Ollila, Olszewski.

Conflict of Interest Disclosures: Dr Olszewski reported research funding from Genentech, TG Therapeutics, Celldex Pharmaceuticals, and Precision Bio; grants from Acrotech Pharma, Adaptive Biotechnologies outside the submitted work. No other disclosures were reported.

Additional Contributions: In addition to the listed authors, we acknowledge the following individuals for their assistance with this study, none of whom were compensated for his or her contributions and all of whom agree to include their names here: John L. Reagan, MD (Brown Alpert School of Medicine); Peter Barth, MD (Brown Alpert School of Medicine); Rabin Niroula, MD; Gerard J. Nau, MD, PhD (Brown Alpert School of Medicine); Rani Chudasama, MD (Brown Alpert School of Medicine); Inna Yakirevich, NP (Division of Hematology/Oncology, Rhode Island Hospital); and Christopher Elco, MD, PhD (Brown Alpert School of Medicine).

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