ANTIBODY RESPONSES AGAINST SARS-COV2 VARIANTS AFTER BOOSTER VACCINATION IN PATIENTS WITH B CELL NON-HODGKIN LYMPHOMA AND CHRONIC LYMPHOCYTIC LEUKEMIA

Andres Chang[1,2], Lilin Lai[2,3,4], Akil Akhtar[2], Susanne L. Linderman[2], Victor M. Orellana-Noia[1], Manpreet Saini[2,5], Rajesh Valanparambil[2], Kristie A. Blum[1], Pamela B. Allen[1], Mary J. Lechowicz[1], Jason Romancik[1], Amy A. Ayers[1,6], Colin B. O'Leary[1], Michael C. Churnetski[1], Melissa Kives[1], Ajay K. Nooka[1], Jean L. Koff[1], Madhav V. Dhodapkar[1], Mehul S. Suthar[2,3], Jonathon B. Cohen[1], and Rafi Ahmed[2]

[1]Department of Hematology and Medical Oncology, Winship Cancer Institute, [2]Emory Vaccine Center, Department of Microbiology and Immunology, [3]Department of Pediatrics, and [4]Yerkes National Primate Research Center, Emory University School of Medicine, Atlanta, GA. [5]International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi, India. [6]Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

EMORY WINSHIP CANCER INSTITUTE
National Cancer Institute-Designated Comprehensive Cancer Center

Background

Non-Hodgkin lymphoma and chronic lymphocytic leukemia (NHL/CLL) patients are at high risk of severe disease and death from COVID-19 disease.

NHL/CLL patients have reduced antibody response after the initial two-dose mRNA vaccine course.

We sought to characterize the antibody response after booster vaccination, focusing on Omicron variants.

Methods

- Antibody binding to the spike protein of multiple SARS-CoV-2 variants was measured with a multiplex assay.
- Peripheral B cells counts by flow cytometry.
- Focus reduction neutralization tests using a live virus was used to measure neutralizing activity against SARS-CoV-2 variants.
- Correlation with clinical variables was assessed.

Table 1. Clinical characteristics

	n	%
Gender		
Female	28	41.8
Male	39	58.2
Age (yrs)		
Median (IQR)	69	(59-75)
Range	37-92	
Race		
White	55	82.1
Non-White	10	14.9
Unknown	2	3
Lymphoma subtype		
CLL/SLL	37	55.2
NHL (all subtypes)	30	44.8
Vaccine manufacturer - initial series		
Pfizer	25	37.3
Moderna	41	61.2
Janssen	1	1.5
Vaccine manufacturer - booster		
Pfizer	23	34.3
Moderna	44	65.7
Booster vaccine		
Homologous	60	89.6
Heterologous	7	10.4

**Includes (n): DLBCL (12), FL (7), MCL (4), WM (3), MZL (1), BL (1), PTCL (1), CLL/DLBCL (1)*

Results

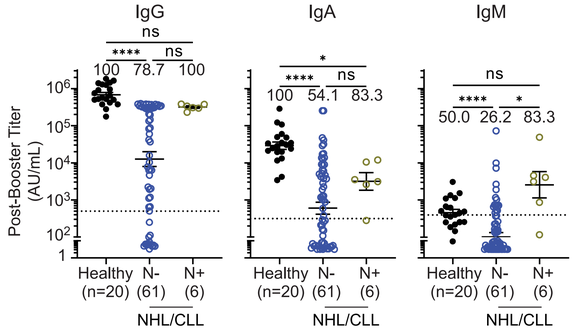


Fig 1. Lower anti-spike antibody binding titers after booster vaccination are observed in NHL/CLL patients compared to healthy controls. Numbers = percent seropositivity rate.

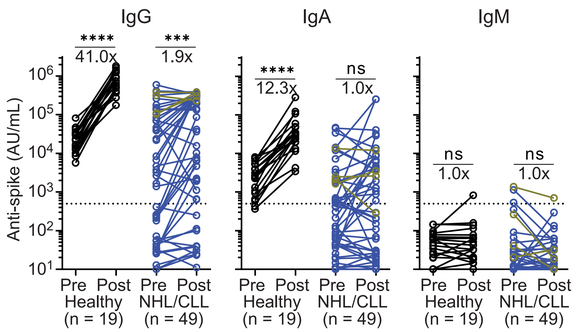


Fig 2. Diminished effect of booster vaccination on antibody titers in NHL/CLL patients. Numbers = median fold change from pre-booster titer after receipt of a booster vaccine.

Table 2. Univariate analyses of clinical variables associated with booster response

	Responder (n) / Evaluable (n)	% Responder	OR	95% CI	P
Prior anti-CD20 monoclonal antibody					
No	6 / 9	66.7	ref	-	-
Yes	12 / 27	44.4	0.4	0.08 -1.94	0.26
≤1 year pre-booster	3 / 14	21.4	ref	-	-
>1 year pre-booster	9 / 13	69.2	8.25	1.45 - 46.86	**0.02**

Responder: anti-spike IgG ≥ 500 AU/mL and a 0.5 log10 increase in antibody titers at least 3 days after booster vaccination. Analysis excludes patients in the "high-titer" group.

No significant correlation was observed with age, gender, race, lymphoma subtype, prior cytotoxic chemotherapy, prior cellular therapy, ongoing Bcl-2 inhibitor, or ongoing BTKi therapy.

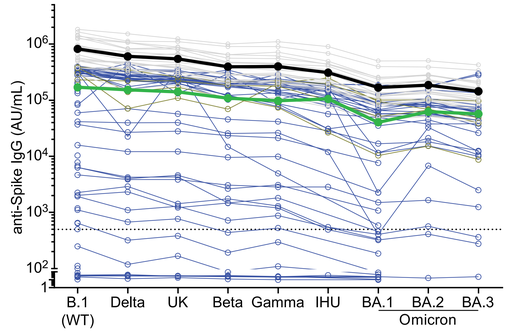


Fig 3. Reduced IgG binding titers against SARS-CoV-2 variant spike. Gray = healthy, blue = N- NHL/CLL, gold = N+ NHL/CLL. Median titers in healthy (black) and NHL/CLL (green) are shown.

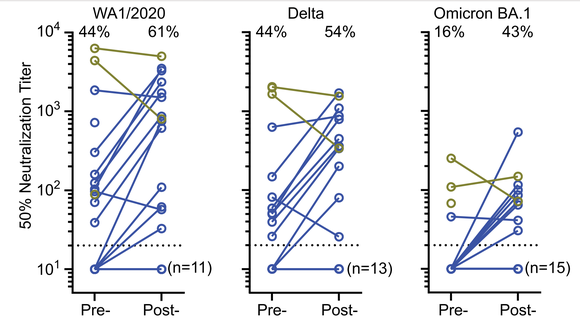


Fig 4. Minimal induction of live-virus neutralization titers against Omicron after booster vaccination.

Conclusions:

- Antibody binding and live-virus neutralization titers against SARS-CoV-2 and its variants including Omicron remain lower than healthy controls in NHL/CLL patients even after booster vaccination.
- Bivalent booster vaccines should be recommended for NHL/CLL patients and close contacts.
- Anti-SARS-CoV-2 prophylactic and treatment agents remain key to protect these patients.

Funding

This work was partly supported by Winship Cancer Institute institutional funds, Emory University internal funds, NIH U54CA260563, P30CA138292, P51OD011132, U19AI090023, R35CA197603, and HHSN272201400004C, the American Society of Hematology Research Training Award for Fellows, and the Leukemia & Lymphoma Society Specialized Center of Research Award.

Contact: Andres.chang@emory.edu
Twitter: @ChangMDPhD