Supplemental material – BLD-2021-012443

Detail of the population subgroups

Subjects were separated into several cohorts: 1) BCL patients on active treatment with anti-CD20 (i.e., rituximab, Obinutuzumab), anti-CD19 (Chimeric antigen receptor therapy against CD19 or tafasitamab-cxix), or Bruton tyrosine kinase inhibitors (BTKi) -based therapies (either as single agent or in combination with chemotherapy drugs or small molecule inhibitors [e.g., venetoclax, lenalidomide, BTKi, etc.]); or chimeric antigen receptor T-cells against CD19 antigen (CART-19); 2) BCL patients on surveillance who had completed B-cell directed treatments within 9 months of vaccination 3) BCL patients on observation either > 9 months after B-cell directed treatments, or treatment naïve. The following volunteers and patients served as controls: 1) Health care providers fully vaccinated, 2) Health care providers previously infected with the SARS-CoV-2 virus, 3) patients with other lymphoid malignancies (i.e., Hodgkin's lymphoma [HL], Multiple myeloma [MM] or T-cell lymphoma [TCL]) therapy and fully vaccinated, and 4) an elderly population of fully vaccinated individuals living in long-term care facilities, tested for antibody production recruited by KSL Diagnostics.

Antibody testing with ability to discern between response to vaccine or to SARS-CoV-2 infection

Testing for antibodies were performed on serum at the KSL Diagnostics laboratories. Cryopreserved patient and control samples from RPCCC were submitted to the testing laboratory, in which personnel was blinded to the study assignment of each sample. Detection of antibodies to spike protein domain 1, the receptor-binding domain (RBD) was performed using KSL chemiluminescence immunoassays (CLIA). The CLIA assay provides qualitative detection of human IgA, IgG, or IgM antibodies to SARS-CoV-2. The test was authorized by NY State and EUA on November 25, 2020 under Project ID No. 84341. Testing of IgA allowed us to evaluate B cell reconstitution, with the presence of IgG class switch. IgM was done to exclude re-infection after vaccination.

Samples are incubated with a magnetic bead that is coated with structural protein (S1 domain) from SARS-CoV-2. After all unbound materials are washed away by magnetic separation, the acridinium ester marker is added for incubation. Following a wash step, SARS-CoV-2 antibodies are detected with a substrate that produces a luminescence reaction with the acridinium ester. Luminescence intensity of acridinium ester is

proportionate to the amount of antibody against novel coronavirus. The test result is expressed by critical value index (COI). If the sample value is less than 0.8 COI, no SARS-CoV-2 antibody is detected. If the value is within 0.8~1.0 COI, the SARS-CoV-2 antibody is undetermined. If the value is greater than 1.0 COI, then SARS-CoV-2 antibody is detected.

As previously described, all SARS-CoV-2 infected patients are found to have higher titer of antibodies against both SARS nucleocapsid protein and spike protein, whereas vaccinated people were only found to have raised antibody against the spike protein.[1,2] To identify patients who raise antibody specifically from vaccine, serology testing for SARS nucleocapsid protein IgA, IgM, and IgG antibodies were also tested to rule out the potential SARS-CoV-2 infection before or during the time of vaccination.

Detection of SARS-CoV-2 nucleocapsid antibodies (NAbs) was performed using the Platelia SARS-CoV-2 total antibody kit (BioRad #72710). The Platelia SARS-CoV-2 Total Antibody assay[3,4] is a one-step antigen capture Enzyme-Linked Immunosorbent Assay (ELISA) for the qualitative detection of total antibodies (including IgM/ IgA/IgG) to SARS-CoV-2 nucleocapsid protein. For this standard ELISA assay, a cut-off control R4 as greater than 0.5 and less than 1.4 should be detected. Specimen results are calculated using the S/CO ratio: Specimen ratio = Specimen OD / OD_MR4. Values are defined as: S/CO <0.8 as negative for the presence of anti-SARS-CoV-2 NAbs; Samples with $0.8 \leq x < 1.0$ are equivocal for the presence of SARS-CoV-2 NAbs; samples ≥ 1.0 are positive for the presence of SARS-CoV-2 Nabs.

Tables

Table 1SM

Characteristic	**All RPCCC patients**	**BCL on/after treatment with B cell directed therapies**	**Lymphoid disorders receiving other treatments or on observation**
	N = 86 (100%)	**N = 65 (75.6%)**	**N = 21 (24.4%)**
Sex (female/male)	41/45 (47.7% F)	28/37 (43% F)	13/8 (61%)
Age: median (range)	70 (35-91)	72 (47-91)	67 (35-88)
Vaccines			
BNT162b2 (Pfizer BioNTech)	40 (47%)	33 (51%)	7 (33%)

mRNA-1273 (Moderna)	45 (52%)	31 (48%)	14 (67%)
J&J	1 (1%)	1 (1%)	0
Disease			
CLL	19 (22%)	15 (23%)	4 (19.5%)
DLBCL	18 (21%)	18 (28%)	0
FL	14 (16%)	10 (15%)	4 (19.5%)
MZL	11 (12%)	9 (14%)	2 (9%)
MCL	8 (9%)	7 (11%)	1 (5%)
WM	5 (6%)	4 (6%)	1 (5%)
HL	2 (2%)	0	2 (9%)
AITL	2 (2%)	0	2 (9%)
CTCL	2 (2%)	0	2 (9%)
ALCL	1 (1.6%)	0	1 (5%)
Grey zone lymphoma	1 (1.6%)	1 (1.5%)	0
Hairy-cell leukemia	1 (1.6%)	0	1 (5%)
Primary CNS lymphoma	1 (1.6%)	1 (1.5%)	0
MM	1 (1.6)	0	1 (5%)

Table 1SM : characteristics of the population

Legend: CLL chronic lymphocytic leukemia, DLBCL diffuse large B-cell lymphoma, FL follicular lymphoma, MZL marginal zone lymphoma, MCL mantle cell lymphoma, WM Waldenstrom macroglobulinemia, HL hodgkin lymphoma, AITL angioimmunoblastic T-cell lymphoma, CTCL cutaneous T cell lymphoma, ALCL anaplastic large cell lymphoma, CNS central nervous system and MM multiple myeloma.

Table 2SM

Variable	All BCL receiving anti-B cell N=65 (100%)	Anti B cell Tx < 9 mo N=52 (80%)	Anti B cell Tx >9 mo N=13 (20%)
Line of treatment prior or during the vaccine			
First	40 (62%)	30 (58%)	10 (77%)
Second	12 (18%)	18 (35%)	1 (8%)
Third or more	13 (20%)	4 (7%)	2 (15%)
Condition of the lymphoma			
CR/PR	59 (91%)	48 (92%)	11 (85%)
SD/PD	6 (9%)	4 (8%)	2 (15%)
Type of treatment			
Anti-CD20 mab single agent	7 (11%)	5 (10%)	2 (15%)
B-cell directed + chemotherapy	37 (57%)	26 (50%)	11 (85%)
Anti-CD20 + small molecules	9 (14%)	9 (17%)	0
BTKi	12 (18%)	12 (23%)	0

Table 2SM. BCL Timing of B-cell directed therapy and vaccine. Small molecules were lenalidomide and venetoclax.

Legend: CR complete remission; PR partial remission; SD stable disease; PD progressive disease; mab monoclonal antibodies; BTKi Bruton Tyrosine Kinases.

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4. Tré-Hardy M, Wilmet A, Beukinga I, et al. Analytical and clinical validation of an ELISA for specific SARS-CoV-2 IgG, IgA, and IgM antibodies. *J Med Virol.* 2021;93(2):803-811.