LYMPHOMA
RESEARCH • FOUNDATION

Proceedings of the COVID-19 Vaccine Panel:

A LYMPHOMA RESEARCH FOUNDATION WHITE PAPER

Introduction

On March 1, 2021, the Lymphoma Research Foundation convened an expert panel of medical and scientific advisors to discuss the current state of research regarding the COVID-19 vaccine and people with lymphoma. The panel discussed recommendations for oncologists caring for people with these cancers, as well as related scientific research and education programming. This white paper reflects the panel discussion and the state of research as of the date of the original panel meeting. Oncologists and other healthcare providers are encouraged to consult the most recent guidance from the Centers for Disease Control and Prevention (CDC) and other federal healthcare agencies when making treatment recommendations. Patients should consult with their own healthcare providers when making treatment decisions.

For additional information, members of the lymphoma community are also encouraged to visit the Lymphoma Research Foundation's COVID-19 Learning Center at lymphoma.org/covid19 and/or contact the LRF Helpline at 800-500-9976 or helpline@lymphoma.org.

Panel Members

Andrew D. Zelenetz, MD, PhD
Panel Chair
Medical Oncologist and Medical Director, Quality Informatic
Memorial Sloan Kettering Cancer Center
Chair, Lymphoma Research Foundation Scientific Advisory Board

Ranjana Advani, MD
Saul A Rosenberg Professor of Lymphoma
Stanford Cancer Institute

Ash A. Alizadeh, MD, PhD
Associate Professor, Divisions of Oncology and Hematology
Stanford Cancer Institute

Lindsey R. Baden, MMSc, MD
Associate Professor of Medicine, Harvard Medical School
Associate Professor and Director of Clinical Research
Department of Medicine, Infectious Diseases
Brigham and Women's Hospital

Nilanjan Chatterjee, PhD
Bloomberg Distinguished Professor
Department of Biostatistics, Bloomberg School of Public Health
Department of Oncology, School of Medicine
Johns Hopkins University

Andrew M. Evens, DO, MSc, FACP
Professor of Medicine, Rutgers Robert Wood Johnson Medical School
Associate Director for Clinical Services, Rutgers Cancer Institute of New Jersey
Director, Lymphoma Program, Division of Blood Disorders and Medical Director, Oncology Service Line, RWJ Barnabas Health

Leo I. Gordon MD, FACP
Abby and John Friend Professor of Cancer Research
Professor of Medicine
Co-Director, Hematologic Malignancy Program
Medical Director, John and Lillian Mathews Cellular Therapy Laboratory
Robert H. Lurie Comprehensive Cancer Center
Northwestern University Feinberg School of Medicine

Thomas M. Habermann, MD
Professor of Medicine
Consultant, Division of Hematology
Mayo Clinic, Rochester

John P. Leonard, MD
Richard T. Silver Distinguished Professor of Hematology and Medical Oncology
Senior Associate Dean for Innovation and Initiatives
Executive Vice-Chair, Joan and Sanford I. Weill Department of Medicine
Weill Cornell Medicine

Izidore S. Lossos, MD
Professor of Medicine
Director, Lymphoma Program and Head, Hematological Malignancies Site Disease Group
Sylvester Comprehensive Cancer Center
University of Miami

Peter Martin, MD
Associate Professor of Medicine
Chief, Lymphoma Program
Weill Cornell Medicine

Sonali M. Smith, MD
Elwood V. Jensen Professor in Medicine
Chief, Section of Hematology/Oncology
University of Chicago Medicine
Chair-Elect, Lymphoma Research Foundation Scientific Advisory Board

Barbara Pro, MD
Professor of Medicine, Division of Hematology and Oncology
Clinical Director, Lymphoma Program
Robert H. Lurie Comprehensive Cancer Center
Northwestern University Feinberg School of Medicine

Michael Satlin, MD
Associate Professor of Medicine
William Randolph Hearst Foundation
Clinical Scholar in Microbiology and Infectious Diseases
Weill Cornell Medicine

Kerry J. Savage, MD, MSc
Professor, Medical Oncology
University of British Columbia
BC Cancer Agency

Laurie H. Sehn MD, MPH
Chair, Lymphoma Tumour Group
BC Cancer Centre for Lymphoid Cancer
Clinical Professor of Medicine
Division of Medical Oncology
University of British Columbia

Adrian Wiestner, MD, PhD
Senior Investigator, Laboratory of Lymphoid Malignancies
National Heart, Lung, and Blood Institute
National Institutes of Health

Presentations

Introduction and Panel Overview

Dr. Andrew Zelenetz, Panel Chair and Chair of the LRF Scientific Advisory Board (SAB), opened the meeting by presenting current data around vaccine response in patients with hematologic malignancies. Earlier studies in patients with hematologic malignancies have demonstrated impaired influenza and pneumococcal vaccine responses, with pooled data showing a protection rate of 30% following vaccination with a single dose of the H1N1 vaccine, compared with protection rates of over 85% in the general population.[1] Attenuated protection from vaccination in onco-hematological patients was also reported for H1N3, influenza B, and pneumococcal vaccines. Furthermore, minimal seroconversion for influenza was observed in patients after treatment with rituximab. Based on these data, assuming no significant vaccine safety issues, vaccination is worthwhile in onco-hematological patients despite the impaired response; however, vaccination should not be expected to eliminate disease risk or reduce risk to the same degree expected in the general population. Physicians may consider alternative strategies, such as creating mini herds through vaccination of household contacts and potentially prophylactic use of antiviral drugs (including anti-SARS monoclonal antibodies) to minimize the morbidity and mortality from such diseases in this high-risk population.

Dr. Zelenetz explained that the presented vaccination data preceded many potentially immunosuppressive targeted therapies for B-cell lymphoma, which has important implications given the role of B-cells in immunologic memory. Current treatments include anti-CD20 antibodies, Bruton tyrosine kinase inhibitors (BTKi), BCL2 BH3 mimetics, PI3K inhibitors (PI3Ki), bispecific antibodies, and chimeric antigen receptor (CAR) T-cells. Immunosuppressive effects of anti-CD20 antibodies are long-lasting B-cell depletion (often ≥9 months), with extended exposure leading to immunoglobulin depletion and risk of long-term hypogammaglobulinemia. Similarly, BTKis diminish B-cell activity while causing B-cell apoptosis and a gradual decline in immunoglobulins. Treatment with BCL2 BH3 mimetics leads to decreased B-cells and T-cells, a dual mechanism which may further diminish patient ability to fight infection. In contrast, PI3Ki treatment results in impaired B-cell development and antigen response but can also increase autoimmunity. Finally, CAR T cell therapy and bispecific antibodies cause profound B-cell depletion, and hypogammaglobulinemia is common.

Vaccine responses vary in patients with lymphoma and other hematological malignancies, and general principles cannot be applied. Response can be influenced by the vaccine technology, underlying disease, and prior treatment. Furthermore, limited data exist on the impact of targeted therapy and CAR T cell therapy on vaccine response. Some therapies may require specific consideration due to a more profound impact on humoral responses. Dr. Zelenetz stressed the need for effective communication to prevent false confidence in patients. Patients who receive a vaccine often believe they have mounted a protective immune response despite education to the contrary, which may lead to changes in behavior such as less masking, more social interaction, or increased likelihood of travel. Physicians must communicate that patients should not change their behavior following COVID-19 vaccination.

Epidemiology of COVID-19 in Lymphoma Patients

Dr. Nilanjan Chatterjee presented several studies that assessed the risks around COVID-19 in lymphoma patients. A national Veterans' Affairs study of COVID-19 infection prevalence and outcome in over 20 thousand cancer patients from the US VA healthcare system's electronic health record showed a higher prevalence in Black and Hispanic/Latino populations and patients with hematological cancer, indicating an increased risk for lymphoma patients.[2] A smaller retrospective multi-center study investigated determinants of COVID-19 outcomes specifically in lymphoma patients.[3] Most of the patients had B-cell non-Hodgkin lymphoma and had received a lymphoma treatment within one year. The authors reported increased risk associated with age and relapsed/refractory lymphoma. However, the survival rate for lymphoma patients without these high-risk factors is comparable to the general population. The UK OpenSAFELY study represents the largest synthetic population cohort available to study COVID-19.[4] Within this large cohort, a detailed investigation of COVID-19 mortality risk was performed in the general population considering different factors, such as age and gender, and comorbid conditions, including cancers. Patients with hematological malignancy were at greater risk for death in a trend reflective of less time from diagnosis. Patients with non-hematological cancers were generally at lower risk for COVID-19 death than those with hematological malignancy.

Dr. Chatterjee reported that although more data are needed to examine the impact of these factors on COVID-19 illness and mortality, specifically among lymphoma patients, his group created a model to predict individual and community-level risk for COVID-19 mortality in the United States.[5] The model combines individual COVID-19 mortality risk factors, including those described for hematological cancers, with community-level risk to provide an estimate of individual-level absolute risk. Dr. Chatterjee concluded his presentation with a demonstration of the prediction model, highlighting that factors such as age, weight, race, and comorbidities substantially increase risk for patients with a recent diagnosis of hematological cancer. A wide variation in COVID-19 mortality risk may exist among this patient population depending on other individual risk factors.

COVID-19 and Patients with Lymphoma or Chronic Lymphocytic Leukemia (CLL)

Dr. Adrian Wiestner introduced the panel to the underlying science behind vaccine response in B-cell malignancies through his presentation on the current literature. Dr. Wiestner first discussed a meta-analysis reporting a COVID-19 mortality risk of 32% for patients with lymphoma and 31% with CLL.[6] Smaller studies focusing specifically on CLL patients reported similar COVID-19 fatality rates.[7–9] In a small case series, the fatality of infection was 29% and the 2 CLL patients that died of COVID-19, had just completed multi-agent therapy that included anti-CD20 antibodies.[9] Additionally, in two multicenter studies, the effect of BTK inhibitors on mortality was reported as absent when treatment was halted and as beneficial when BTKis were continued.[7,8]

To understand vaccine response in people with hematological malignancy, Dr. Wiestner reviewed a study investigating the vaccine efficacy of the adjuvanted recombinant zoster vaccine (Shingrix).[10] About one-third of the patients were vaccinated during immunosuppressive cancer treatments, and the remaining patients were vaccinated after treatment completion. Humoral vaccine responses were reduced for the combined hematological malignancy population and more so for the B-cell non-Hodgkin lymphoma and CLL sub-groups. No diagnosis-dependent difference was observed in the cellular vaccine response. Notably, the 2 vaccinated patients that developed herpes zoster had received a rituximab-containing regimen close to the time of vaccination.

Dr. Wiestner shared data from his group showing antibody response to influenza vaccination is possible in patients receiving BTKi; a seroconversion rate of 26% was determined after seasonal influenza vaccine in CLL patients treated with ibrutinib and overall, up to 74% of patients achieved seroprotective titers against influenza after vaccination.[11] To investigate the vaccine response rate for a new antigen versus a recall antigen, CLL patients that were treatment naïve or receiving BTKi were vaccinated against either recombinant hepatitis B or shingles.[12] De novo immune response to hepatitis B vaccine was nearly absent in CLL patients on BTKi and impaired in treatment-naïve patients. In contrast, recall immune response to the Shingrix vaccine was not significantly different between CLL patients on BTKi and treatment-naïve patients. The results demonstrate that vaccine response can depend on the administered vaccine and treatment status. In agreement with this data, high rates of humoral and T-cell responses to Shingrix vaccination occurred in patients with CLL on BTKi therapy without recent rituximab treatment.[13]

Of note, inhibition of BTK may be a therapeutic strategy to treat severe COVID-19 by targeting excessive host inflammation.[14] A small study showed better COVID-19 outcomes in patients treated with a BTKi and led to 2 confirmatory randomized controlled trials (Calavi program), which did not meet their primary endpoints.[15] Results of other trials with BTKi interventions in COVID infection are awaited. Another therapeutic strategy in immunodeficient patients could be convalescent plasma, which clinically benefitted a CLL patient with severe COVID-19.[16] The convalescent plasma had a uniquely high-titer of neutralizing antibody and led to a rapid clinical recovery. Investigating different preparations of convalescent plasma, these investigators found that neutralization titers can fluctuate greatly among convalescent plasmas, and concluded that the neutralizing activity should be tested in both plasma donors and recipients before therapy.

COVID-19 Vaccines

Dr. Mini Kamboj presented an overview of the three highly effective COVID-19 vaccines to the panel. The Pfizer BioNTech and Moderna mRNA vaccines demonstrated high efficacy against SARS-CoV-2 infection and the prevention of symptomatic COVID-19 illness, respectively.[17,18] The vaccines' real-world effectiveness has been demonstrated with reduced asymptomatic infection and continued efficacy in areas with predominant circulation of the B.1.1.7 variant.[19,20] Furthermore, the mRNA vaccines continue to have minimal adverse events reported in the real-world setting.[21,22] Emergency use authorization has recently been granted for Janssen's recombinant adenoviral vector COVID-19 vaccine.[23] The vaccine is replication-incompetent, which is critical for cancer patients because there is no risk of infection from the vaccine. Advantages over mRNA vaccines include its single-dose and easier handling. The vaccine is highly effective against moderate to severe COVID-19 illness in multiple regions, including those with predominant circulation of the B.1.351 variant. The Janssen vaccine offers a strong protection from severe illness, including variants, and the vaccine prevents asymptomatic infection.

The current Advisory Committee on Immunization Practices recommendations state no preference of one vaccine over another, vaccine efficacy is not directly comparable as the trials were performed in the context of different variants, and all vaccines offer strong protection against severe disease. Patients with a contraindication to the mRNA vaccine may receive the Janssen vaccine.[22] Vaccine efficacy will not be immediately available for certain populations because they were excluded from clinical trials, including people with cancer, children, and pregnant and breastfeeding individuals.

Vaccine response with anti-B cell antibodies is currently based on experience with other vaccines[24,25] Anti-CD20 therapies attenuate vaccine responses due to humoral immune responses being severely impaired from the rapid and prolonged B cell depletion that lasts at least 6-9 months. The theoretical benefit of offering the COVID-19 vaccine

to patients being treated with anti B-cell antibodies are the potential cellular-mediated vaccine responses, but data is lacking to support this. With high community infection rates, vaccination is recommended at the earliest opportunity, and if feasible, patients should be prioritized to receive the vaccine before starting therapy. Patient education and reinforcing nonpharmaceutical interventions (NPI) for infection prevention are essential to protect patients receiving anti-B cell antibodies.

Current Vaccine Recommendations

Dr. Laurie H. Sehn compiled the vaccine recommendations from the CDC, ASH, and NCCN. Many institutions have generated their own recommendations, taking these guidelines into account. Dr. Sehn explained that tables are helpful for practitioners to guide the timing of vaccine administration with respect to different treatments, and the Memorial Sloan Kettering Cancer Center's (MSKCC) recommendation document is very comprehensive and should be consulted when creating guidelines. Guidelines specific to patients with lymphoma are listed here.

CDC guidelines for immunocompromised persons

- Data on safety and efficacy not available
- Immunocompromised persons can receive if they have no contraindication for vaccination
- Immunocompromised persons must be properly counseled on possible diminished benefit and advised to maintain COVID precautions
- Antibody testing to assess post-vaccination immunity is not recommended
- Re-vaccination after immune competence is regained is not recommended (Dr. Sehn acknowledged that this recommendation may change as more of the population has become vaccinated and more vaccine becomes available and if data emerges on need for re-vaccination in this population)

ASH General Guidelines for Hematologic Malignancies

- Risk to benefit should be weighed for each patient, taking into account community risk
- Full vaccination is recommended at least 2-4 weeks prior to immunosuppressive therapy, transplant, or splenectomy (Dr. Sehn explained that this recommendation is based on data from the mRNA trials showing a minimum of 2 weeks for the vaccine response)
- In patients already receiving immunosuppressive therapy, consider vaccine 3-6 months post treatment for optimal benefit to obtain the maximal humoral and cellular response if the patient is at lower risk for COVID, although it is reasonable and safe to proceed regardless of anticipated benefit
- Influenza vaccine is also recommended in addition to influenza/COVID vaccination of all household contacts and caregivers

ASH Lymphoma-specific Guidelines

- Vaccination is recommended prior to initiating therapy when feasible
- Avoid highly immunosuppressive therapy prior to vaccination (rituximab, bendamustine, etc.)—consider alternatives, minimize cycles of treatment, and avoid maintenance
- Rituximab may blunt humoral immune response for a prolonged time after treatment, although T-cell responses may persist
- Delay treatment (esp. rituximab) until 2 weeks after second vaccine dose when feasible
- Recommended timing should take into account: COVID-19 risk, capacity to self-isolate, expected duration of treatment and immunosuppression, and vaccine availability

Discussion

Overall, panel members agreed that evidence is being generated rapidly and that the dynamics of the pandemic are continually shifting based on vaccination of the broader population and emergence of new variants, among other factors. The body of evidence used to generate the above guidelines continues to evolve and guidance presented here is in no way static. The current situation requires ongoing assessment of research as it is published and collaborative work to translate research outcomes to clinical guidance.

COVID-19 testing

Regarding COVID-19 testing, the CDC does not recommend retesting those who have tested positive and instead uses the 10- to 20-day rule of being symptom free. However, at many medical institutions, stricter policies have been put into place for transplants and infusions that require two consecutive negative tests as a test of cure. The stricter policies are based on data showing that patients with profound immunosuppression who have recently undergone hematopoietic stem-cell transplantation or received cellular therapies may shed viable SARS-CoV-2 for at least 2 months.[26] Currently, no consensus exists for determining active infection, and results can vary based on the CT count of the assay or detection of the positive versus negative strand. The small subset of individuals who develop a chronic persistent infection are commonly lymphoma patients who have had B-cell therapy. It was noted that some centers advocate for a sustained negative PCR as a test of cure for patients being treated for hematological malignancies.

Vaccination and treatment

Panelists discussed if they should recommend modifying treatment to allow patients first to get vaccinated. The panelists agree that treatment should not be modified for curative intent. If possible, panelists agree to avoid starting anti-CD20 therapy until after vaccination and consider different treatment choices, such as BTKi instead of rituximab (in appropriate clinical situations). Regarding maintenance therapy, it should be continued if given recently. Measuring lymphocyte subsets at Sloan Kettering revealed that patients who received rituximab consistently had zero B-cells around 6 months and started to recover around 9 months. Patients treated with CD20 antibody, a bispecific, or CAR-T cells may require a long time to recover immune function. Therefore, holding maintenance therapy is only useful if it was planned months ahead of time. These patients should receive the vaccination for the possible benefit from the innate immune response, but it is critical that they are counseled on impaired vaccine effectiveness and preventative measures must remain in place.

Generally, a second vaccine dose elicits a stronger immune response, and in vitro evidence indicates that 2 doses would protect more against variants. The Janssen vaccine has an ongoing trial for a second dose: FDA clearance was sought for the single-dose vaccine in the interest of time. The recommendation of waiting 2 weeks after the vaccination before the start of therapy if feasible but is somewhat arbitrary and could result in a long treatment delay, in particular for patients receiving the two-dose vaccine. For this reason, the Janssen vaccine may be more practical for these patients. Moreover, because the Janssen vaccine is replication-deficient, it can be administered to patients receiving targeted therapy as live-attenuated vaccines are generally contraindicated. Although probably not the optimal response time, a substantial immune response does appear after 7 days following inoculation with the mRNA vaccines while the earliest protection was observed at 7-11 days in the Janssen vaccine trial. After the 2-week window following vaccination, when an anti-CD20 antibody is given, cells that have differentiated to plasma cells may be protected, but memory B cells are at risk.

Vaccination counseling
Panelists are concerned that in areas of high community spread, vaccination could lead to infections due to patients' over-confidence resulting in risky behavior. Counseling patients about the lack of data and the likelihood of an impaired immune response is essential. Preventative measures and NPIs must be sustained. Furthermore, as guidelines emerge for vaccinated people, physicians must put them into context for the lymphoma patient population.

Important areas of discovery
Panelists agree that the underlying mechanism of risk for severe disease varies both in the general population and among patients with lymphoid malignancies, and there is no overarching theme which can help in identifying those at highest risk. A question remains if immunosuppression can be beneficial to prevent COVID-19 severe disease. However, some immunosuppressed individuals develop a chronic persistent infection. Importantly, lymphoma patients also respond differently to COVID-19 treatments; for example, not all respond to convalescent plasma. Panelists believe that these inconsistencies may be related to the timing of prolonged immunosuppression from lymphoma treatments and interventions aimed at preventing the inflammatory response characteristic of COVID-19. The role of the innate and adaptive immune response in COVID-19 infection and in the context of novel lymphoma therapies is also a consideration.

Currently, a protective COVID-19 antibody or T cell response is undefined, and the dominant response for the clinical vaccine remains undetermined. Furthermore, vaccine responses may not be shared among different vaccine platforms. Many infer that antibodies to the spike protein and nucleocapsid are surrogates for protection, but that has not been confirmed. The durability, waning, and consequence of vaccination have not yet been determined. Compounding the complexities presented by these gaps in knowledge, variants are not equal and partial protections with the full-length stabilized spike protein may require re-tooling of the vaccine through immune bridging versus large-scale trials.

Anticipating regulatory pathways and making recommendations in a more proactive rather than reactive manner would have been ideal, but this was impossible due to the lack of data around cancer patients in these trials. As clinical data are compiled, recommendations should be made on how to measure response in these patients. Challenges that remain include what to recommend to local community physicians and patients at the present, and how to inform future recommendations in a data-driven manner when data is rapidly changing.

Future research areas

- Clinical studies are needed with lymphoma patients to measure vaccine responses
  - — Vaccine companies have thus far not included many cancer patients in trials and none have made an effort to enroll patients with lymphoma
  - — Funding for such studies must be prioritized
  - — Several panelists have been attempting to measure vaccine response in their patients, but there is no prospective or concerted effort to do so
    - Lack of communication exists between vaccination sites and oncologists' offices regarding date and vaccine type
    - Single-institution studies are running their own, non-standardized tests with different timing
    - A common time to test and what to test should be established to synthesize data through a concerted effort
    - Compiling the data in its current format in a database such as the ASH COVID registry is very difficult, but concerted efforts could make it possible
    - Companies have been funding anti-SARS-CoV2 antibodies
- Development of a lymphoma-specific model that predicts COVID risk would be beneficial
  - — A wide variation in COVID-19 mortality risk exists among lymphoma patients, dependent on compounding risk factors, such as comorbidities, treatments, and regional risk
  - — By including lymphoma-specific risk factors, such as hypogammaglobulinemia, and with a large enough cohort of patients, Dr. Chatterjee's model could be refined specifically for patients with lymphoma
- Study on the benefit of prophylactic infusion of anti-SARS-CoV-2 monoclonal antibodies will require significant resources but is a good opportunity for collaboration and is particularly attractive for patients with therapy-induced loss of B-cells.

Recommendations

The panel discussed distinct areas where the Lymphoma Research Foundation might direct resources to ameliorate issues faced by the lymphoma community. Panelists agree that practical guidelines are necessary for physicians and patients, and recommendations are needed to gather information to inform updated guidelines as data-driven conclusions are made.

Practical recommendations for physicians and patients

- Develop sensible and evidence-based patient and provider guidelines
  - This should include directions and support for patients to retain records and information related to their inoculation
- Generate tables for general practitioners to guide vaccination around the timing of different treatments
  - Encourage physicians to consult ASH and the comprehensive Memorial Sloan Kettering Cancer Center recommendation document
- Create guidelines for different community spread levels and different local vaccination levels
- Create discussion points to communicate during vaccination counseling
- Advocate for a sustained negative PCR as a test of cure for patients being treated for hematological malignancies

Recommendations for data collection

- Continue to collect data as they emerge and refine recommendations accordingly
  - The panelists emphasized a need for ongoing communication between specialists to keep recommendations up to date
- Generate a specific list of questions for patients based on a common clinical scenario to assess if the existing data can answer these questions
  - For example: transplant patients, CHOMP patients, etc.
- Determine a consensus on how to gather the information needed for observational studies
  - Universal data on every patient is not needed, just sufficient information to predict how the lymphoma population will react to vaccination
  - Use commercial spike assays, and determine a common T cell assay
  - Because patients get vaccinated outside of oncology practices, provide patients and providers with a method to record vaccine received, date, time, and location of vaccination
  - Determine a common time to test and what to test (B- and T-cell vaccine responses) in the context of different treatments to synthesize data through a concerted effort
  - Determine a way to compile the data, perhaps through the ASH COVID registry

Other recommendations

- This meeting will likely need to be ongoing and convene at regular intervals to provide timely and evidence-based information to the lymphoma community
- Advocate that in the future, the evaluation of vaccine responses be part of new therapy development; in the phase 2 studies, there should be an evaluation of the response to de novo antigens and recall antigens
- The LRF could work to engage the current administration and other policymakers to drive federal funding to research projects that will benefit patients with cancer, especially those with hematological malignancies
- Consider engaging Israeli public health officials to share vaccination experience around vaccination of lymphoma patients at various oncological milestones during disease history

References

Additional references cited in the virtual meeting chat[27–29]

1. La Torre G, Mannocci A, Colamesta V, D'Egidio V, Sestili C, Spadea A. Influenza and Pneumococcal Vaccination in Hematological Malignancies: a Systematic Review of Efficacy, Effectiveness, and Safety. *Mediterr J Hematol Infect Dis.* 2016;8(1):e2016044. doi:10.4084/MJHID.2016.044
2. Fillmore NR, La J, Szalat RE, et al. Prevalence and Outcome of COVID-19 Infection in Cancer Patients: A National Veterans Affairs Study. *JNCI: Journal of the National Cancer Institute*. 2020;(djaa159). doi:10.1093/jnci/djaa159
3. Lamure S, Duléry R, Di Blasi R, et al. Determinants of outcome in Covid-19 hospitalized patients with lymphoma: A retrospective multicentric cohort study. *EClinicalMedicine*. 2020;27:100549. doi:10.1016/j.eclinm.2020.100549
4. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020;584(7821):430-436. doi:10.1038/s41586-020-2521-4
5. Jin J, Agarwala N, Kundu P, et al. Individual and community-level risk for COVID-19 mortality in the United States. *Nature Medicine*. 2021;27(2):264-269. doi:10.1038/s41591-020-01191-8
6. Vijenthira A, Gong IY, Fox TA, et al. Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients. *Blood*. 2020;136(25):2881-2892. doi:10.1182/blood.2020008824
7. Mato AR, Roeker LE, Lamanna N, et al. Outcomes of COVID-19 in patients with CLL: a multicenter international experience. *Blood*. 2020;136(10):1134-1143. doi:10.1182/blood.2020006965
8. Scarfò L, Chatzikonstantinou T, Rigolin GM, et al. COVID-19 severity and mortality in patients with chronic lymphocytic leukemia: a joint study by ERIC, the European Research Initiative on CLL, and CLL Campus. *Leukemia*. 2020;34(9):2354-2363. doi:10.1038/s41375-020-0959-x
9. Fürstenau M, Langerbeins P, De Silva N, et al. COVID-19 among fit patients with CLL treated with venetoclax-based combinations. *Leukemia*. 2020;34(8):2225-2229. doi:10.1038/s41375-020-0941-7
10. Dagnew AF, Ilhan O, Lee W-S, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis. *Lancet Infect Dis.* 2019;19(9):988-1000. doi:10.1016/S1473-3099(19)30163-X
11. Sun C, Gao J, Couzens L, et al. Seasonal Influenza Vaccination in Patients With Chronic Lymphocytic Leukemia Treated With Ibrutinib. *JAMA Oncol*. 2016;2(12):1656-1657. doi:10.1001/jamaoncol.2016.2437
12. Pleyer C, Ali MA, Cohen JI, et al. Effect of Bruton tyrosine kinase inhibitor on efficacy of adjuvanted recombinant hepatitis B and zoster vaccines. *Blood*. 2021;137(2):185-189. doi:10.1182/blood.2020008758
13. Zent CS, Brady MT, Delage C, et al. Short term results of vaccination with adjuvanted recombinant varicella zoster glycoprotein E during initial BTK inhibitor therapy for CLL or lymphoplasmacytic lymphoma. *Leukemia*. Published online October 30, 2020:1-4. doi:10.1038/s41375-020-01074-4
14. Roschewski M, Lionakis MS, Sharman JP, et al. Inhibition of Bruton tyrosine kinase in patients with severe COVID-19. *Science Immunology*. 2020;5(48). doi:10.1126/sciimmunol.abd0110

15. Astrazeneca. Update on CALAVI Phase II trials for Calquence in patients hospitalised with respiratory symptoms of COVID-19. Published November 12, 2020. Accessed March 6, 2021. https://www.astrazeneca.com/media-centre/press-releases/2020/update-on-calavi-phase-ii-trials-for-calquence-in-patients-hospitalised-with-respiratory-symptoms-of-covid-19.html

16. Honjo K, Russell RM, Li R, et al. Convalescent plasma-mediated resolution of COVID-19 in a patient with humoral immunodeficiency. *Cell Rep Med*. 2021;2(1):100164. doi:10.1016/j.xcrm.2020.100164

17. Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *New England Journal of Medicine*. 2020;383(27):2603-2615. doi:10.1056/NEJMoa2034577

18. Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *New England Journal of Medicine*. 2021;384(5):403-416. doi:10.1056/NEJMoa2035389

19. Hall VJ, Foulkes S, Saei A, et al. Effectiveness of BNT162b2 mRNA Vaccine Against Infection and COVID-19 Vaccine Coverage in Healthcare Workers in England, Multicentre Prospective Cohort Study (the SIREN Study). *SSRN: Preprints with the Lancet*. Published online February 22, 2021. doi:10.2139/ssrn.3790399

20. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. *New England Journal of Medicine*. 2021;0(0):null. doi:10.1056/NEJMoa2101765

21. Shimabukuro T, Nair N. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine. *JAMA*. 2021;325(8):780-781. doi:10.1001/jama.2021.0600

22. ACIP Meeting. Presented at the: March 1, 2021. https://www.youtube.com/watch?v=1hcB6cqSVxY

23. JANSSEN BIOTECH, INC. *COVID-19 Vaccine Ad26.COV2.S VAC31518 (JNJ-78436735)*. FDA VRBPAC Briefing Document; 2021:1-118. Accessed March 6, 2021. https://www.fda.gov/media/146219/download

24. Yri OE, Torfoss D, Hungnes O, et al. Rituximab blocks protective serologic response to influenza A (H1N1) 2009 vaccination in lymphoma patients during or within 6 months after treatment. *Blood*. 2011;118(26):6769-6771. doi:10.1182/blood-2011-08-372649

25. Bedognetti D, Zoppoli G, Massucco C, et al. Impaired response to influenza vaccine associated with persistent memory B cell depletion in non-Hodgkin's lymphoma patients treated with rituximab-containing regimens. *J Immunol*. 2011;186(10):6044-6055. doi:10.4049/jimmunol.1004095

26. Aydillo T, Gonzalez-Reiche AS, Aslam S, et al. Shedding of Viable SARS-CoV-2 after Immunosuppressive Therapy for Cancer. *New England Journal of Medicine*. 2020;383(26):2586-2588. doi:10.1056/NEJMc2031670

27. Abdul-Jawad S, Baù L, Alaguthurai T, et al. Acute Immune Signatures and Their Legacies in Severe Acute Respiratory Syndrome Coronavirus-2 Infected Cancer Patients. *Cancer Cell*. 2021;39(2):257-275.e6. doi:10.1016/j.ccell.2021.01.001

28. Lamure S. High incidence of persistent Covid-19 among patients with lymphoma treated with B-cell depleting immunotherapy. Presented at the: AACR Virtual Meeting: COVID-19 and Cancer; February 5, 2021.

29. Lee LYW, Cazier J-B, Starkey T, et al. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. *The Lancet Oncology*. 2020;21(10):1309-1316. doi:10.1016/S1470-2045(20)30442-3

LYMPHOMA
RESEARCH • FOUNDATION

National Headquarters
Wall Street Plaza
88 Pine Street, Suite 2400
New York, NY 10005

LRF Helpline
(800) 500-9976
Helpline@lymphoma.org

lymphoma.org