

Proceedings of the
COVID-19 and Lymphoma Panel:
October 25, 2022

A LYMPHOMA RESEARCH FOUNDATION WHITE PAPER

Introduction

On October 25, 2022 the Lymphoma Research Foundation convened two expert panels of medical and scientific advisors as part of an ongoing series on the impact of the COVID-19 pandemic on people with lymphoma. The panels discussed current recommendations regarding COVID-19 prevention and treatment for people with lymphoma, as well as the impact of the COVID-19 pandemic on clinical lymphoma research.

This white paper reflects the panel discussion and the state of research as of the date of the above. 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.

The Foundation is grateful to the friends and family of Dr. Robert Schroeder whose support made this program possible.

Panel Participants

Lindsey Baden, MD

Harvard Medical School

Robert Chen, MD

AstraZeneca

Andres Chang, MD, PhD

Emory University School of Medicine

Jonathon B. Cohen, MD, MS

Winship Cancer Institute

Lisa Baumann Kreuziger, MD, MS

Medical College of Wisconsin and COVID-19
Treatment Guidelines Panel Member

Emily Landon, MD

University of Chicago

Matthew Lunning, DO

University of Nebraska Medical Center

Lindsay M. Morton, PhD

National Cancer Institute Panel Steering
Committee Member and
LRF Scientific Advisory Board Member

Lisa M. Rimsza, MD

Mayo Clinic, Arizona

LRF Scientific Advisory Board Member

Lisa Roth, MD

Weill Cornell Medicine

LRF Scientific Advisory Board Member

Kerry J. Savage, MD

BC Cancer, Vancouver

LRF Scientific Advisory Board Member

Eduardo M. Sotomayor, MD

Tampa General Hospital Cancer Institute

LRF Scientific Advisory Board Member

Sonali M. Smith, MD

University of Chicago

Panel Steering Committee Member and

Chair, LRF Scientific Advisory Board

Andrew D. Zelenetz, MD, PhD

Memorial Sloan Kettering Cancer Center

Panel Steering Committee Chair and

LRF Scientific Advisory Board Member

Opening Remarks

Though much of the world has moved on, immunocompromised individuals such as lymphoma patients remain at risk. Panel chair and immediate past chair of the LRF Scientific Advisory Board, Dr. Andrew Zelenetz, acknowledged that it is becoming increasingly challenging to manage and mitigate these risks as the world moves forward. Oncologists are tasked with providing patients the right advice so that they don't continue living in isolation out of fear of infection, but so that they also understand their unique risk profiles.

To this end, two panels were convened to discuss current recommendations for immunocompromised individuals with regard to the COVID-19 pandemic, as well as what the lymphoma research community needs to do to move forward.

Panel One: **Current recommendations for people who are moderately or severely immunocompromised**

Moderator

Andrew D. Zelenetz, MD, PhD, Memorial Sloan Kettering Cancer Center

Panelists

Lindsey Baden, MD, Harvard Medical School

Andres Chang, MD, PhD, Emory University School of Medicine

Emily Landon, MD, University of Chicago

Lisa Baumann Kreuziger, MD, MS, Medical College of Wisconsin and COVID-19 Treatment Guidelines Panel Member

Sarah Quinlan, Lymphoma Research Foundation

Discussion

Vaccination and booster recommendations

Dr. Zelenetz kicked off the discussion by noting that even among vaccine believers, medical professionals are starting to see some vaccine resistance. He acknowledged that some of this pushback is reasonable given the occurrence of high-profile individuals who have developed COVID-19 shortly after receiving boosters.

Dr. Lindsey Baden of Harvard Medical School echoed these concerns in discussions, noting that he worries about "COVID fatigue" and patients wondering why they should get vaccinated if they are still going to get sick. Dr. Emily Landon, a hospital epidemiology and adult infectious disease doctor at UChicago Medicine, acknowledged that it is difficult to tailor discussions with patients so that they understand the risks and potential long-term implications of COVID-19 illness, but so that aren't so scared that they are constantly living in fear.

Current recommendations for COVID-19 vaccination are that everyone who is eligible should receive a booster this fall. Therefore, there is a need to unify messaging to help unvaccinated and unboosted individuals, particularly those who are immunocompromised, understand the role of vaccination and why it is still important in order to motivate individuals to action.

Dr. Landon emphasized that there is a need for patients and providers to stop thinking of the COVID-19 vaccine as simply a tool to prevent acute infection. People who are vaccinated are less likely to develop COVID-19,

but they are not *unlikely*. Rather, the role of vaccination is now two-fold: to **prevent severe illness** and poor outcomes with infection, and to **develop community advantage**. This means that vaccination is important not only for immunocompromised individuals, but those around them as well. Dr. Landon also suggested that there are emerging data to suggest that longer intervals before vaccination are associated with lower levels of protection against hospitalization (for both older and younger individuals), highlighting the need to encourage patients to get their booster as soon as they are eligible. Panelists also discussed the potential role of vaccination in preventing long-term complications of COVID-19, which could have serious neurological and cardiovascular implications, though these effects are still speculative.

For people who have recently had COVID-19 illness, the current recommendation is to wait 2 months before administering a booster to help extend immunity. Panelists agreed, though, that waiting 3 months may be better to help spread out immunity. However, they also noted that these intervals may need to be tailored for patients who have recently received (or are currently receiving) B cell-depleting therapy, with Evusheld used as needed in the interim. See below for a full discussion on the future of Evusheld in the current phase of the pandemic.

In addition to vaccines, additional precautionary measures should be taken to mitigate risks as needed, which may involve wearing a mask when possible and avoiding large crowds when case rates are high. Panelists agreed that these recommendations should not be “black and white”, but rather based on the patient’s own personal risk tolerance and situational nuances. To help with understanding risk, Dr. Landon noted that the current CDC map used by many outlets to show community case rates is misleading and is actually a measure of how sick patients are with COVID-19 rather than the case counts. She recommended that for immunocompromised individuals and their providers, the “Community Transmission” view in the CDC COVID Data Tracker¹ map is a more sensitivity measure of community spread.

Booster strains

Panelists also discussed whether vaccine strains correlate with efficacy and how that may influence their use in the vaccination series. Some panelists suggested that for naïve individuals, initial vaccination with the current bivalent vaccine may offer better protection earlier in the series, but others cautioned against using vaccines in a context for which there is no human data available. While this may inherently feel like the correct approach, scientifically there are no data yet to support the use of the BA.4/5 bivalent booster in the primary vaccine series.

Dr. Landon suggested, though, that **original antigenic preference** may influence how vaccines are ordered in the future. As is seen with influenza, she noted that there is emerging evidence that the body preferentially makes antibodies against the original SARS-CoV-2 strain to which it was exposed. Delaying vaccination against the circulating variant may therefore result in lower levels of neutralizing antibodies (nAbs) to the strains of interest, potentially resulting in lower levels of protection. However, Dr. Baden noted that there are not enough data to show that strain-specific nAbs are the “holy grail” for protection and may not directly correlate with immunity. The initial vaccines still offer good protection against severe illness, and though there may be some temporal waning, there is still evidence to show that vaccinating and boosting in the recommended sequence still has value until there is research to demonstrate a superior approach.

Dr. Andres Chang, a physician scientist at Emory University School of Medicine, added that even if original antigenic preference is a concern, people receiving B cell-depleting therapies, in theory, have a chance to have that memory erased or lessened, which may result in better responses to variant-specific boosters. Panelists agreed that

1. Centers for Disease Control and Prevention. COVID Data Tracker: COVID in your community. Available from: <https://covid.cdc.gov/covid-data-tracker/#datatracker-home>

following recovery from the immunosuppressive effects of therapy—which may take several months—represents an ideal time to boost patients with strain-specific boosters. Actively immunocompromised individuals should be boosted every 6 months.

T cell responses

Panelists also emphasized that, though data are limited, there is evidence to suggest that vaccination elicits robust T cell responses that can be meaningful for lymphoma patients. Dr. Zelenetz shared his experiences with a small pilot study in which patients with chronic lymphocytic leukemia (CLL) did not develop antibody responses to vaccination but were still protected from severe outcomes including death. Helping patients understand these benefits may help them better understand the importance of vaccination despite their B cell-depleted status. Such discussions should be made within the scientific context of T cell activity—T cells cannot prevent infection, but they can help clear infected cells to protect against severe illness.

Antibody products: prevention and treatment

Panelists indicated they are concerned about the use of mAb therapies for the prevention COVID-19 moving forward. The changing composition of circulating strains has reduced the efficacy of Evusheld, and while panelists indicated they will continue to give Evusheld as long as they can, they also indicated they expect this won't be for much longer. Boosters will be much more important for prevention moving forward for immunocompromised individuals, as panelists also believe it is unlikely new mAb products will be brought to market. Without government intervention to buy up stocks and with increasing confusion over which antigens to target, panelists suggested it is unlikely new products will be brought to market in a timely fashion.

Dr. Baden also noted that there is a reemerging debate about the use of convalescent plasma (CCP) for the treatment of COVID-19 in immunocompromised individuals. Panelists agreed this can be a promising option, especially when COVID-19 is diagnosed early, but also noted that there are many unanswered questions that remain that make it difficult to find effective donors (ie, what in CCP is an accurate measure or correlate of protective capacity?).

Recommendations

Dr. Zelenetz concluded the panel discussion by emphasizing that medical field is now in a place where vaccination is going to become the most important tool to prevent COVID-19 illness in immunocompromised individuals as the world moves forward and other preventatives/therapeutics become less available. To that end, the panel recommended two key messages that the LRF can help disseminate:

- **Vaccination and ongoing boosters are important for immunocompromised patients:** This applies not only to patients, but also their close contacts to develop community advantage. COVID-19 and influenza vaccinations can be given at the same time.
- **Clinics and hospitals should continue masking:** The most recent guidance from the CDC regarding masking in healthcare settings was noted to be “problematic”, in that there are many exceptions and caveats written in to protect immunocompromised individuals that are buried in footnotes. These exceptions can be difficult for media outlets and hospital administrators to identify and understand. Immunocompromised patients (and employees) are everywhere, and ongoing masking in healthcare settings is needed to continue protecting these patients and the clinic infrastructure. For immunocompromised individuals, panelists recommended KF94, KN95, and N95 masks, which provide the highest levels of protection, particularly when others are not masking. Masking will also help provide extra protection within the context of the “devastating” flu and RSV season that is expected.

Panel Two:
Pandemic impact on lymphoma/CLL clinical trials

Moderator

Lisa Roth, MD, Weill Cornell Medicine

Panelists

Robert Chen, MD, Global Head of Lymphoma Clinical Development and Strategy at AstraZeneca
Jonathon B. Cohen, MD, MS, Winship Cancer Institute
Matthew Lunning, DO, University of Nebraska Medical Center

Discussion

Impact of COVID-19 pandemic on clinical research

Panelists agreed that overwhelming the most burdensome lasting impact of the COVID-19 pandemic has been staffing issues. Many clinical sites have lost staff or have had members switch to remote or hybrid roles, which has created challenges building and maintaining momentum for clinical research. Staff shortages means that the people who are in the clinic have to prioritize care of patients and cannot devote the attention they once could to activating and conducting clinical research. Many staff members have also been forced to take on additional responsibilities to account for shortages, further limiting their time to commit to clinical research.

Dr. Jonathan Cohen of the Winship Cancer Institute noted that despite the many challenges of the pandemic, one positive was that many companies and regulatory agencies allowed for the use of telemedicine to support clinical research, which has helped keep many patients on trial. While this change has been appreciated, panelists agreed there is a need for more flexibility in clinical trial conduct. Panelists acknowledged that certain requirements and rigidity are needed to help keep patients safe, particularly within the context of early phase trials, these kinds of strict requirements can create logistical challenges for already overburden healthcare systems. There is a need for pharmaceutical companies and clinical research organizations (CROs) to be more intentional about identifying what restrictions are needed to maintain patient safety and study integrity and where there is flexibility to accommodate for clinical strain and patient convenience. Dr. Zelenetz emphasized that approved alternatives to standard operating procedures (eg, use of electronic consent) need to be standardized to help prevent confusion between referring hospitals/clinics and research centers. Similarly, Dr. Matthew Lunning of the University of Nebraska Medical Center noted that there is a need for more clarity and support navigating Part 11 Compliance requirements as these types of electronic adaptations are made.

Declines in research applications

Research applications to the LRF declined during the past cycle. Panelists feel that this is likely a universal phenomenon driven by clinical burnout. Clinicians and researchers were forced to take on a lot of responsibility during the pandemic. Panelists suggested that many clinical researchers are taking time to “reset” and regain control of their mental health and work-life balance and may feel overwhelmed at the thought of putting together a research application at the moment. Dr. Cohen also suggested that for Career Development Awards in particular, investigators may feel they will not be competitive if the pandemic affected their ability to collect preliminary data or participate in research-sharing activities.

Panelists emphasized that there is likely a direct relationship between staffing shortages and declining research applications. Junior investigators in particular are forced to fill in gaps that may exist due to loss of research support staff, increasing their already-heavy workload. Additionally, panelists shared that they have anecdotally noticed more turnover in grants administration offices, which could further decrease the amount of support available as newer employees navigate these systems. At many institutions, promotions committees have not adapted promotion criteria in the wake of the pandemic, which panelists felt already failed to recognize the value of clinical research. Junior investigators may therefore feel overwhelmed at the idea of committing a significant amount of their time without the personnel available to support them.

Recommendations

Based on the discussions, panelists recommended the following opportunities for LRF to help support lymphoma research in the wake of the COVID-19 pandemic:

- **Advocate to increase flexibility in clinical trial requirements:** While certain requirements are needed to maintain patient safety and security, more flexibility is needed to adapt to new challenges in the healthcare system (eg, staffing shortages, closed sites). This includes flexibility with regard to the intensity of clinical events and windows as well as increased use of telemedicine and electronic consent. With this, there is a need to help investigators navigate requirements for Part 11 Compliance.
- **Increase awareness of LRF among lymphoma trainees:** Panelists indicated that their involvement with LRF was a natural extension of their mentors' involvement, and that many trainees in the lymphoma field may not have the same level of existing connection. To help engage with lymphoma trainees, panelists suggested hosting a fellowship reception at the American Society of Hematology annual meeting, as well as making LRF educational programming available to trainees.

Summary and Final Recommendations

Dr. Zelenetz concluded the meeting by reiterating that while many people have moved on from the pandemic, the lymphoma patient population is still at risk. There is an urgent need to help these patients navigate their new realities so that they can get back out into the world while still staying safe. Similarly, there is a need to help the research community navigate the new challenges they face so that clinical research can move forward and continue to help serve patients.

In addition to the recommendations described above, panelists agreed that there is a need to document the recommendations described in this meeting in a way that is patient friendly, to help lymphoma patients navigate risks within the context of their own personal circumstances. Such materials should link to CDC and NIH recommendations as often as possible, as recommendations change often and this will alleviate the need for frequent updates.

Moving forward, the panel expects to meet only as new challenges arise that uniquely affect lymphoma patients.



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