It’s Not Over Yet: The Ongoing Impact of COVID-19 for Those with CLL/SLL

August 24, 2022

11 AM PT, 12 PM MT
1 PM CT, 2 PM ET
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Speakers

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Johns Hopkins University School of Medicine

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Executive Vice President and Chief Medical Officer
CLL Society
COVID-19 Treatment Considerations

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Johns Hopkins University School of Medicine

August 24, 2022
Disclosures

• Funding related to CCP
  • U.S. Department of Defense (JPEO-CBRND and DHA), Bloomberg Philanthropies, State of Maryland, NIH (NIAD and NCATS), Mental Wellness Foundation, Moriah Fund, Octapharma, HealthNetwork Foundation and the Shear Family Foundation

• Other funding
  • Ansun, F2G, Zeteo

• Personal fees: Celltrion, Immunome, Adagio

• DSMB: Karyopharm, Intermountain Health, Adamis
The patient is a 56-year-old woman with history of CLL and low immunoglobulins. Despite multiple COVID-19 vaccine injections she has failed to develop a durable antibody response. She is now in the midst of her 3rd COVID-19 related hospitalization. The first was 3 months previously and she was treated with 5 days of remdesivir, a course of steroids and was discharged on home oxygen. The second was two weeks previously for an episode of presumed bacterial pneumonia. She has not felt well in months and is now in hospital with mildly low oxygen, fever to 101.5 and SARS-COV-2 PCR positivity with cycle threshold of 17 (a way to measure how much virus the patient harbors).
# Risks for Poor COVID-19 Outcomes in People with Cancer

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>COVID-19 severity OR (95% CI)</th>
<th>30-day mortality OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, per decade</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;40 years</td>
<td>0.91 (0.72-1.15)</td>
<td>0.58 (0.35-0.97)</td>
</tr>
<tr>
<td>Age &gt;40 years</td>
<td>1.38 (1.31-1.45)</td>
<td>1.75 (1.59-1.93)</td>
</tr>
<tr>
<td><strong>Sex, male versus female</strong></td>
<td>1.47 (1.31-1.65)</td>
<td>1.46 (1.20-1.77)</td>
</tr>
<tr>
<td><strong>Race and ethnicity, versus non-Hispanic white</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>1.46 (1.27-1.68)</td>
<td>1.38 (1.09-1.75)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.38 (1.16-1.64)</td>
<td>1.31 (0.96-1.80)</td>
</tr>
<tr>
<td>Other</td>
<td>1.27 (1.05-1.53)</td>
<td>0.97 (0.70-1.36)</td>
</tr>
<tr>
<td><strong>Type of malignancy, versus solid tumor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematological neoplasm</td>
<td>1.70 (1.46-1.99)</td>
<td>1.44 (1.10-1.97)</td>
</tr>
<tr>
<td>Multiple</td>
<td>1.21 (1.01-1.44)</td>
<td>1.30 (1.00-1.70)</td>
</tr>
<tr>
<td><strong>Cancer status, versus remission or no evidence of disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active and responding</td>
<td>0.84 (0.67-1.04)</td>
<td>0.79 (0.52-1.18)</td>
</tr>
<tr>
<td>Active and stable</td>
<td>0.97 (0.81-1.16)</td>
<td>1.06 (0.77-1.44)</td>
</tr>
<tr>
<td>Active and progressing</td>
<td>2.19 (1.80-2.67)</td>
<td>2.88 (2.13-3.90)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1.93 (1.55-2.41)</td>
<td>2.19 (1.56-3.07)</td>
</tr>
<tr>
<td><strong>Modality of active anticancer therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytotoxic chemotherapy, yes versus no</td>
<td>1.28 (1.04-1.58)</td>
<td>1.61 (1.15-2.24)</td>
</tr>
<tr>
<td>Immunotherapy, yes versus no</td>
<td>0.86 (0.64-1.16)</td>
<td>0.91 (0.56-1.47)</td>
</tr>
<tr>
<td>Targeted therapy, yes versus no</td>
<td>1.09 (0.87-1.36)</td>
<td>0.90 (0.63-1.31)</td>
</tr>
<tr>
<td>Endocrine therapy, yes versus no</td>
<td>0.79 (0.61-1.03)</td>
<td>0.68 (0.43-1.09)</td>
</tr>
<tr>
<td>Locoregional therapy, yes versus no</td>
<td>1.18 (0.93-1.50)</td>
<td>0.96 (0.65-1.42)</td>
</tr>
<tr>
<td>Other, yes versus no</td>
<td>0.97 (0.47-2.00)</td>
<td>1.31 (0.44-3.94)</td>
</tr>
</tbody>
</table>

Grivas et al, Annals of Oncology 2021
## Risks for Poor Outcome in B-lymphoid Malignancies

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Multivariable AOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study populations (ref = Patients with nonrecently treated B-lymphoid malignancies)</td>
<td></td>
</tr>
<tr>
<td>Nonrecently treated control population</td>
<td>1.16 (0.90-1.49)</td>
</tr>
<tr>
<td>Recently treated control population</td>
<td>0.75 (0.61-0.93)</td>
</tr>
<tr>
<td>Patients recently treated for B-lymphoid malignancies</td>
<td>2.30 (1.58-3.36)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Multivariable AOR (95% CI)</th>
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<tbody>
<tr>
<td>Study populations (ref = Patients with nonrecently treated B-lymphoid malignancies)</td>
<td></td>
</tr>
<tr>
<td>Nonrecently treated control population</td>
<td>0.82 (0.61-1.10)</td>
</tr>
<tr>
<td>Recently treated control population</td>
<td>0.92 (0.63-1.34)</td>
</tr>
<tr>
<td>Patients recently treated for B-lymphoid malignancies</td>
<td>1.34 (0.85-2.11)</td>
</tr>
</tbody>
</table>
Seroconversion in Immune Compromised Patients (After 2 Doses of Vaccine)

- RR 0.39 (0.32 to 0.46)
  - Organ transplant
- RR 0.63 (0.57 to 0.69)
  - Heme malignancy
- RR 0.75 (0.69 to 0.82)
  - Immune disease
- RR 0.90 (0.88 to 0.93)
  - Solid tumor cancer
- RR 1.00 (0.98 to 1.01)
  - HIV

Lee et al BMJ. 2022
Immunization for Immune Compromised

• Up to date means
  • Completed primary series
    • 3 mRNA vaccines or 1 J&J and 1 mRNA or 2 Novavax
      AND
  • #1 booster if it has been 3 months since primary series
      AND
  • #2 booster if it has been 3 months since first booster

Activity of mAb’s vs. Omicron Sublineages

<table>
<thead>
<tr>
<th></th>
<th>Delta</th>
<th>BA1</th>
<th>BA2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bamlanivimab</td>
<td>&gt;9,000</td>
<td>&gt;9,000</td>
<td>&gt;9,000</td>
</tr>
<tr>
<td>Etesivimab</td>
<td>3.8</td>
<td>&gt;9,000</td>
<td>&gt;9,000</td>
</tr>
<tr>
<td>Casirivimab</td>
<td>0.58</td>
<td>&gt;9,000</td>
<td>&gt;9,000</td>
</tr>
<tr>
<td>Imdevimab</td>
<td>1.2</td>
<td>&gt;9,000</td>
<td>693</td>
</tr>
<tr>
<td>Adintentivam</td>
<td>4.5</td>
<td>198</td>
<td>&gt;9,000</td>
</tr>
<tr>
<td>Regadavimab</td>
<td>23</td>
<td>&gt;9,000</td>
<td>&gt;9,000</td>
</tr>
<tr>
<td>Sotrovimab</td>
<td>280</td>
<td>1,508</td>
<td>&gt;9,000</td>
</tr>
<tr>
<td>Tixagevimab</td>
<td>3.2</td>
<td>&gt;9,000</td>
<td>&gt;9,000</td>
</tr>
<tr>
<td>Cilgavimab</td>
<td>8.5</td>
<td>1,988</td>
<td>9.3</td>
</tr>
<tr>
<td>Evusheld</td>
<td>2.6</td>
<td>715</td>
<td>23</td>
</tr>
</tbody>
</table>

IC_{50} (ng/ml).

Bruel T et al Nature Medicine 2022
Yamasoba D et al bioRxiv 2022.05.03.490409
### Antiviral Options Authorized for Treatment of COVID-19

<table>
<thead>
<tr>
<th>Medication</th>
<th>Route</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>mAb (bebtelovimab)</td>
<td>IV</td>
<td>Outpatient or inpatient if reason for admission is not COVID-19</td>
</tr>
<tr>
<td>Nirmatrelvir and ritonavir</td>
<td>PO</td>
<td>Drug interactions with ritonavir: Outpatient only</td>
</tr>
<tr>
<td>Molnupiravir</td>
<td>PO</td>
<td>Efficacy questions and fetal harm: outpatient only</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>IV</td>
<td>Inpatient or outpatient</td>
</tr>
<tr>
<td>Convalescent plasma</td>
<td>IV</td>
<td>Inpatient or outpatient</td>
</tr>
<tr>
<td>Evusheld</td>
<td>IM</td>
<td>PREVENTION: Pre-exposure prophylaxis</td>
</tr>
</tbody>
</table>
Evusheld FDA Information

• Initial dose: 300 mg of tixagevimab and 300 mg of cilgavimab administered as two separate consecutive intramuscular injections.

• Repeat dose: 300 mg of tixagevimab and 300 mg of cilgavimab every 6 months. Repeat dosing should be timed from the date of the most recent EVUSHIELD dose.
Convalescent Plasma in Patients With Hematologic Cancers and COVID-19

Thompson, MA et al JAMA Oncol. 2021

Table:

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI) for death within 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall population</td>
<td></td>
</tr>
<tr>
<td>No. of events/No. of patients at risk (%)</td>
<td>223/966 (23.1)</td>
</tr>
<tr>
<td>Convalescent plasma</td>
<td>19/143 (13.3)</td>
</tr>
<tr>
<td>No convalescent plasma</td>
<td>204/823 (24.8)</td>
</tr>
<tr>
<td>Crude analysisa</td>
<td>0.47 (0.30-0.76)</td>
</tr>
<tr>
<td>Multivariable analysisb</td>
<td>0.60 (0.37-0.97)</td>
</tr>
<tr>
<td>Propensity score matchingc</td>
<td>0.52 (0.29-0.92)</td>
</tr>
</tbody>
</table>
Treatment of B Cell Depleted Patients with Persistent COVID-19 and Negative Antibodies

- **Gharbharan A, et al., *Clinical Infectious Diseases*, 2022**
  - Patients:
    - Twenty-five B-cell–depleted patients (24 following anti-CD19/20 therapy)
    - Symptomatic for a median of 26 days
    - Antibody negative
  - Treatment: Convalescent plasma with high neutralizing antibody titers
  - Outcomes: Twenty-one (84%) recovered

- **Kenig A, et al., *Clinical Immunology*, 2021**
  - Patients
    - Eight B cell depleted patients
    - Prolonged disease course and delayed viral clearance
    - Covid Convalescent Plasma (CCP) used an add-on therapy to standard medical treatment
  - All patients showed remarkable clinical and laboratory improvement
Contact Information

• Email: sshoham1@jhmi.edu
• Twitter: @ShohamTxlD
CLL Society’s COVID-19 Action Plan

Robyn Brumble, RN, MSN
Director of Scientific Affairs
CLL Society
Complete Prior to COVID-19 Exposure
Known Exposure, Positive Result, and How to Quarantine

**CHECKLIST FOR KNOWN EXPOSURE TO COVID-19 WITHOUT A POSITIVE TEST RESULT**

- Closely monitor for symptoms of COVID-19. Symptoms can appear anywhere from 2-14 days after exposure and may or may not include headache, fever or chills, cough, shortness of breath or difficulty breathing, increased fatigues, worsening muscle or body aches, headache, loss of taste or smell, sore throat, congestion, runny nose, nausea, vomiting, and diarrhea.
- Contact your healthcare provider(s) right away to arrange for possible urgent treatment with the anti-COVID-19 monoclonal antibodies, regardless of whether or not you have had a positive test or symptoms.
- Immediately schedule appointments for testing 3-5 days following the date of known exposure. Availability for testing can be limited during times of surging cases.

**TESTING RECOMMENDATIONS FOR COVID-19**

- The CDC recommends testing 3-5 days following the date of the known exposure, even without symptoms. But if you begin to have symptoms, arrange to get tested right away. If possible, have both the rapid and PCR tests performed. If both are not available, the PCR test is most preferred due to increased accuracy. Know that if you test negative, you were not infected at the time your sample was collected. The test result only means that you did not have COVID-19 at the time of testing. Continue to take steps to protect yourself and others by wearing a mask and distancing. If you develop symptoms, you should immediately get tested. If you test positive, refer to the COVID-19 Action Plan for the next steps.

**QUARANTINE RECOMMENDATIONS FOR CLL**

- If you received a negative PCR test result AND if no symptoms have been detected during daily monitoring, quarantine can end after Day 10.
- For those that did not get tested and never experienced any symptoms of COVID-19, quarantine must last for the full 14 days following exposure.

**HOUSEHOLD QUARANTINE PLAN**

- **Why Is It Important To Have A Quarantine Plan In Place Before You Become Infected with COVID-19?**
  - Receiving a COVID-19 diagnosis can be stressful and confusing, especially if you are not prepared. Having a self-quarantine plan will help everyone in the household know exactly what to do should the virus infect someone within the home. In addition to this checklist, learn as much as you can in advance about standard infection control precautions that may help decrease the possibility of spread. Place this document within your COVID-19 planning folder to refer to if needed.

  - **Have plenty of masks available.** Everyone in the household should plan on wearing a tightly-fitted mask (preferably an N95) over their nose and mouth as much as possible, especially when in direct contact with anyone else in the home.
  - **Keep your distance from others.** Stay in a designated room by yourself and use a bathroom separate from the one used by others in the household. Keep your bedroom and bathroom door closed when possible. Have someone else prepare meals and leave them outside your bedroom door.
  - **Do not leave your home (unless necessary for medical care).** Identify family, friends, or community groups to help deliver groceries, medications, and other supplies to your front door. Have their contact information readily available as part of your quarantine plan.
  - **If living with others, increase ventilation within your home.** Open windows and outside doors (when the weather permits), operate airflow fans or run a window air conditioner with the vent control open to increase the indoor/outdoor airflow.
  - **Have necessary supplies on hand.** Consider creating a kit that includes items such as thermometers for each person in the home, electrolytes, teas, over-the-counter medications, cleaning supplies, hand sanitizer, disposable gloves, Kleenex, etc. Speak with your healthcare provider about what vitamins or over-the-counter medications might be helpful to have readily available as well.
  - **Wipe down high-touch areas every day with a disinfectant.** This includes door knobs, light switches, phones, remote controls, appliances, sink, toilet, countertops, etc. Let someone else disinfect high-touch surfaces in the common areas of the home. But you should also clean and disinfect your designated sick room and bathroom if possible.
  - **Do not share any items with others in your home.** This includes clothes, drinking glasses, eating utensils, towels, or bedding. It is important to wash all items used by the infected person thoroughly with soap and water after using them.
What Do I Do If I Do Get COVID-19?

COVID-19 ACTION PLAN

Do These Things After Testing Positive for COVID-19

ACTIVATE YOUR PLAN! ACT EARLY-EVEN IF YOU FEEL FINE. REMEMBER, TIME IS OF THE ESSENCE.

☐ Access your COVID-19 Planning Folder.
☐ Read through your COVID-19 Planning Checklist and instructions again.
☐ Contact your healthcare provider(s) immediately to discuss arranging urgent treatment with the anti-COVID-19 monoclonal antibodies and any other possible early therapies as soon as possible.
☐ Activate your Household Quarantine Plan.

IMPORTANT PEOPLE TO CONTACT

☐ Contact anyone you have been around in the previous 48 hours and inform them of your positive test result. By notifying close contacts of possible exposure, you may be helping them prevent the spread of COVID-19 to their friends and family.
☐ Someone from the health department may call you. This is completely normal, and it is important to answer the call to assist with contact tracing, which may also help slow the spread.
☐ Call your healthcare provider(s) to notify them of your positive test result.
☐ Stay in touch with them periodically to ask questions and/or inform them of your status. And do not hesitate to call your healthcare provider(s) to report any symptoms that are severe or concerning to you.

SCHEDULED APPOINTMENTS

☐ If you have an in-person medical appointment that cannot be avoided, call the office ahead of time to remind them you have been diagnosed with COVID-19. This will help the office put measures in place to protect the staff and other patients when you arrive.

KEEP A LOG OF YOUR VITAL SIGNS AND SYMPTOMS

☐ Begin recording a list of all measured vital signs, especially oxygen saturation levels and temperatures.
☐ Keep track of when you experience any new symptoms such as cough, chills, shortness of breath, fatigue, muscle/body aches, vomiting, diarrhea, or loss of taste/smell.
☐ Include the time and date when you are logging them.
☐ Call your healthcare provider(s) to inform them if your oxygen saturation is consistently reading below 95%, fever >100.4, or if with worsening symptoms.

SEEKING EMERGENCY CARE

☐ Call 911 immediately if emergency warning signs for COVID-19 develop such as difficulty breathing, rapid breathing, oxygen saturation consistently reading <92%, persistent pain or pressure in the chest, difficulty swallowing, agitation, confusion, or discolored lips/nail beds.
☐ Should you need to seek emergency care via ambulance, you must request to be taken to the hospital that you have already determined ahead of time can provide you with rapid access to critical COVID-19 therapies. If they are not informed, they are required to transfer you to the nearest local hospital.
☐ Take your COVID-19 Planning Folder along with you to the hospital so you have quick access to the important documents (the ‘Official Statement for Prioritizing CLL Patient’s Emergency Room Care’).
☐ Most importantly, ADVOCATE for your best care! Remember, EARLY administration of critical COVID-19 therapies, such as convalescent plasma and SARS-CoV-2 monoclonal antibodies, is extremely important for those who are immunocompromised (as recommended by Emergency Use Authorization and other clinical guidelines). Data shows both reduced morbidity and mortality in CLL patients with both of these treatments.

AFTER YOUR DISEASE HAS RUN ITS COURSE

☐ Please consult with your healthcare provider(s) to find out when you can safely be around others. If you have any symptoms, it is important to get tested again. Routine testing after COVID-19 is not advised in the general population. However, your healthcare provider may recommend repeated testing, as some CLL patients have difficulty clearing the virus that causes COVID-19 and may remain contagious after symptoms resolve.
Where to Find the COVID-19 Action Plan On CLL Society’s Website
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COVID-19 Action Plan

Checklists for Chronic Lymphocytic Leukemia (CLL)
Preparing for Pre- and Post-COVID-19 Exposure

Downloading and completing the CLL Society's COVID-19 Action Plan could save your life.

Complete and print this action plan, which will help you prepare in advance for possible exposure, testing positive, time sensitive therapies, and home management, including what you need for safe isolation, and much more. Preparing in advance can minimize the panic that many experience when exposed or diagnosed because you will have a written plan to guide you. If you do only one thing to protect yourself and your loved ones during the pandemic, please complete your family’s COVID-19 Action Plan. The life you save might be your own.
Important Takeaways

• Complete the checklists ahead of time-BE PREPARED!

• Keep them in an easily accessible place, such as a folder

• Discuss your plan with others within the household

• If you have known exposure, symptoms, or a positive test result-pull out the plan and act fast! Time is of the essence.
Poll Questions
Audience Questions & Answers
This program was made possible by grant support from

AstraZeneca

BeiGene

Bristol Myers Squibb

Janssen

Pharmacyclics
Thank You for Attending!

Please take a moment to complete our post-event survey, your feedback is important to us.

If you’re question was not answered, please feel free to email asktheexpert@cllsociety.org.

Join us on October 26th for our virtual event on therapy sequencing.

CLL Society is invested in your long life. Please invest in the long life of the CLL Society by supporting our work.

cllsociety.org/donate-to-cll-society/