Performing a COVID-19 Risk Assessment: Understanding What Has Changed Now That the Government Response Has Scaled Down

June 27, 2023

10:30 AM PT, 11:30 AM MT, 12:30 PM CT, 1:30 PM ET
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Speakers

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COVID-19 and Immunocompromised Individuals in 2023

Ghady Haidar, MD
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June 27, 2023
Outline

• Brief COVID-19 update
• Vaccine guidance
• COVID-19 therapies
• Protracted SARS-CoV-2 infection
• Available clinical trials for immunocompromised individuals
COVID-19 in Spring 2023

Green is good! (low # of hospitalizations)

Weekly Update for the United States

Hospitalizations
- Hospital Admissions (In Past Week)
  - Total: 8,256
- Trend in Hospital Admissions
  - -11% in past week

Deaths
- % Due to COVID-19 (In Past Week)
  - 1.3%
- Trend in % COVID-19 Deaths
  - -13.3% in past week

Vaccinations
- % with Updated Booster Dose
  - 17.0%

CDC, as of June 1, 2023
Burden of COVID-19 in the Immunocompromised

• ~ 3% of the US population are considered immunocompromised, including all of those with CLL/SLL

• According to the CDC: In 2022 12.2% of COVID-19 hospitalizations were immunocompromised individuals
  • More ICU admissions vs immunocompetent
  • More inpatient deaths vs immunocompetent
  • Regardless of vaccination

• Difficult to track numbers

Singson et al, MMWR / July 8, 2022 / 71(27);878–884
COVID-19 in 2023

• XBB era
  ▪ Mostly XBB1.5, others (e.g., Arcturus, XBB1.16)
• On a practical basis, no real differences for management

https://covid.cdc.gov/covid-data-tracker/#variant-proportions
## COVID-19 Symptoms

- Cough
- Fever
- Myalgia
- Headache
- Dyspnea (new or worsening over baseline)
- Sore throat
- Diarrhea
- Nausea/vomiting
- Anosmia or other smell abnormalities
- Ageusia or other taste abnormalities
- Rhinorrhea and/or nasal congestion
- Chills/rigors
- Fatigue
- Confusion
- Chest pain or pressure

Most patients with confirmed COVID-19 have fever and/or symptoms of acute respiratory illness. However, various other symptoms have been associated with COVID-19; this list is not inclusive of all reported symptoms. These symptoms are also not specific for COVID-19, and the predictive value of a single symptom in the diagnosis of COVID-19 is uncertain.

**COVID-19:** coronavirus disease 2019.

**Reference:**

- Does not include all symptoms
- Symptoms may change with new COVID-19 variants and can vary depending on vaccination status
  - E.g., conjunctivitis with XBB1.16
- No symptom can rule in/out COVID-19
- Low threshold to get tested
Vaccination Recommendations in 2023

Recommended COVID-19 vaccines for people who ARE moderately or severely immunocompromised, aged 6 years and older, mRNA vaccines, May 2023*

*For product-specific dosages, administration intervals, additional dose information, and options for heterologous dosing, see Table 2 in the Interim Clinical Considerations for Use of COVID-19 Vaccines.

Key

- Moderna
- Pfizer-BioNTech
- Moderna OR Pfizer-BioNTech

Updated Vaccine Guidance

• Overall, shift to bivalent vaccines

• Immunocompromised individuals may receive 1 additional bivalent vaccine dose at least 2 months following the last recommended bivalent COVID-19 vaccine dose
  ▪ Open-ended > 2 months after that (guidance unclear)

• Vaccinate the "bubble"
  ▪ Individuals > 65 years old may receive an additional bivalent vaccine > 4 months after their last one
## Outpatient COVID-19 Therapies in 2023

<table>
<thead>
<tr>
<th>Drug</th>
<th>Nirmatrelvir/r (Paxlovid)</th>
<th>Remdesivir</th>
<th>Molnupiravir</th>
<th>Convalescent plasma*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
<td>✓</td>
<td>?</td>
</tr>
<tr>
<td><strong>Ease of delivery</strong></td>
<td>✓ ✓ ✓ (oral)</td>
<td>XXX (IV)</td>
<td>✓ ✓ ✓ (oral)</td>
<td>XXX (IV)</td>
</tr>
<tr>
<td><strong>Drug Interactions</strong></td>
<td>!!<strong>XXX</strong>!!</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td><strong>Safe during pregnancy</strong></td>
<td>? (RTV safe)</td>
<td>✓ ✓</td>
<td>XXX</td>
<td>✓ ✓</td>
</tr>
<tr>
<td><strong>NIH recommendation</strong></td>
<td>Alla</td>
<td>BIIa</td>
<td>CIIa</td>
<td>Insufficient evidence in IC; some may use</td>
</tr>
</tbody>
</table>

**Test early, treat early!**

Adapted with permission from Raj Gandhi MD and Annie Luetkemeyer MD, CROI 2022
Protracted SARS-CoV-2 Infection

• Not the same as “long COVID-19” because there is an active infection where individuals are still shedding the virus

• Prolonged SARS-CoV-2 replication in immunocompromised individuals
  ▪ Cancer, solid organ transplant, AIDS, and other
  ▪ Case reports/case series

• Intra-host evolution → how new variants emerge within immunocompromised individuals

• Limited antiviral arsenal available to treat
Protracted Infections For Up to 268 Days!

Why do we think this occurs?
Not the same as “paxlovid rebound”
How should an immunocompromised individual be monitoring for this?
  - Home antigen testing—how often and for how long?
What if symptoms persist or re-occur?
  - Continue to isolate/mask
  - When to consult with an infectious disease doctor
Recommendations for Treating Protracted COVID-19

- Use the same antivirals as other patients, with “fine print”
- Use a combination of antivirals? → insufficient evidence
- Give antivirals longer than standard duration? → insufficient evidence
- Non-committal about the use of convalescent plasma

https://www.covid19treatmentguidelines.nih.gov/special-populations/immunocompromised/
How to Manage Protracted Infection: Unconventional Approaches

Open Forum Infectious Diseases

BRIEF REPORT

Successful Treatment of Prolonged Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Patients With Immunodeficiency With Extended Nirmatrelvir/Ritonavir: Case Series

Madison Breeden, Samuel L. Aitken, Ji Hoon Baang, Misty Gravelin, Daniel R. Kaul, Adam S. Lauring, Lindsay A. Petty, and Kevin S. Gregg

1Division of Infectious Diseases, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA, 2Department of Pharmacy, University of Michigan, Ann Arbor, Michigan, USA, 3Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, Michigan, USA, and 4Michigan Institute for Clinical and Health Research, University of Michigan, Ann Arbor, Michigan, USA

- We don’t know
- No clinical trials
- Have been using trial and error
  - 4 B-cell malignancy patients
  - 2-8 months of illness
  - All previously received remdesivir
  - 2/4 previously received paxlovid
  - 2/4, previously received the monoclonal antibody bebtelovimab
  - Success with giving a longer course of paxlovid (up to 21 days vs the standard 5 days)
Treating with Viral-Specific T-Cells?

1. Collect PBMCs from SARS-CoV-2 convalescent donors
2. Isolate PBMCs
3. Expose to SARS-CoV-2-specific peptides
4. Stimulate T-cell-peptide mix
5. Cryopreserved SARS-CoV-2-specific T cells
6. SARS-CoV-2-specific T cells
7. Infuse into IC patient with COVID-19
Treating with Viral-Specific T-Cells?

• SARS-CoV-2 viral-specific T-cells (VSTs) were given to 6 immunocompromised patients with protracted COVID-19 infection
  ▪ 4 had blood cancer, 2 had lung transplants
  ▪ 3 patients had partial responses after failing other therapies but then died
  ▪ 2 patients completely recovered, but the role of VSTs in recovery was unclear due to the concomitant use of other antivirals
  ▪ 1 patient had not responded to 2 courses of remdesivir and experienced sustained recovery after VST administration

• Not currently available
• Needs further study
# COVID-19 Clinical Trials for the Immunocompromised

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Conditions</th>
<th>Interventions</th>
<th>Locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not yet recruiting</td>
<td>OPTimisation of Antiviral Therapy in Immunocompromised COVID-19 Patients: a Randomized Factorial Controlled Strategy Trial</td>
<td>COVID-19, Immunodeficiency</td>
<td>Drug: Paxlovid 5 days, Drug: Paxlovid 10 days, Drug: Vekury</td>
</tr>
<tr>
<td>Recruiting</td>
<td>T CELL THERAPY OPPOSING NOVEL COVID-19 INFECTION IN IMMUNOCOMPROMISED PATIENTS</td>
<td>SARS-CoV-2 Infection</td>
<td>Biological: Coronavirus-specific T cell (CST), Children's National Hospital Washington, District of Columbia, United States</td>
</tr>
<tr>
<td>Recruiting</td>
<td>Study Understanding Pre-Exposure pRophylaxis of NOVel Antibodies (SUPERNova)</td>
<td>COVID-19, SARS-CoV-2</td>
<td>Biological: AZD5156 (Sentinel Safety Cohort), Biological: Placebo (Sentinel Safety Cohort), Biological: AZD7442 (EVUSHELD™) (Main Cohort), Biological: AZD3152 (Main Cohort), Research Site Birmingham, Alabama, United States, Research Site Little Rock, Arkansas, United States, Research Site Little Rock, Arkansas, United States</td>
</tr>
</tbody>
</table>

### Treatments
- **Paxlovid**: 5 vs 10 days (treatment)
- **T-cells**: (treatment)
- **Convalescent plasma**: (treatment)
- **New monoclonal antibody**: (prevention) (e.g., Invivyd, AstraZeneca)

Visit CLL Society’s Homepage for More Trials!
In Summary

- COVID-19 burden for the general public right now is lower compared to before, but immunocompromised patients remain at higher risk.
- Vaccination guidance has shifted to bivalent vaccines, please get boosted!
- Outpatient COVID-19 therapies do work → tested early and let your provider know you tested positive
  - Be aware that drug interactions exist with Paxlovid—work with your CLL healthcare provider.
- Protracted SARS-CoV-2 infection in immunocompromised patients is a real concern and research is needed.
- There are several clinical trials ongoing, so additional help is on the horizon!
COVID-19 Personal Risk Assessment & Action Plan

Robyn Brumble, MSN, RN
Director of Scientific Affairs & Research
CLL Society

June 27, 2023
Outline

• COVID-19 personal risk assessment
• Changes in light of the Public Health Emergency (PHE) ending
• Where to find the most accurate COVID-19 information
• Advocating for your best (and safest) care
• CLL Society’s COVID-19 Action Plan
COVID-19 Risk Assessment

Definition: Using a framework to help assess the personal risk that COVID-19 poses to our personal health, implementing tools to mitigate those risks, and then making a personal decision as to whether the risk of the activity is worth taking.
Assessing Risks of the Environment

• Knowing the rate of transmission in the community
• What is the setting of the activity (social distancing, indoors, outdoors, is there good ventilation)
• What is the size of the gathering
• Is anyone else going to be masked
• Are any of the individuals you are gathering with ideally willing to test and isolate for several days prior to meeting
• What is the vaccination status of others in attendance
Changes Since the End of the PHE

• CDC’s ability to collect and share certain data are very limited and there is a longer lag in reporting
• COVID-19 death counts will remain, but the source of the data has changed
• Case numbers are no longer being highlighted by the CDC’s COVID Data Tracker
• At-home tests are no longer required to be provided free of charge by insurance providers
What Remains the Same

• Hospitals are still required to report data through the end of 2024.
• Test positivity numbers will remain, but the source of information has changed and lag about a week behind when they are reported.
• Vaccines remain mostly free available (for now)
• Treatments for COVID-19 remain available for free while the government’s stockpile lasts.
• Wastewater surveillance and genomic sequencing for the type of variants that are present will remain in place through 2024.
• Telehealth coverage
• FDA’s Emergency Use Authorization
Shared Responsibilities and Interventions

- Get vaccinated
- Wash your hands frequently
- Keep your distance when not vaccinated
- Report positive cases and exposures
- Wastewater testing
- Enhanced cleaning
- Public health policy enforcement
- Wear a facial covering
- Regular testing
- Avoid school, work when sick
- Quarantine and isolation
- Enhanced building ventilation
- Education and awareness activities

This illustration was adapted from the Swiss Cheese Model developed by James Reason, Ph.D.

Remember to continue the basics of infection control for yourself!
Remember to continue the basics of infection control for yourself!
Paradigm Shift to the Individual

• How many risk factors do you have that would make you at higher risk for poorer outcomes?
• Will you be wearing a high quality KN95 or N95 facemask?
• Are you fully vaccinated?
• When available, have you received your COVID-19 pre-exposure prophylaxis monoclonal antibody therapy?
• Can you distance yourself from others at the gathering?
• Do you have your COVID-19 Action Plan up-to-date and know what to do to act fast if you should test positive?
• What is the benefit to you of participating in the activity?
Where to Find Timely and the Most Accurate COVID-19 Statistics

- Wastewater data doesn’t lie and is not dependent upon how many people take a COVID-19 test or states reporting!
  - Biobot Analytics
  - National Wastewater Surveillance System
Managing Your Risks As Masks Are Disappearing in Healthcare Settings

- Wear a well-fitted quality N95 mask
- Utilize telehealth options when appropriate
- Request appointments early in the morning before the waiting areas become full
- When scheduling an appointment ask them to put a note in your chart that you are immunocompromised and requests masks be worn by healthcare staff
- If urgent care or emergency care is needed, request to be placed in an isolated area while you wait
- You have the right to safe healthcare! Never hesitate to ask staff that will be in contact with you to please wear a mask.
COVID-19 Action Plan

Be Prepared to Fight Back Against COVID-19
Complete Prior to COVID-19 Exposure

Directions for Completing the COVID-19 Planning Checklist

The COVID-19 planning checklist is designed to help individuals prepare for the potential exposure to COVID-19. It is important to complete this checklist as early as possible to ensure adequate preparations are made.

1. Obtain an oxygen (O2) pulse oximeter (O2 saturation monitoring device) and have it readily available in your home. Inexpensive O2 pulse oximeters can be purchased on Amazon or from your local drug store.

2. Have a reliable digital thermometer available. If you only have oral thermometers in your home, consider purchasing one for each member of the household to prevent spreading the virus to other family members.

3. Know ahead of time where you will go to get tested for COVID-19, and confirm you will perform the necessary testing:
   - The location you choose should be willing to offer you both the rapid test and the PCR test at the same time. Remember, the Rapid test can indicate evidence of COVID-19 infection, but the PCR is typically more accurate. (Please note, some rapid tests will not detect variants).
   - Always err on the side of caution and get tested right away should you experience any respiratory symptoms, or if you have known exposure to COVID-19. Do not dismiss allergy or cold symptoms!
   - The earlier you know, the earlier you can receive treatment, which is of utmost importance.

4. High titer convalescent plasma should be administered early after diagnosis and is authorized under the EUA (Emergency Use Authorization) for the treatment of hospitalized patients with COVID-19 and impaired immunity. That would include CLL patients. It is not used in severe COVID-19. Convalescent plasma may need to be administered more than once.

5. Monoclonal antibodies directed against the COVID-19 spike protein have proven to help high-risk patients and should be given within 10 days of diagnosis and can be given outpatient. The earlier the better! You must investigate ahead of time which hospitals in your area provide rapid access to this critical COVID-19 treatment! COVID-19 monoclonal antibody therapies are not available everywhere and are mostly likely not available at your local small community hospital. So please spend time finding out exactly where you can access them quickly should you need them. It is also important to understand the criteria that makes you eligible for this critical COVID-19 treatment should there be any pushback when you advocate for receiving it:
   - Search this map to find the hospitals in your area that have monoclonal antibody therapy available, and make it part of your plan to visit their emergency room if COVID-19 treatment becomes necessary.

COVID-19 PLANNING CHECKLIST

Complete Prior To Exposure

- Obtain Necessary Monitoring Supplies
  - Oxygen Monitoring Device (Pulse Oximeter)
  - Digital Thermometer for Each Individual in the Household

- Know Where to Go for COVID-19 Testing
  - Ensure Testing Facility Will Perform BOTH the Rapid Test & the PCR Test
  - Name of Testing Location:

- Determine Where Critical COVID-19 Treatments Are Available Nearby
  - Convalescent Plasma:
  - Monoclonal Antibodies:

- Healthcare Team Contact Information
  - CLL Provider’s Contact Info:
  - List of All Healthcare Providers and Place in Planning Folder

- Personal Paperwork to Place in COVID-19 Planning Folder
  - Copy of Living Will, Power of Attorney, and Advance Directives
  - Insurance Cards

- CLL Society Documents to Place in COVID-19 Planning Folder
  - CLL Society’s Official Statement for Prioritizing CLL Patients Emergency Room Care related to COVID-19

- Quarantine Plan
  - Complete Quarantine Plan Checklist and Place a Copy in Planning Folder
  - Discuss Quarantine Plan with Others in the Household

Please Refer to the COVID-19 Planning Checklist Directions Sheet for Detailed Instructions
How to Quarantine Appropriately
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 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 staying awake, 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.
In Summary

- Performing a COVID-19 personal risk assessment is still important.

- Continue to have situational awareness and know where to obtain the most accurate COVID-19 statistics for your area.

- Keep up-to-date on vaccines, continue to mask, and take all other infection control measures.

- Revisit your COVID-19 Action Plan from time to time to make sure the information within it is still correct.

- Discuss your COVID-19 Action Plan with others in the household.
Poll Question
Audience Questions & Answers
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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 July 12th for our next “Ask Me Anything” event on Facebook Live and Zoom.

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/