COVID-19: Are Monoclonal Antibodies What the CLL Community Has Been Waiting For?

December 2, 2021

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Speakers

Welcome
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Communications Director
CLL Society

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MS Ed
Executive Vice President and
Chief Medical Officer
CLL Society

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Director of Scientific Affairs
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& Rheumatology
Rochester Regional Health Clinical
Associate Professor of Medicine
University of Rochester School of
Medicine and Dentistry
Understanding and Minimizing CLL/SLL Patients’ Risks with COVID-19

Dr. Brian Koffman
Executive Vice President and Chief Medical Officer of CLL Society
CLL/SLL Is a Cancer of the Immune System

• For many, CLL was a nagging background to an otherwise full life.

• Though CLL patients have long been known to be immunocompromised (IC), it was often ignored or simply handled by avoiding sick friends and relatives and perhaps careful handwashing.

• The COVID-19 pandemic changed everything for many as CLL’s inherent (IC) status became a constant and potentially life-threatening disability.
Risk of COVID-19 Infection After Vaccination

• The IC making up only 2.7% of the U.S. adult population.
• The rate of breakthrough cases among vaccinated people who are not IC was <1%.
CDC on Poor Outcomes in the IC

• Are more likely to get severely ill from COVID-19.
• Higher risk for:
  • Prolonged SARS-CoV-2 infection and shedding
  • Viral evolution (mutations) during infection and treatment in hospitalized patients
  • Low antibody/neutralization titers to SARS-CoV-2 variants
• Are more likely to transmit SARS-CoV-2 to household contacts.
• CLL patients hospitalized with COVID-19 have had a historical high mortality rate of ~30%, now closer to 10%.
Should the IC Undergo Antibody Testing Following COVID-19 Vaccination?

According to the CDC:

• Utility of serologic testing or cellular immune testing to assess immune response to COVID-19 vaccination has not been established.

• Exact correlation between antibody level and protection from COVID-19 remains unclear.

• Commercial antibody and cellular immune testing may not be consistent across laboratories.

• Serologic (antibody) testing or cellular immune testing outside of the context of research studies is not recommended at this time.
Passive Versus Active Immunity

• A strong **active** immune response involves a complicated set of hand-offs and passes between different cells in our immune system. We as CLL patients fumble the ball a lot.

• In most cases it is better to teach someone to fish than to hand them cooked fish (or sushi). In our case, we may never successfully fish on our own and may end up going hungry.

• Fortunately, there is a good source of prepared fish (sushi) in the form of monoclonal antibodies (mAb).

• If we could get enough pre-made “neutralizing” antibodies against the COVID-19 spike (S) protein, then those antibodies would be expected to **passively** protect us.
When Do Monoclonal Antibodies Help?

Just About Any Time!

Currently Authorized and Available For:
1. Early in mild to moderate COVID-19 as an outpatient
2. Exposed to COVID-19 but have not yet tested positive (this is called post-exposure prophylaxis)

Coming Real Soon:
• Pre-Exposure Prophylaxis (PrEP)

Experimental:
• In severe cases where the patient is not making their own antibodies
A Layered Approach Leads to Better COVID-19 Protection

The “Swiss Cheese” analogy recognizes that **NO SINGLE INTERVENTION** is perfect at preventing the spread of COVID-19. But when multiple preventative measures are layered on top of the other, the chance of prevention becomes greater.

Add a cheese wedge for:
- Monoclonal Antibodies
- Antivirals
- Better Therapies

The future is looking much safer!!
Monoclonal Antibodies for COVID-19 in CLL

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Rochester Regional Health
Clinical Associate Professor of Medicine
University of Rochester School of Medicine & Dentistry

December 2, 2021
Outline

• Background of immunodeficiency
• Proposed evaluation of immunodeficiency
• Therapeutic options for COVID-19
Risk of Infection

**Summary of Findings**

<table>
<thead>
<tr>
<th>Category</th>
<th>MM</th>
<th>CLL</th>
<th>MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of patients</td>
<td>50</td>
<td>45</td>
<td>50</td>
</tr>
<tr>
<td>% of patients with ≥ 2 infections</td>
<td>78</td>
<td>84</td>
<td>18</td>
</tr>
<tr>
<td>Period in years under observation (average ± 50)</td>
<td>1.58 ± 1.4</td>
<td>3.17 ± 2.4</td>
<td>2.17 ± 3.2</td>
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<tr>
<td>Average annual infection rate</td>
<td>0.026</td>
<td>0.009</td>
<td>0.002</td>
</tr>
<tr>
<td>Total No. of infections</td>
<td>102</td>
<td>71</td>
<td>9</td>
</tr>
<tr>
<td>% of infections while receiving therapy</td>
<td>36</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Total mortality</td>
<td>56</td>
<td>30</td>
<td>11</td>
</tr>
<tr>
<td>% of deaths primarily due to infections</td>
<td>50</td>
<td>63</td>
<td>9</td>
</tr>
<tr>
<td>Site of Infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>49(9)</td>
<td>36(6)</td>
<td>4(1)</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>22</td>
<td>13</td>
<td>4</td>
</tr>
<tr>
<td>Ectodermal</td>
<td>1(1)</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Septicemia</td>
<td>10(5)</td>
<td>4(4)</td>
<td>0</td>
</tr>
<tr>
<td>Meningitis</td>
<td>7(4)</td>
<td>1(1)</td>
<td>0</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
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**Pathogens**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>MM</th>
<th>CLL</th>
<th>MI</th>
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<tbody>
<tr>
<td>Total identified</td>
<td>73</td>
<td>54</td>
<td>8</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>26(9)</td>
<td>9(2)</td>
<td>8</td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>10(3)</td>
<td>14(6)</td>
<td>1</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>13(2)</td>
<td>11(3)</td>
<td>2</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>6(1)</td>
<td>6(5)</td>
<td>1</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>4(1)</td>
<td>7(2)</td>
<td>3</td>
</tr>
<tr>
<td>Hemophilus influenzae</td>
<td>5(2)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Klebsiella enterobacter</td>
<td>4(1)</td>
<td>2(1)</td>
<td>0</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Mycobacterium tuberculosis</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>1</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Myxoma africana</td>
<td>0</td>
<td>2(1)</td>
<td>0</td>
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</tbody>
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Immune Components

- Complement proteins
- Neutrophils & phagocytes
- T cells
- Antibodies
Proposed Immune Evaluation

- **Antibody Level**
  - IgG, IgM, IgA

- **Antibody Function**
  - Vaccine Responses

- **T Cell Counts**
  - Lymphocyte Subsets

**Current State**

Infection

Pneumonia

*Streptococcus pneumoniae*

Vaccination

Infection #1 Cause of Morbidity & Mortality

Vaccines lead to antibody production

B cells make antibodies

CLL is a B cell cancer

B cells are dysfunctional in CLL

Patients with CLL have suboptimal antibody response

COVID-19 Vaccine in Blood Cancers

COVID-19 Pfizer Vaccine in CLL

COVID-19 Pfizer Vaccine in CLL

COVID-19 mRNA Vaccine 3rd Dose

Three doses of an mRNA COVID-19 vaccine in solid-organ transplant recipients

- No serious adverse events were reported after administration of the 3rd dose, and no acute rejection episodes occurred (n=99)

CDC ACIP Meeting July 22, 2021.
COVID-19 Treatment – Monoclonal Antibodies

Casirivimab w/ imdevimab (Regeneron), Bamlanivimab + etesevimab (Eli Lilly), Sotrovimab (GSK)
COVID-19 Treatment Outcomes

- Quicker decrease in viral load
- Quicker resolution of symptoms
- Decreased rate of hospitalization
- No increased risk of side effects as compared to placebo
Eligible Patients

**Treatment of mild to moderate COVID-19 in adults and pediatrics (≥ 12 years) with positive results for SARS-CoV-2 testing and are at high risk for progressing to severe COVID-19 and/or hospitalization.**

**NOT authorized for use in:**

- Hospitalized due to COVID-19
- Who require oxygen therapy due to COVID-19
- Require an increase in baseline oxygen flow rate due to COVID-19
Subcutaneous REGEN-COV Antibody Combination to Prevent Covid-19

COVID-19 Prophylaxis – EUA Pending

AZD7442 PROVENT Phase III prophylaxis trial met primary endpoint in preventing COVID-19

PUBLISHED
20 August 2021

20 August 2021 07:00 BST

77% reduced risk of developing symptomatic COVID-19

First long-acting antibody combination to prevent COVID-19
Summary

• Individuals with CLL have immune dysfunction
• Infections are the #1 cause of complications in CLL
• Vaccines are recommended but response is often suboptimal
• COVID-19 pandemic poses increased risk to individuals with CLL, due to suboptimal vaccine responses
• Individuals with CLL should be aware of additional therapeutic options for management of COVID-19
Thank You

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CLL Society’s COVID-19 Action Plan

Robyn Brumble, RN, MSN
Director of Scientific Affairs
CLL Society
Complete Prior to COVID-19 Exposure

Directions for Completing the COVID-19 Planning Checklist

CLL Society highly encourages individuals living with CLL to prepare ahead of time and have a comprehensive COVID-19 Plan ready in place just in case you have either a known exposure or receive a positive test result. The following are guidelines to assist you in completing your personalized COVID-19 Planning Checklist. Please keep all printed information in a designated COVID-19 Planning Folder that can be easily accessed if needed.

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 also 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 most 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 make you eligible for receiving this critical COVID-19 treatment should there be any pushback when you advocate for receiving it.

   a. 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.
Known Exposure, Positive Result, and How to Quarantine

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

READ THROUGH YOUR COVID-19 PLANNING FOLDER AND ACTIVATE YOUR HOUSEHOLD QUARANTINE PLAN

- 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 fatigue, 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 due to delays in processing of samples.

TESTING RECOMMENDATIONS FOR COVID-19

- The CDC recommends testing 3-5 days following the date of 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. Both are not available, the PCR test is much 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 the others by wearing a mask and distancing.
- If symptoms develop, but you had a negative test, you should immediately get retested.
- 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 no symptoms have been detected during daily monitoring, quarantine may 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 as 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 sharing with others, increase ventilation within your home. Open windows and outside doors (when the weather permits), operate air/vent 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 list 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 doorknobs, light switches, phones, remote controls, appliances, sinks, 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 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 difficult breathing, rapid breathing, oxygen saturation consistently reading <95%, persistent pain or pressure in the chest, difficulty staying awake, confusion, or discolored lips/tongue.
☐ 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 mortality 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.

Please visit cll.org for more information.
Where to Find the COVID-19 Action Plan On CLL Society’s Website
Important Take Aways

• 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

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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

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