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

December 2, 2021

9:30 AM PT, 10:30 AM MT, 11:30 AM CT, 12:30 PM ET

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Speakers





Welcome
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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



44%

Share of hospitalized breakthrough case patients in the US who are immunocompromised

- The IC making up only 2.7% of the U.S. adult population.
- The rate of breakthrough cases among <u>vaccinated</u> 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)

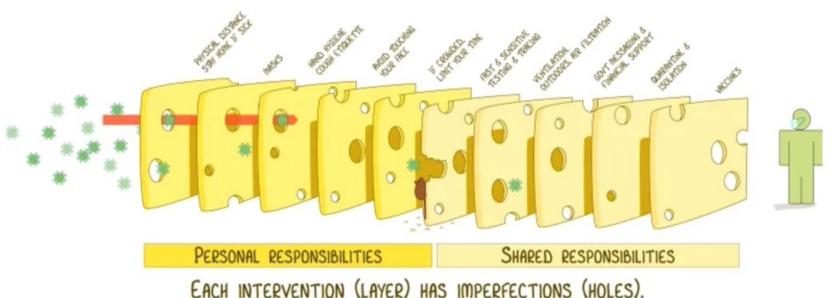
Experimental:

In severe cases where the patient is not making their own antibodies

A Layered Approach Leads to Better **COVID-19 Protection**

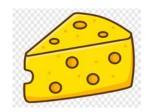
The "Swiss Cheese" analogy recognizes that **NO SINGLE INTERVENTION** is perfect at preventing the spread of COVID-19. But when multiple preventative measures are layered on top of the other, the chance of prevention becomes greater.





Add a cheese wedge for:

- Monoclonal Antibodies
- Antivirals
- **Better Therapies**



MULTIPLE LAYERS IMPROVE SUCCESS.

The future is looking much safer!!



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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 &
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December 2, 2021

Outline

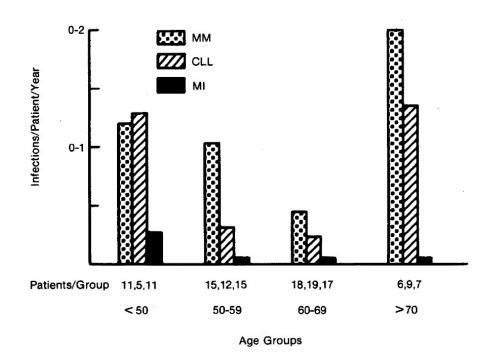
- Background of immunodeficiency
- Proposed evaluation of immunodeficiency
- Therapeutic options for COVID-19



Risk of Infection

Category	мм	CLL	МІ
Total No. of patients % of patients with	50	45	50
≥1 infection	78	84	18
Period in years under observation (average ± SD) Average annual	1.58 ± 1.4	3.17 ± 2.4	2.17 ± 3.2
infection rate	0.026	0.009	0.002
Total No. of infections % of infections	102	71	9
while receiving therapy	36	37	
Total mortality % of deaths primarily	36	30	11
due to infections	50	63	9
Site of infection Pulmonary	49(9)†	36(6)	4(1)
Urinary tract	22	13	4
Ectodermal	11(1)	14	1
Septicemia	10(5)	4(4)	0
Meningitis	7(4)	1(1)	0
Miscellaneous	3	3	0
Pathogens Total identified	73	54	8
Pneumococcus	26(3)‡	9(2)	8
Staphylococcus	10(3)	14(6)	1
Escherichia coli	13(2)	11(3)	2
Pseudomonas	6(1)	6(5)	1
Proteus mirabilis	4(1)	7(2)	3
Haemophilus influenzae	5(2)	2	0
Klebsiella enterobacter	4(1)	2(1)	0
Streptococcus	2	2	0
Meningococcus	0	1	0
Mycobacterium tuberculosis	2	1	0
Herpes zoster	1	4	0





Immune Components



Complement proteins Neutrophils & phagocytes Immune System Antibodies T cells

Proposed Immune Evaluation

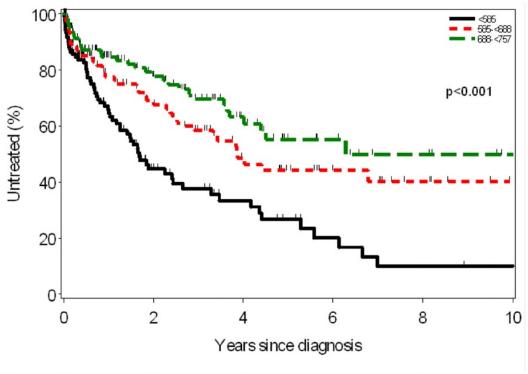




• IgG, IgM, IgA

Vaccine Responses

LymphocyteSubsets



Parikh. Cancer 2015; 121(17): 2883.

Antibody Function

T Cell Counts

Current State



Infection

Pneumonia

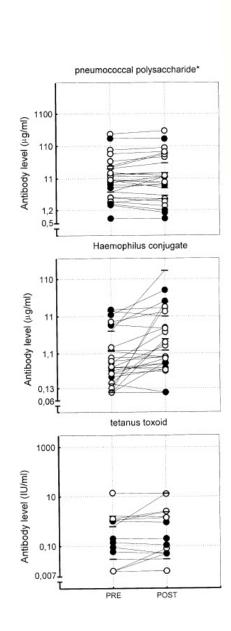
Streptococcus pneumoniae

Vaccination

Infection #1 Cause of Morbidity & Mortality

Vaccination in CLL

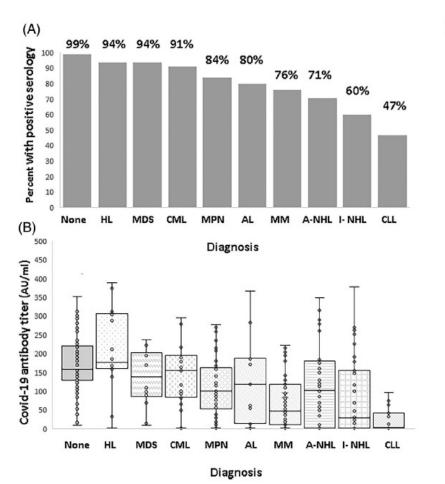
Vaccines lead to antibody production B cells make antibodies CLL is a B cell cancer B cells are dysfunctional in CLL Patients with CLL have suboptimal antibody response

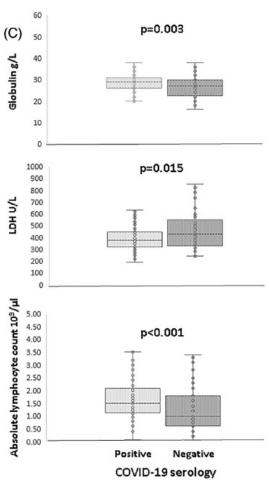




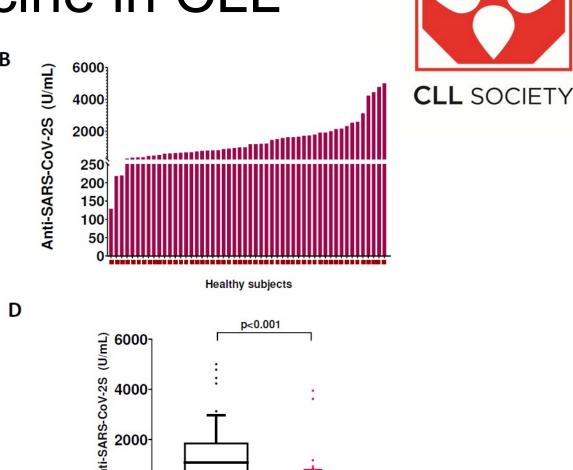
COVID-19 Vaccine in Blood Cancers

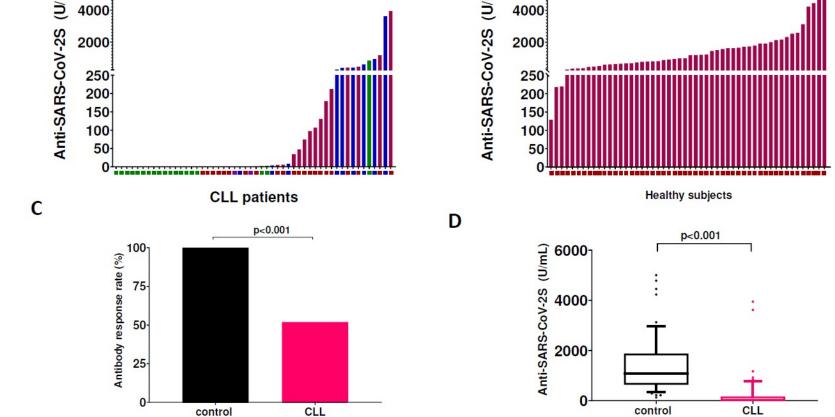






COVID-19 Pfizer Vaccine in CLL

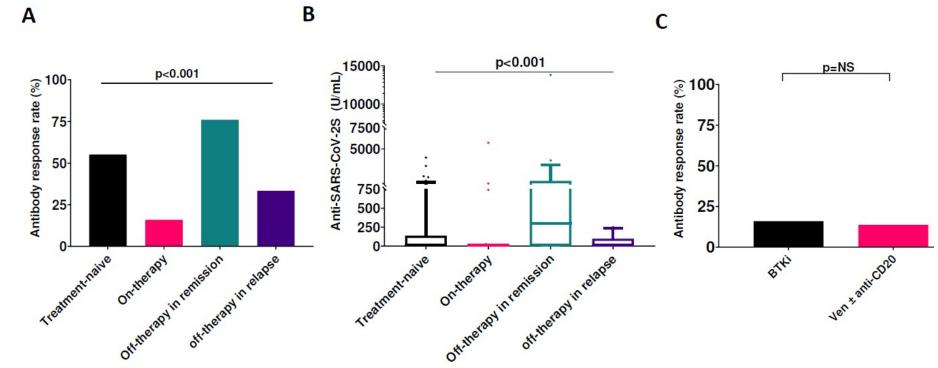




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COVID-19 Pfizer Vaccine in CLL

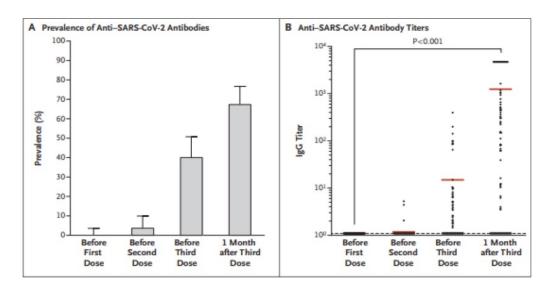




COVID-19 mRNA Vaccine 3rd Dose



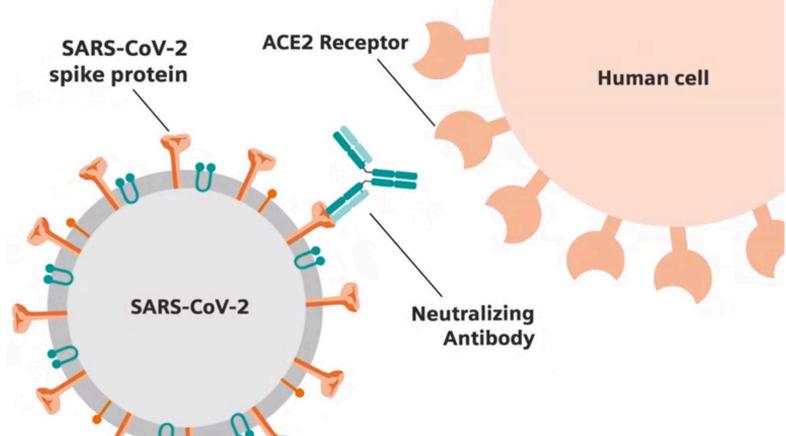
Three doses of an mRNA COVID-19 vaccine in solid-organ transplant recipients



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

COVID-19 Treatment – Monoclonal Antibodies





Casirivimab w/ imdevimab (Regeneron), Bamlanivimab + etesevimab (Eli Lilly), Sotrovimab (GSK)

COVID-19 Treatment Outcomes



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Quicker decrease in viral load

Decreased rate of hospitalization

Quicker resolution of symptoms

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 COVID19 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

COVID-19 Prophylaxis

The NEW ENGLAND JOURNAL of MEDICINE



ORIGINAL ARTICLE

Subcutaneous REGEN-COV Antibody Combination to Prevent Covid-19

M.P. O'Brien, E. Forleo-Neto, B.J. Musser, F. Isa, K.-C. Chan, N. Sarkar, K.J. Bar, R.V. Barnabas, D.H. Barouch, M.S. Cohen, C.B. Hurt, D.R. Burwen, M.A. Marovich, P. Hou, I. Heirman, J.D. Davis, K.C. Turner, D. Ramesh, A. Mahmood, A.T. Hooper, J.D. Hamilton, Y. Kim, L.A. Purcell, A. Baum, C.A. Kyratsous, J. Krainson, R. Perez-Perez, R. Mohseni, B. Kowal, A.T. DiCioccio, N. Stahl, L. Lipsich, N. Braunstein, G. Herman, G.D. Yancopoulos, and D.M. Weinreich, for the Covid-19 Phase 3 Prevention Trial Team*

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

shahzad.mustafa@rochesterregional.org 585-922-8350



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CLL Society's COVID-19 Action Plan

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

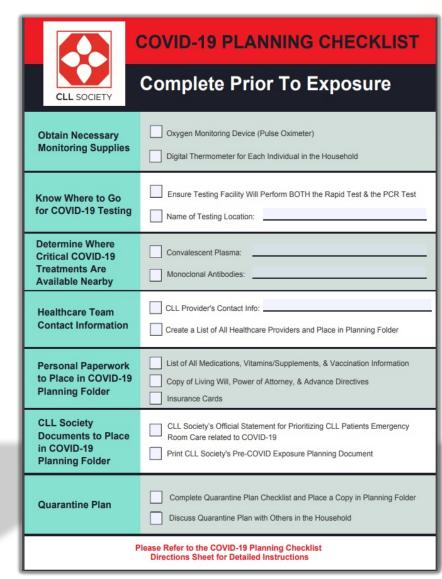
Complete Prior to COVID-19 Exposure



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 already 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.

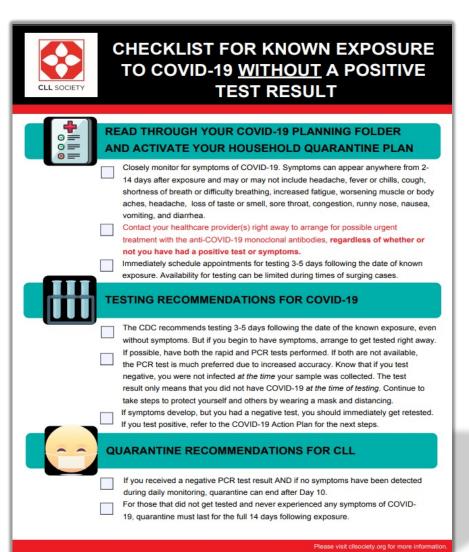
- 1) Obtain an oxygen (O2) pulse oximeter (O2 saturation monitoring device) and have it readily available in your home. Inexpensive O2 pulse oximeters can be purchased on Amazon or from your local drug store.
- 2) Have a reliable digital thermometer available. If you only have oral thermometers in your 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 they 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
- 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:
 - 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.





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Known Exposure, Positive Result, and How to Quarantine





HOUSEHOLD QUARANTINE PLAN



Why Is It Important To Have a Quarantine Plan in Place Before You Become Infected with COVID-19?

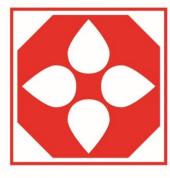
Receiving a COVID-19 diagnosis can be stressful and confusing, especially if you are not prepared. Having a self-quarantine plan will help everyone in the household know exactly what to do should the virus infect someone within the home. In addition to this checklist, learn as much as you can in advance 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.

advance about standard infection control precautions that m 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 N-95) 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 attic/window 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 doorknobs, 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 dishes, drinking glasses, eating

utensils, towels, or bedding. It is important to wash all items used by the infected person thoroughly

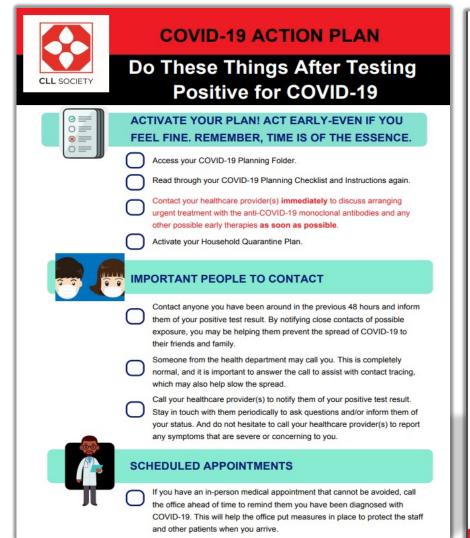
with soap and water after using them.



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For more information, please visit cllsociety.org

What Do I Do If I Do Get COVID-19?

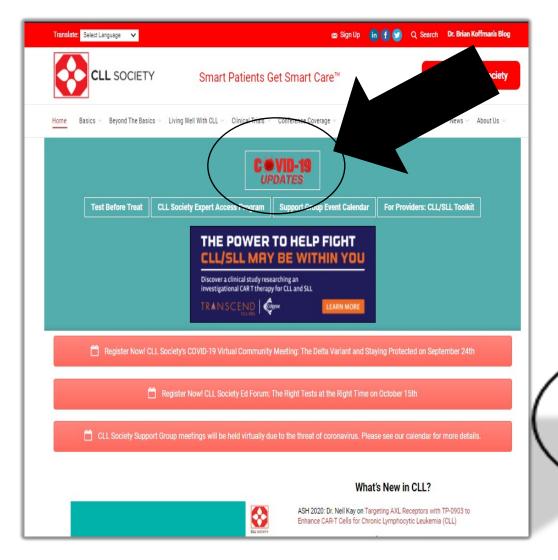






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Where to Find the COVID-19 Action Plan On CLL Society's Website







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













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

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/