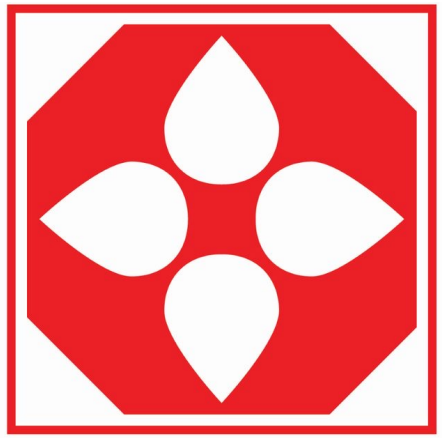


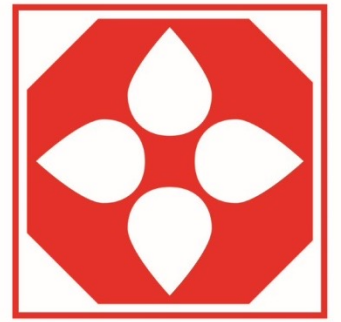
CLL SOCIETY

Smart Patients Get Smart Care™

COVID-19 Virtual Community Meeting: Contagion, Variants, and Vaccines

March 26, 2021

11:00 AM PT, 12:00 PM MT, 1:00 PM CT, 2:00 PM ET



This program was made possible by grant support from

Speakers

Welcome: Patricia Koffman
Co-Founder and Communications Director
CLL Society

Moderator: Brian Koffman, MDCM (retired), MS Ed
Co-Founder, Executive Vice President, and Chief Medical Officer, CLL Society

Speaker: Steven T. Rosen, MD
Provost and Chief Scientific Officer, City of Hope National Medical Center and Director, Comprehensive Cancer Center and Beckman Research Institute

CLL SOCIETY

Speakers

Speaker: Alexey V. Danilov. MD, PhD
Professor, Department of Hematology and Associate Director, Lymphoma Center at City of Hope National Medical Center

Speaker: Susan J. Leclair, PhD, CLS (NCA)
Chancellor Professor Emerita
University of Massachusetts
Dartmouth, Senior Scientist, Forensic DNA Associates, LLC

Speaker: Sanjeet Singh Dadwal, MD
Chief, Division of Infectious Diseases at City of Hope National Medical Center

CLL SOCIETY

Agenda

2:00 PM ET Welcome, Overview, Panel Introductions, Audience Poll

2:05 PM ET Panelist Comments

2:25 PM ET Q&A with CLL Community Participants

3:25 PM ET Concluding Comments

CLL SOCIETY

CLL SOCIETY

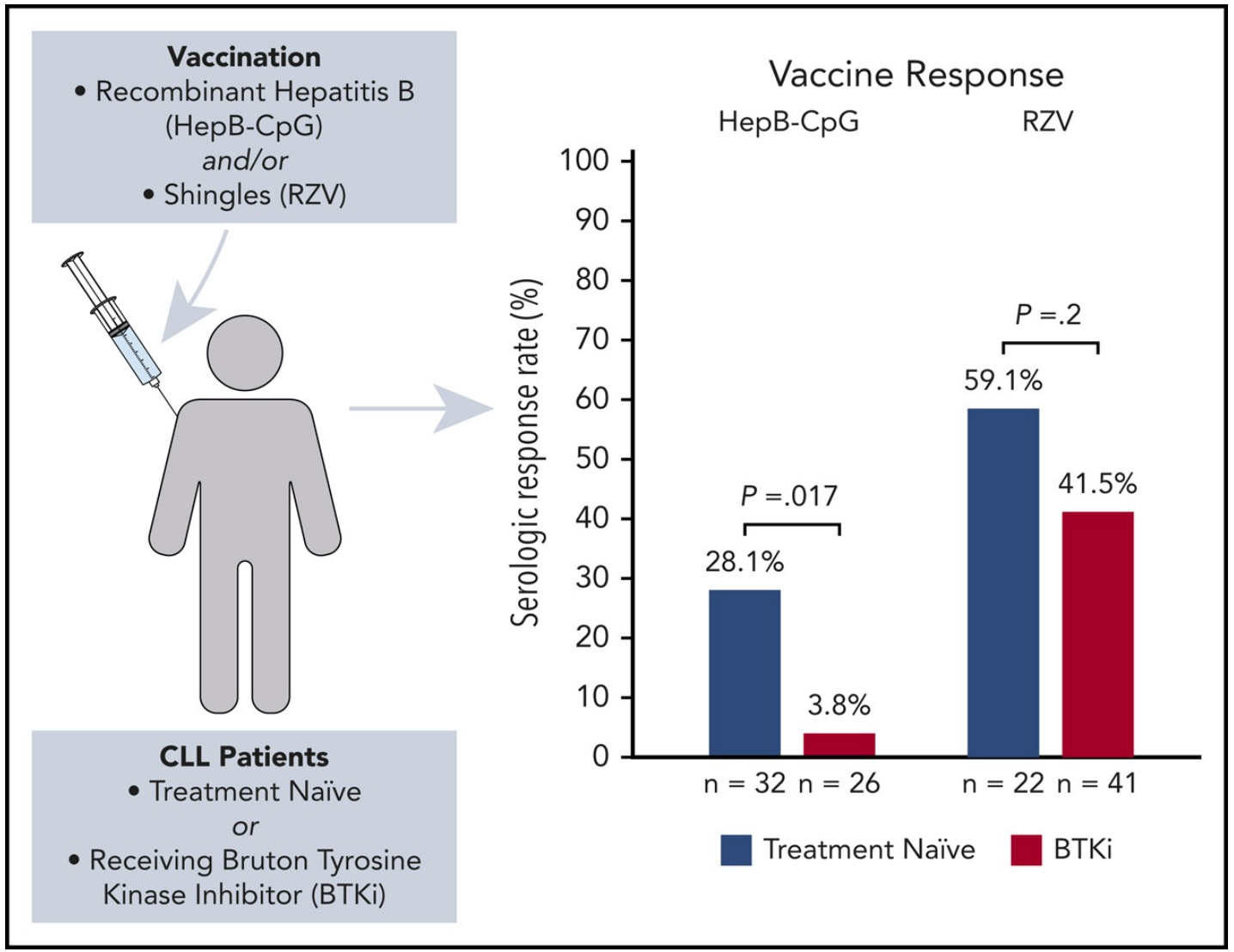
Smart Patients Get Smart Care™

COVID-19 Vaccine Update

Steven T. Rosen, MD

March 26, 2021

Efficacy of Vaccinations in CLL While Undergoing Treatment



CLL SOCIETY

Pleyer et al, Blood 2021

SARS-CoV-2 Vaccines

CLL SOCIETY

- Vector vaccines (COVID nucleic acid coding for spike protein in a replication incompetent adenoviral vector)
  - Astra-Zeneca (AZD 1222)
  - Janssen/ J and J (Ad26.COV2.S)
- mRNA vaccines (coated mRNA for spike protein)
  - Moderna (mRNA-1273)
  - Pfizer BioNTech (BNT162b2)
- Protein subunit vaccines
  - Novovax (spike protein covered in nanoparticles)

https://www.nytimes.com/interactive/2021/health/how-covid-19-vaccines-work.html

COVID-19 Vaccines

*EUA

Vaccine	Efficacy	Prevention of hospitalization	Mortality	Number of doses
AstraZeneca	76% (82% after boost)(included some variants)	2 vaccine arm (early), 16 placebo	None vaccine 1 in control arm in interim analysis	2 (standard refrigeration)
Janssen/J and J*	67% (77/85% against severe disease at 14/28 days); inc some variants	2 cases vaccine group, 29 cases placebo	None vaccine 7 in control	1 (standard Refrigeration)
Moderna*	94% (no variants)	0 cases vaccine group, 30 placebo	0 vaccine 1 in control	2 -20 freezer then 30 days refrigerator
Pfizer*	95% (no variants)	1 case vaccine 9 cases placebo	0 vaccine 0 control	2 -80 freezer then 5 days refrigerator
Novovax	(not official) 96% (no variants)	0 cases vaccine 5 cases placebo	“vaccine 100% effective”	2 Standard refrigeration

CLL SOCIETY

CLL SOCIETY

Smart Patients Get Smart Care™

Antigen and Antibody Testing for SARS-CoV2

Susan J. Leclair, PhD, CLS(NCA)
Chancellor Professor Emerita
University of Massachusetts

March 26, 2021

Two Types of Antigen Testing: PCR & Rapid

CLL SOCIETY

PCR (Polymerase Chain Reaction)
• Tests for genetic materials of the virus.
• Most Sensitive 0-4 days after the onset of symptoms.
• Important if you are trying to limit contagion (i.e., large gatherings).
• Most people want quick results, so this is not used.
• Only gives the status the day of the test. May be negative on day #1 post exposure, but positive on day #2.
• There are issues with accuracy after ten days.
• Test can be positive in the "Long" COVID patients.
• Requires sophisticated equipment and trained scientists. Not performed in clinics, physician's office, laboratories, etc.
• History of supply issues, which limits the ability to test.

Two Types of Antigen Testing: PCR & Rapid

CLL SOCIETY

Rapid (Antigen)
• Has value only if it is a positive result.
• A negative test indicates you either do not have the virus, or you may have the virus-but not enough to test positive.
• Most people utilize this test out of anxiety (i.e., airplanes).
• This test is more susceptible to error (i.e., false negatives).
• There are issues with accuracy after seven days.
• Requires sophisticated techniques and personnel (some have tried to perform these without, which has resulted in poor quality control and inaccurate results).
• History of supply issues has limited the ability to test.

Two Different Antibody Tests for COVID-19

CLL SOCIETY

Antibodies to Nucleocapsid (N) Protein:

- Positive 10 – 18 days after symptoms, or 2-3 weeks after exposure to COVID-19
- Positive in patients who have been infected with the SARS-CoV-2 virus
- May diminish or disappear over time
- Best to have two different tests to see if the titer rises:
  - The first immediately or as soon as one knows about exposure
  - The second 7-10 days later
- Nucleocapsid (N) protein will be *negative* post vaccine unless the person had COVID-19

Antibodies to Spike (S) Protein:

- Positive 14-20 days after full vaccination is complete
- Positive only in people who have been vaccinated
- May diminish or disappear over time

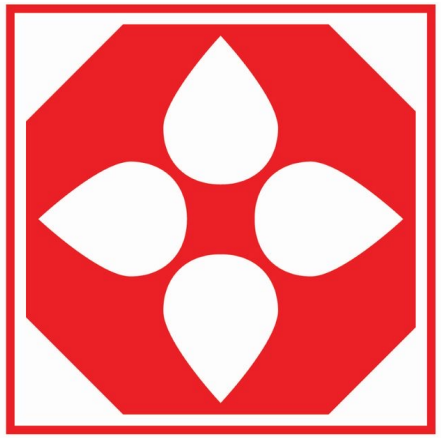
Difficulties with false negatives and false positives for both (N) and (S) antibodies

What Do the Antigen and Antibody Test Results Mean?

CLL SOCIETY

POSITIVE Antigen Testing	NEGATIVE Antigen Testing
• You DO have the virus.	• You do NOT have the virus.
• There is no way to determine the severity of the course of the infection.	• It is possible that you have the virus but in such small numbers that the test cannot detect them.

POSITIVE Antibody Testing	NEGATIVE Antibody Testing
• You did come into contact with the virus sufficient to generate an antibody response.	• You *may* have come into contact with the virus, but have not yet generated a detectable concentration of antibodies, or the timeframe isn't yet sufficient.
• It is NOT known if these antibodies are protective or not.	• You did once upon a time come into contact with the virus, but the concentration of antibodies is below level of detection.



CLL SOCIETY

Smart Patients Get Smart Care™

CLL & COVID-19

Alexey Danilov, MD, PhD

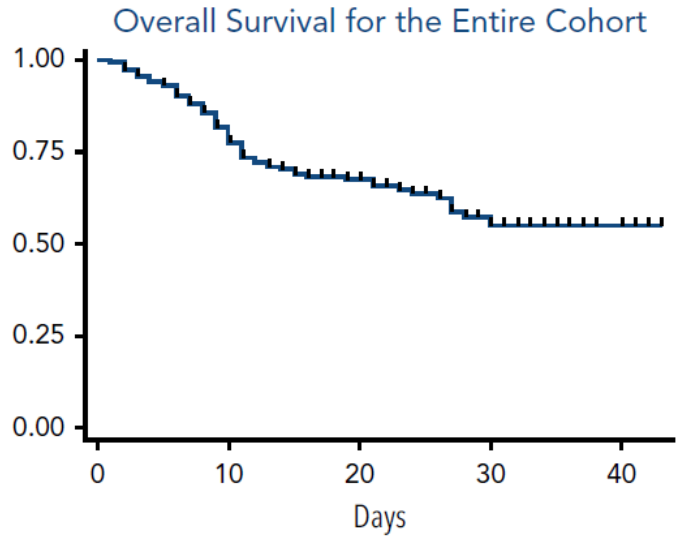
March 26, 2021

The Risk of COVID-19 in Those With CLL

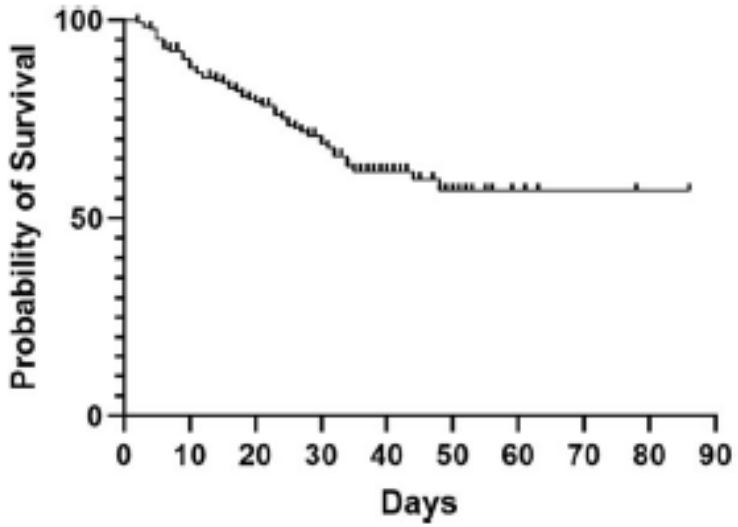
- So far, 15 studies, 517 patients in a meta-analysis - 31% risk of dying
- Hospitalization rates may be lower with ibrutinib than with chemotherapy?
- Data biased towards sicker patients – not a true sample of everyone who contracted COVID-19

CLL SOCIETY

US Cohort



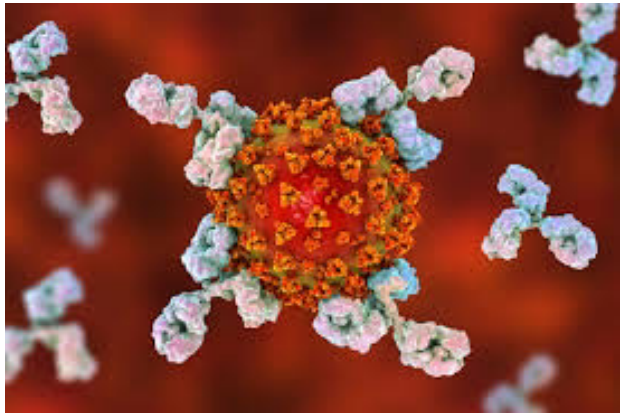
Euro Cohort



Vijenthira et al, 2020
Mato et al, 2020
Scarfo et al, 2020

Pre- and Post-Exposure Prophylaxis

- Phase III double-blind, placebo-controlled study of AZD7442 for pre-exposure prophylaxis of COVID-19 in adults (PROVENT)
  - No history of COVID-19 infection or vaccine
- Phase III double-blind, placebo-controlled study of AZD7442 for post-exposure prophylaxis of COVID-19 in adults (STORM CHASER)
  - Potential exposure within 8 days to a specific identified individual with laboratory-confirmed SARS-CoV-2 infection
  - Symptomatic or asymptomatic
  - No prior vaccine



Antibodies to Spike protein

What If I Contract COVID-19?

CLL SOCIETY

- Mild disease:
  - Isolation
  - Monitoring symptoms and temperature
  - Symptomatic management
  - Pulse oximetry (>88%)
- Moderate or severe disease:
  - Hospital admission

Emerging Agents to Treat COVID-19

CLL SOCIETY

- **Bamlanivumab**-A neutralizing antibody against spike protein (IV administration):
  - Randomized study (BLAZE-1) in patients with ‘mild or moderate’ COVID-19
  - Symptoms but not hospitalized
  - Authorized for emergency use by the FDA
  - Accelerated viral clearance

- **Molnupiravir (MK-4482)**-A “ribonucleoside analog” that inhibits proliferation of RNA-based viruses:
  - Phase 2 study of the drug in patients with symptomatic SARS-CoV-2 infection showed a reduction in time (days) to negativity of infectious virus isolation in nasopharyngeal swabs
  - There were no study-related serious adverse events.

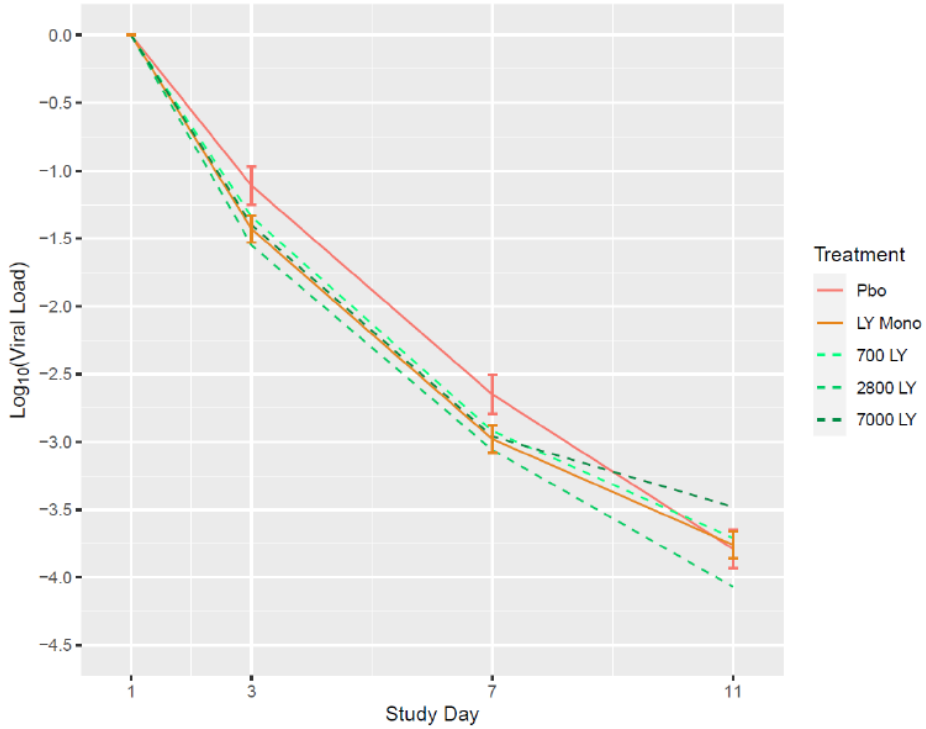
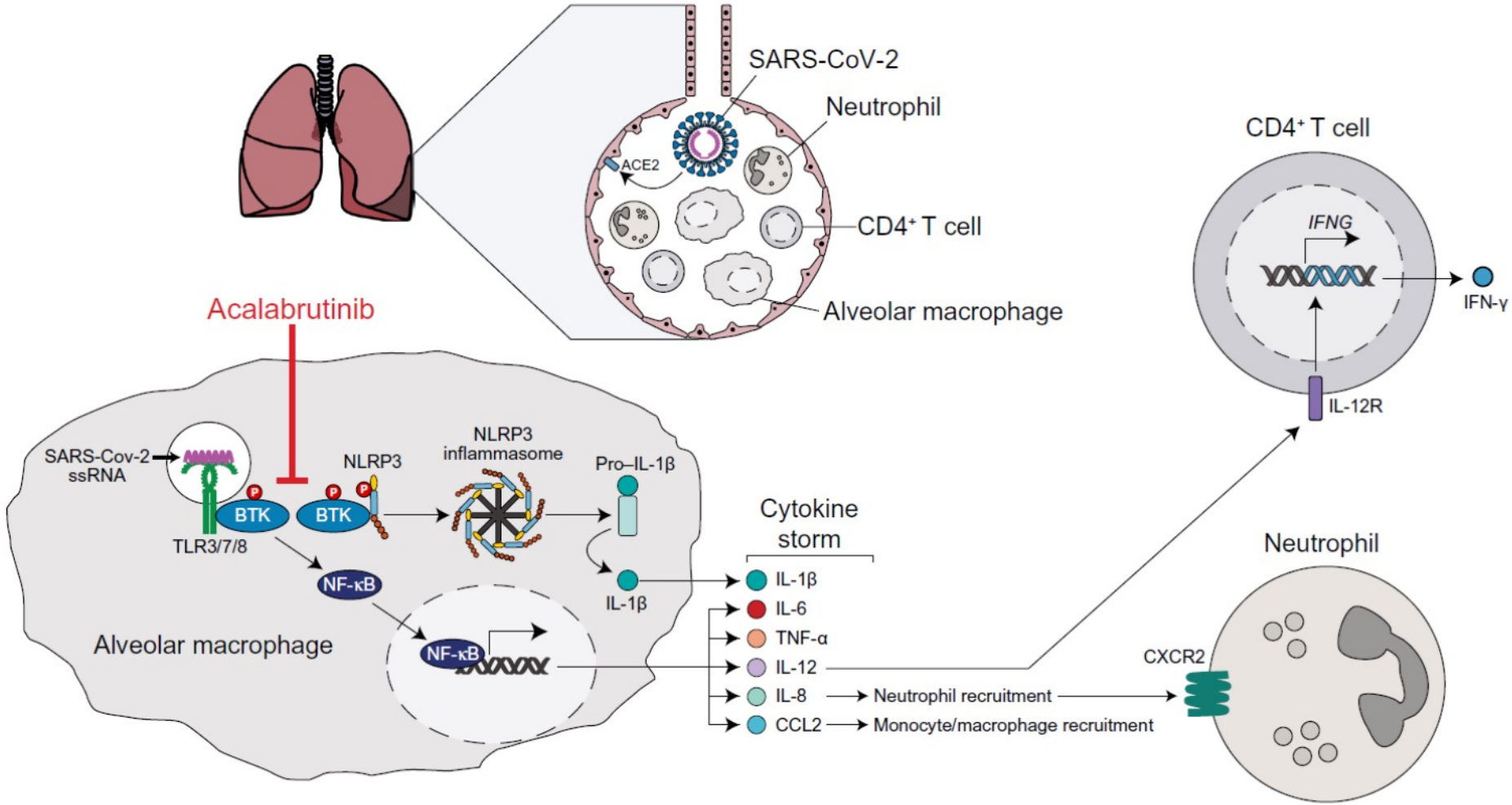


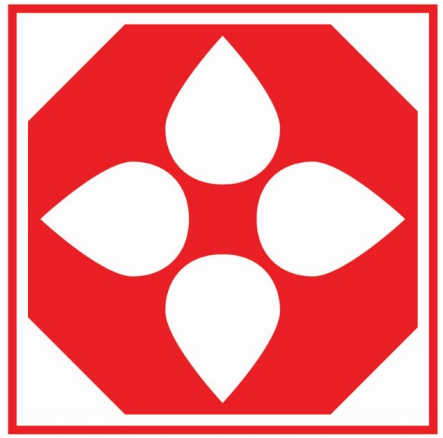
Figure 1: SARS-CoV-2 viral load change from baseline by visit.

Could BTK Inhibitors Impact COVID-19

CLL SOCIETY



Roschewski et al, 2020 Science Immunology



CLL SOCIETY

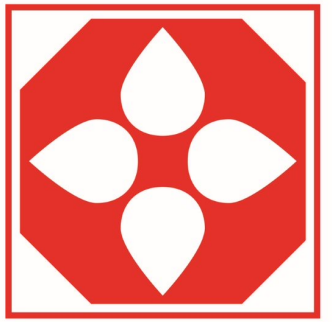
Smart Patients Get Smart Care™

The Current Status of COVID-19 Treatment for CLL

Sanjeet Dadwal, MD

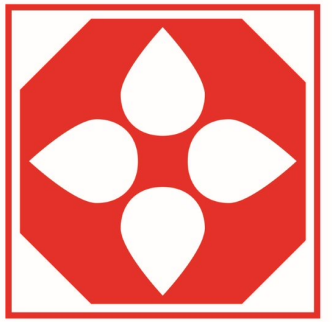
March 26, 2021

Special Features of COVID-19 in CLL



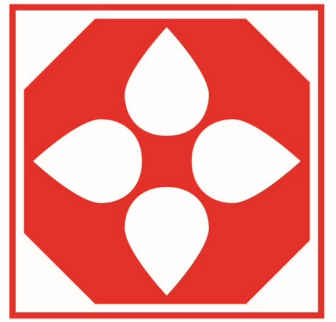
- Prolonged B cell deficiency in patients on active therapy with B-cell depleting agents
- Agents like ibrutinib – have pleotropic effects
- Lack of development of humoral immunity
- Role of T-cell immune responses unclear and not well studied
- Prolonged shedding of SARS-CoV-2 after initial infection with or without later progression to pneumonia
- Potential delay of therapy in those with prolonged shedding

Available Therapeutics for COVID-19



- Approved antiviral – so far, only Remdesivir
- Emergency use authorization:
  - Monoclonal antibodies – two products (caveats – relating to variants)
  - High titer convalescent COVID-19 plasma
- Immune modulators
  - Dexamethasone
  - IL-6 inhibitors: tocilizumab and sarilumab
- Anticoagulation
- Prevention: Vaccines

What Do We Know About Antivirals



- Remdesivir:
  - FDA approved for hospitalized patients with moderate to severe COVID19
  - No impact on survival, but hastens recovery
  - Is there a role for early treatment in CLL patients?
  - Ongoing clinical trials for outpatient treatment in patients with mild disease
- No other approved agents
- Molnupiravir (Merck)– oral antiviral in clinical trials

Immunomodulators for Supportive Care

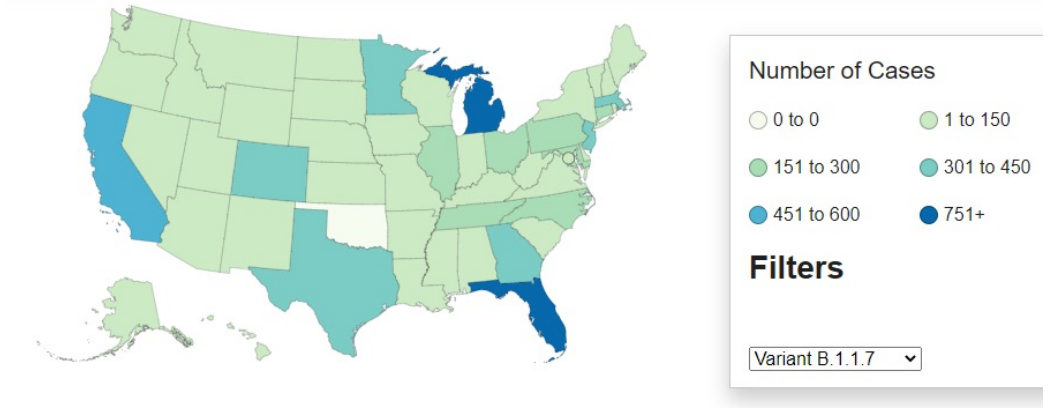
CLL SOCIETY

- Tocilizumab
- Sarilumab
- Baracitinib
- Anticoagulation

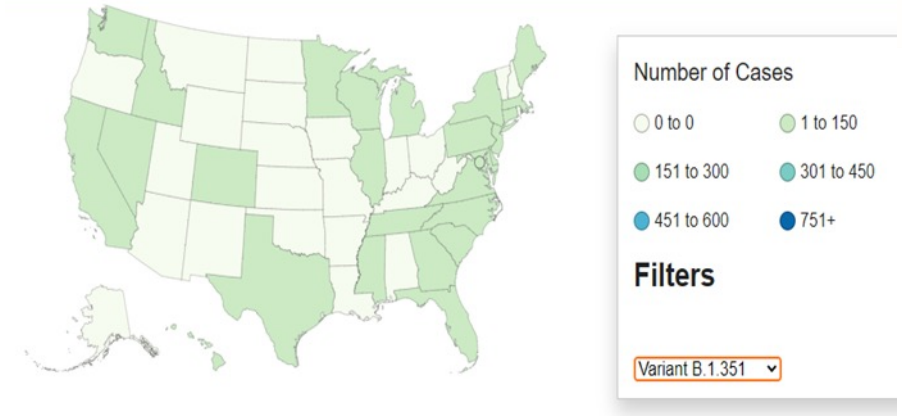
Variants

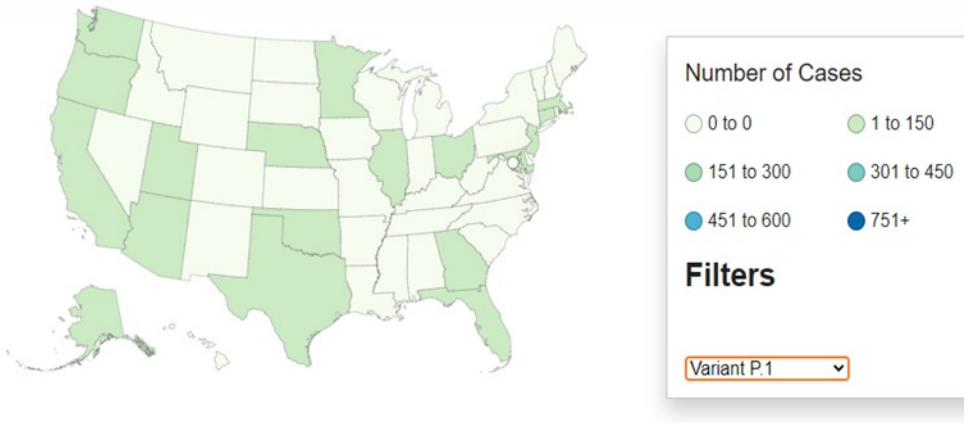
CLL SOCIETY

B1.1.7 – UK strain



B.1.351 – SA strain





P.1 – Brazilian strain

Variants

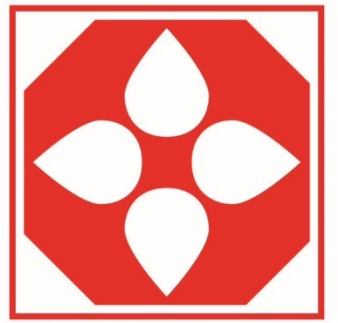
Result of mutations in the spike protein

What is its impact on:

1. Transmissibility
2. Severity of illness
3. Response to treatment
4. Response to convalescent plasma
5. Response to monoclonal antibodies
6. Response to vaccines

CLL SOCIETY

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

Join us for the **CAR-T Ed Forum** taking place on Wednesday, April 21

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/