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

[AbbVie and Adaptive Biotechnologies logos]
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
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
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
Efficacy of Vaccinations in CLL While Undergoing Treatment

**Vaccination**
- Recombinant Hepatitis B (HepB-CpG)
  - and/or
- Shingles (RZV)

**CLL Patients**
- Treatment Naïve
- Receiving Bruton Tyrosine Kinase Inhibitor (BTKi)

**Vaccine Response**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Serologic response rate (%)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>HepB-CpG</td>
<td>28.1%</td>
<td>32</td>
</tr>
<tr>
<td>RZV</td>
<td>59.1%</td>
<td>22</td>
</tr>
<tr>
<td>Treatment Naïve</td>
<td>P = .017</td>
<td></td>
</tr>
<tr>
<td>BTKi</td>
<td>41.5%</td>
<td>41</td>
</tr>
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Pleyer et al, Blood 2021
SARS-CoV-2 Vaccines

• 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)

### COVID-19 Vaccines

*EUA*

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

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

## 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

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:
  o The first immediately or as soon as one knows about exposure
  o 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?

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

<table>
<thead>
<tr>
<th>POSITIVE Antibody Testing</th>
<th>NEGATIVE Antibody Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>• You did come into contact with the virus sufficient to generate an antibody response.</td>
<td>• 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.</td>
</tr>
<tr>
<td>• It is NOT known if these antibodies are protective or not.</td>
<td>• You did once upon a time come into contact with the virus, but the concentration of antibodies is below level of detection.</td>
</tr>
</tbody>
</table>
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
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
What If I Contract COVID-19?

- Mild disease:
  - Isolation
  - Monitoring symptoms and temperature
  - Symptomatic management
  - Pulse oximetry (>88%)

- Moderate or severe disease:
  - Hospital admission
Emerging Agents to Treat COVID-19

- **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

Roschewski et al, 2020 Science Immunology
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 COVID-19
  • 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

- Tocilizumab
- Sarilumab
- Baricitinib
- Anticoagulation
Variants

- 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
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.

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