CLL Society
Global Virtual Patient & Caregiver Educational Forum
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:00 PM</td>
<td>Welcome and Introduction</td>
<td>Patricia Koffman, CLL Society</td>
</tr>
<tr>
<td>12:15 - 1:05</td>
<td>Definitions, Diagnosis, Test Before Treat, and Early Management in CLL</td>
<td>SPEAKERS: Neil E. Kay, MD, Mayo Clinic, Rochester, MN&lt;br&gt;Ryan W. Jacobs, Levine Cancer Institute and&lt;br&gt;Altrium Health, Charlotte NC&lt;br&gt;MODERATOR: Brian Koffman, MDCM (retired) MS Ed, CLL Society</td>
</tr>
<tr>
<td>1:05 – 1:15</td>
<td>Being Your Own Advocate</td>
<td>SPEAKERS: Nathan Ferguson and Doreen Zetterlund, Patient Advocates&lt;br&gt;MODERATOR: Brian Koffman, MDCM (retired) MS Ed, CLL Society</td>
</tr>
<tr>
<td>1:15 – 1:25</td>
<td>Session Break</td>
<td></td>
</tr>
<tr>
<td>1:25 – 2:15</td>
<td>Frontline therapy options, plus measuring response including MRD</td>
<td>SPEAKERS: Joseph Flynn, DO, MPH, FACP, Norton Cancer Institute, Louisville KY&lt;br&gt;Anthony Mata, MD, MSCE, Memorial Sloan Kettering Cancer Center, New York City, NY&lt;br&gt;MODERATOR: Brian Koffman, MDCM (retired) MS Ed, CLL Society</td>
</tr>
<tr>
<td>2:15 – 2:20</td>
<td>CLL Society Resources Presentation</td>
<td>Carly Boos, MEd, MBA CLL Society</td>
</tr>
<tr>
<td>2:20 – 3:10</td>
<td>2nd line and later therapies</td>
<td>SPEAKERS: Matthew Davids, MD, MMSc, Dana Farber Cancer Institute, Boston MA&lt;br&gt;Jose F. Leis, MD, PhD, Mayo Clinic, Phoenix AZ&lt;br&gt;MODERATOR: Brian Koffman, MDCM (retired) MS Ed, CLL Society</td>
</tr>
<tr>
<td>3:10 - 3:20</td>
<td>CLL-specific Patient &amp; Caregiver Support Groups</td>
<td>SPEAKER: Terry Evans, CLL Society</td>
</tr>
<tr>
<td>3:20 – 3:30</td>
<td>Moderated Discussion Session Break</td>
<td>MODERATOR: Patricia Koffman, CLL Society</td>
</tr>
<tr>
<td>3:30 – 3:40</td>
<td>Flash Presentations</td>
<td>SPEAKERS: Sameer A. Parikh, MBBS, MD, Mayo Clinic, Rochester, MN</td>
</tr>
<tr>
<td>3:40 – 3:50</td>
<td>Clinical Trials</td>
<td>John C. Byrd, MD, The Ohio State Comprehensive Cancer Center, Columbus OH</td>
</tr>
<tr>
<td>3:50 – 4:00</td>
<td>Vaccines</td>
<td>Adrian Wiesner, MD, PhD, National Institutes of Health (NIH), Bethesda, MD</td>
</tr>
<tr>
<td>4:00 – 4:10</td>
<td>CAR-T</td>
<td>Joseph A. Fraietta, PhD, Perelman School of Medicine, Philadelphia, PA</td>
</tr>
<tr>
<td>4:10 – 4:20</td>
<td>COVID-1</td>
<td>Lindsey Roeker, MD, Memorial Sloan Kettering Cancer Institute, New York City, NY</td>
</tr>
<tr>
<td>4:20 – 4:50</td>
<td>Audience Q&amp;A with all flash presentation speakers</td>
<td>MODERATOR: Brian Koffman, MDCM (retired) MS Ed, CLL Society</td>
</tr>
<tr>
<td>4:50 – 5:00</td>
<td>Thank you and closing session</td>
<td></td>
</tr>
</tbody>
</table>
This program was made possible by grant support from
Housekeeping Reminders

• Please direct your questions to speakers or CLL Society staff using the Q&A box (located at the bottom of your screen). Questions can only be seen by staff and speakers. The audience is muted.

• Please complete the short survey emailed to you after the event. Your response will help CLL Society plan future events.

• The forum is being recorded and will be available along with the presentation slides on our website via the Support Groups/Education page on cllsociety.org.

• Please explore your screen to view resources, speaker bios, the post-event survey, and a link to donate to CLL Society.
Polling Questions
Definitions, Diagnosis, **Test Before Treat™** and Early Management in CLL

**Moderator:** Brian Koffman, MDCM (retired), CLL Society

**Speakers:**
Neil E. Kay, MD, Mayo Clinic, Rochester, MN
Ryan W. Jacobs, MD, Atrium Health, Charlotte, NC
CLL/SLL: The Prelude and the Beginning

• Diagnosis
• What is MBL
• What is CLL/SLL
• Testing at time of diagnosis
• Causes and familial CLL
• Infections and second cancer screenings
Watch and Wait and Starting Treatment

• Watch and Wait
• Early management
• Auto-immune complications
  • AIHA (auto-immune hemolytic anemia)
  • ITP (immune thrombocytopenic purpura)
• Testing needed to do or repeat before treatment starts
• Indications for therapy
AUDIENCE Q&A
Being Your Own Advocate

Speakers: Doreen Zetterlund, Actor, Patient Advocate

Nathan Ferguson, RN, Co-Facilitator
Nashville CLL Society Support Group, Patient Advocate

Moderator: Dr. Brian Koffman, CLL Society Co-founder, EVP and Chief Medical Officer
Frontline Therapy Options, Measuring Response, Including MRD

**Moderator:** Brian Koffman, MDCM (retired), CLL Society

**Speakers:**
Joseph Flynn, DO, MPH, FACP, Norton Cancer Institute, Louisville, KY
Anthony Mato, MD, MSCE, Memorial Sloan Kettering Cancer Center, New York City NY
CLL/SLL: Frontline Therapy

- Factors in deciding on first therapy
- Any role for chemo-immunotherapy?
- Targeted therapy options
  - Continuous versus limited duration
  - Single agent versus combinations
  - Clinical trials
CLL/SLL: MRD and Response

• Traditional ways to measure response
• MRD
  • What
  • Which test
  • Why
  • When
• Factors in deciding when to stop therapy, when to continue, and when to start a new therapy
AUDIENCE Q&A
Polling Question
CLL Society
Resources

Carly Boos, MEd, MBA
Executive Director
CLL Society
2nd Line and Later Therapies

Moderator: Brian Koffman, MDCM (retired), CLL Society

Speakers:
Matthew Davids, MD, MMSc, Dana Farber Cancer Institute, Boston, MA
Jose F. Leis, MD, PhD, Mayo Clinic, Phoenix, AZ
CLL/SLL: 2\textsuperscript{nd} Line Therapies

- Factors in deciding on later line of therapy
- Relapsed, refractory, or intolerant
- Re-testing
- Treatment options including clinical trials
CLL/SLL: 3rd Line and Later Therapies

- 3rd line and later options
- New therapies or combinations of past therapies
- Clinical trials
- Role of allogeneic hematopoietic stem cell transplant
- Role for palliative care and hospice in CLL
AUDIENCE Q&A
CLL-Specific Patient & Caregiver Support Groups

Speaker: Terry Evans
Director, CLL Society Support Groups

Moderator: Patricia Koffman
Co-Founder and Communications Director
CLL Society
Polling Question
Flash Presentations

1. **Richter Transformation**: Sameer A. Parikh, MBBS, MD, Mayo Clinic
2. **Clinical Trials**: John C. Byrd, MD, The Ohio State Comprehensive Cancer Center
3. **Vaccines**: Adrian Wiestner, MD, PhD, NHLBI and NIH
4. **CAR-T**: Joseph A. Fraietta, PhD, Perelman School of Medicine
5. **COVID-19**: Lindsey Roeker, MD, Memorial Sloan Kettering Cancer Institute
Richter Transformation of CLL

Sameer Parikh, MBBS, MD
Mayo Clinic, Rochester, MN
What a Patient Needs to Know

- What is Richter transformation?
- Risk factors
- Symptoms
- Diagnosis
- Treatment
Definition of Richter Transformation

THE AMERICAN JOURNAL OF PATHOLOGY

Volume IV

July, 1928

Number 4

Report of Case

Clinical History: W. H., Shipping clerk, age 46 years. Entered Bellevue Hospital June 14, 1926, complaining of swelling on the left side of neck, duration seven weeks.

Family History and Past Personal History: Irrelevant.

Present Illness: Seven weeks ago the patient noticed a swelling on the left side of the neck which increased gradually in size. It was not painful. The patient had occasional pains in the epigastrium and suprapubic regions, of short duration, which had no relation to meals, defecation or exertion. He had lost a great deal of weight in the last two months.

Physical Examination: (Positive findings only.) Adult white male, appears chronically ill. Marked emaciation. Eyes: Petechial hemorrhages in palpebral conjunctivae. Neck: Masses of nodes in left cervical region, anterior and posterior chains. The individual nodes appear to be about 2 cm. in diameter. There are smaller ones in both supraclavicular regions. The nodes are firm and

- First described by Dr. Maurice Richter (a pathologist at New York’s Bellevue Hospital) in 1928

- 2016 WHO definition: development of an aggressive B-cell lymphoma in CLL:
  - Diffuse large B-cell lymphoma (95%)
  - Hodgkin lymphoma (4%)
  - Histiocytic sarcoma (<1%)

Richter MN, Amer J Path, 1928
Annual Incidence Of Transformation

- From the Mayo clinic 2000-2011
- Median follow-up 4 years: 2.3% of pts developed RS (median was 1.8 years)
- 47% transformed prior to treatment
- All patients 0.5% per year.
- After treatment it appears to increase to 1%/yr

Parikh et al, BJH; 2013
Risk Factors for Transformation

- Key risk factors:
  - Del17p by FISH
  - NOTCH1 mutation
  - TP53 mutation
Symptoms and Initial Evaluation

- **Symptoms:**
  - Rapidly enlarging lymph node or nodes
  - Fever
  - Fatigue

- **Laboratory findings:**
  - Increased serum lactate dehydrogenase (LDH)
  - Increased serum calcium
  - Anemia and low platelets

- **Initial work-up:**
  - PET scan
  - Bone marrow biopsy
Diagnostic and Additional Workup in Richter Transformation

• Diagnosis:
  • Biopsy of an accessible node that is most FDG-avid or “lights up” most on PET scan

• CLL and Lymphoma tests:
  • FISH
  • Complex karyotype
  • Next generation sequencing

• Clonal relationship between CLL and Richter transformation:
  • Molecular studies
Standard Treatment of Richter Transformation

- No standard treatment for Richter transformation of CLL
  - Clinical trial participation and expert care strongly recommended

- Clonal relationship to underlying CLL:
  - clonally unrelated typically has better prognosis

- No prior CLL therapy:
  - Patients with no prior CLL therapy do better

- Prior CLL therapy was with chemoimmunotherapy (such as FCR or BR):
  - Consider R-CHOP based therapy in combination with a BTKi or venetoclax*

* these treatments are not FDA approved
Standard Treatment of Richter Transformation

- Prior CLL therapy included ibrutinib/acalabrutinib or venetoclax:
  - Switch the novel agent and combine with R-CHOP based therapy*
  - Novel-novel combinations; such as ibrutinib+venetoclax+anti-CD20*
  - Some data supporting the use of PD1 inhibitors such as nivolumab/pembrolizumab with BTK inhibitors*

- **Long term strategy:**
  - “Stem cell” transplant
  - CAR-T

* these treatments are not FDA approved
Current Clinical Trials of Richter Transformation

• **Chemotherapy + novel agent:**
  - R-CHOP/R-EPOCH + venetoclax (NCT03054896)
  - R-CHOP + acalabrutinib (STELLAR, NCT03899337)

• **Novel agents:**
  - Obinutuzumab + high dose steroids + lenalidomide (NCT03113695)
  - PI3 kinase inhibitors with venetoclax (NCT02535286, NCT03534323)
  - DTRM-555 + pomalidomide + everolimus (NCT04305444)
  - ARQ-531 (novel BTK inhibitor; NCT03162536)
Current Clinical Trials of Richter Transformation

- **PD1 inhibitor based treatments:**
  - Pembrolizumab + ibrutinib/idelalisib (NCT02332980)
  - Nivolumab + ibrutinib (NCT02420912)
  - Nivolumab + copanlisib (NCT03884998)
  - Ateolizumab + venetoclax + obinutuzumab (NCT02846623)
  - Nivolumab + duvelisib (NCT03892044)
  - Tislelizumab + zanubrutinib (CLL RT-1; NCT04271956)

- **Bispecific antibodies:**
  - Blinatumomab (NCT03121534)
  - XmAb13676 (NCT02924402)
Thank you!
parikh.sameer@mayo.edu

Rochester, Minnesota
Scottsdale, Arizona
Jacksonville, Florida
Clinical Trials - What You Need to Know

John C. Byrd, MD
The Ohio State University and the Leukemia and Lymphoma Society
What it Takes for a Drug to Get to a Clinical Trial in CLL?

• Laboratory identification of a target relevant to the disease—you can help here

• Creation of a compound, peptide/antibody, or cell product that eliminates CLL cells in the lab

• Demonstration that the compound works in mouse models of CLL or related diseases

• Acceptable drug properties
  • Pharmacology
  • Toxicology
  • Absent harmful interactions with other drugs, etc.

• Filing of an investigational new drug (IND application)
Type of Drug Clinical Trials

• Phase 1 trial: Identify the effective dose of drug
• Phase 2 trial: Demonstrate safety and efficacy in a setting of a single disease at a given time point (i.e. relapse). Not compared to standard therapy.
• Phase 3 non-randomized trial: Examine efficacy in a much larger patient group where no available therapy exists (registration enabling)
• Phase 3 randomized trial: Compare to a standard therapy for the disease for superior efficacy or safety. This is the case in most CLL trials.
• Phase 4 study trial: Done after drug approval to address FDA concern or pursue a different approach (investigator initiated study or IIT)
Process of Clinical Trial Participation

• Physician caring for you presents one or you find one (clinicaltrials.gov) to discuss

• Informed consent counseling—coordinator presents study to you and provides written document for you to read

• Informed consent signing—coordinator has you sign after all your questions are answered and decision is made to proceed with this

• Screening—testing (lab, exam, imaging, etc.) to be sure you are eligible for the trial and it is safe for you to participate

• Treatment—begins after successful screening and continues until you have adverse side effect or progression on treatment

• Follow-up—time after therapy ceases where study team will follow you
Why Are Clinical Trials Important?

• In 1991 when I started my training as an intern, there was only one effective therapy for CLL and virtually all patients who became symptomatic with their disease would die from it

• Clinical trials have brought forth a plethora of therapies (fludarabine, rituximab, alemtuzumab, ofatumumab, ibrutinib, idelalisib, venetoclax, and acalabrutinib) for CLL patients
  • Life expectancy now even with need for treatment is similar to patients age and sex matched who do not have CLL

• Clinical trials have taught us other things do not work or have unacceptable side effects with only minimal exposure of patients

• Clinical trials often have increased monitoring and oversite, which often results in even better patient outcome
How to Know if Trial is Right for You?

• Does the phase of the study match where I am at in my disease?
  • Phase 1—heavily pre-treated CLL where there are less options
  • Phase 1b —prior treated CLL
  • Phase 2 early—prior treated CLL until efficacy and safety demonstrated
  • Phase 2 late-Phase 4—previously untreated and treated CLL

• Does my doctor think this is the best thing for me?

• Is the requirements of the study doable for me based upon travel requirements, monitoring, imaging, insurance and costs, etc.?

• Recognizing the importance of clinical trials, does my gut tell me that this is a good option for me?
Other Important Questions

• What if the trial does not work for me?
  • There is nothing wrong with you—sometimes therapies don’t work
  • Just because one trial drug does not help your condition, another trial drug could so avoid becoming discouraged

• What if I am harmed by the trial?
  • Injury that occurs to a patient in a trial relative to hospital costs, etc. is often paid by your insurance; in the consent form details are provided

• Can I withdraw from the trial if my response is not good enough or the medication is not making me feel well?
  • Yes, at any time

• Could the trial cost me more out-of-pocket costs?
  • Yes, while the research costs are covered by the trial, it is likely you will have extra visits which may increase cost. “Standard of care” is usually your responsibility.
A concluding statement about clinical trials:

Clinical trials are for the patients, NOT patients for the clinical trials.
Vaccines

Adrian Wiestner, MD/PhD
National Heart, Lung, and Blood Institute, NIH
Vaccines in patients with CLL

Background
• Vaccines are effective in reducing risk of infections in the general population
• There is little data on vaccine responses in CLL patients
• Vaccine response rates in CLL patients have been variable in small studies
• To seasonal influenza vaccines 15-65% of patients respond

Recommendations

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Safe for CLL Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Routine Non-Live Vaccines</strong></td>
<td></td>
</tr>
<tr>
<td>Influenza (Afluria, Fluarix, Flucelvax, Fluzone)</td>
<td>✔</td>
</tr>
<tr>
<td>Pneumonia (Pneumovax-23)</td>
<td>✔</td>
</tr>
<tr>
<td>Pneumonia (Prevnar-13)</td>
<td>✔</td>
</tr>
<tr>
<td>Shingles (Shingrix)</td>
<td>✔</td>
</tr>
<tr>
<td>Hepatitis B (Engerix, Recombivax, Heplisav)</td>
<td>✔</td>
</tr>
<tr>
<td>Tetanus, Diphtheria and Pertussis (TDaP)</td>
<td>✔</td>
</tr>
<tr>
<td><strong>Travel Non-Live Vaccines</strong></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A (TWINRIX, HAVRIX, VAQTA)</td>
<td>✔</td>
</tr>
<tr>
<td>Meningococcus (MenACWY)</td>
<td>✔</td>
</tr>
<tr>
<td>Intramuscular Typhoid (Typhim Vi)</td>
<td>✔</td>
</tr>
</tbody>
</table>

Not recommended: live vaccines
Pneumonia vaccination

Suggested Schedule for Immunocompromised Individuals

- **Prevnar 13**
  - 2 Months

- **Pneumovax 23**
  - Every 5 Years

- **Pneumovax 23**
Influenza vaccination

High-Dose or Standard Dose Influenza Vaccine?

<table>
<thead>
<tr>
<th></th>
<th>IIIV3-HD (N=15,990)</th>
<th>IIIV3-SD (N=15,993)</th>
<th>Relative Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol-defined influenza-like illness</td>
<td>228 (1.4)</td>
<td>301 (1.9)</td>
<td>24.2 (9.7 to 36.5)‡</td>
</tr>
</tbody>
</table>

DiazGranados, NEJM 2014

CDC Recommendation: **No preference** for any one flu vaccine type. Any age appropriate flu vaccine is fine.

Avoid: FluMist Intranasal Live Virus Vaccine
Do vaccines work when I am treated with a BTK inhibitor?

Yes, to some degree – at least for the seasonal flu vaccine: 27% of CLL patients being treated with ibrutinib responded to the seasonal influenza vaccine.

*Sun et al, Jama Oncology 2016*
Ongoing NIH vaccine trials

Shingrix (Shingles vaccine)
- ‘Chickenpox’ virus remains dormant for life
- Can reactivate and cause shingles (herpes zoster) and nerve pain
- 1 out of 3 people in the U.S. will develop shingles in their lifetime
- Risk of shingles increases with age and when the immune system is weakened
  ✓ Immune system memory response

Heplisav (Hepatitis B vaccine)
- Hepatitis B virus can cause liver damage
- Currently incurable
- ~850,000 people in US affected
- Vaccine recommended for:
  - People with chronic health conditions
  - Healthcare workers
  ✓ Immune response to new infection

Chris Pleyer, MD
Vaccine side effects

Almost all reactions are mild and resolve within 2-3 days

<table>
<thead>
<tr>
<th>Adverse Reactions within 7 days of Vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Reaction</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Any ≥ Grade 3</td>
</tr>
</tbody>
</table>

**Local Reactions (Any Grade)**
- Soreness: 23.7% (HEPLISAV) vs 82.8% (SHINGRIX)
- Redness: 0.9% (HEPLISAV) vs 38.4% (SHINGRIX)
- Swelling: 0.9% (HEPLISAV) vs 26.5% (SHINGRIX)

**Systemic Reactions (Any Grade)**
- Fatigue: 12.6% (HEPLISAV) vs 45.7% (SHINGRIX)
- Headache: 11.8% (HEPLISAV) vs 39.6% (SHINGRIX)
- Muscle Aches: 8.5% (HEPLISAV) vs 49% (SHINGRIX)
- Fever: 0.6% (HEPLISAV) vs 23.9% (SHINGRIX)

**Impressions so far:**
- Safety as reported, both in patients on watch & wait and in patients treated with BTK inhibitors
- Response rate to Shingrix vaccine ~40-50% - compared to >90% in the general population
- Response rate to Heplisav under investigation
Participate in vaccine trials

- Diagnosis of CLL or SLL
- On watch & wait, on BTK inhibitor or venetoclax
- No prior vaccination with Shingrix, no shingles infection in the past 1 year
- No prior hepatitis B infection or vaccination
- Not being treated with IVIG

Clinic visit
Blood draw
Vaccine dose #1

Clinic visit
Blood draw
Vaccine dose #2

Clinic visit
Blood draw
Test response

0 months
3 months
6 months

Contact:
Susan Soto: sotos@nhlbi.nih.gov
Pia Nierman: Pia.Nierman@nih.gov
CAR T cell Therapy for CLL

Joseph A. Fraietta, PhD
University of Pennsylvania
Why are CAR T cells Referred to as “Living Drugs” Engineered to Fight CLL and other Cancers?

- The immune system we are born with is often not equipped to win the battle against cancer
- A patient’s own T cells can be engineered to make artificial receptors (CARs) allowing them to seek out and destroy tumors
What are the Phases of CAR T cell Therapy of CLL?

1. **Remove blood from patient to get T cells**
2. **Make CAR T cells in the lab**
   - Insert gene for CAR
   - Chimeric antigen receptor (CAR)
3. **Grow millions of CAR T cells**
4. **CAR T cells bind to cancer cells and kill them**
   - CAR T cell
   - Cancer cell
   - Antigens
5. **Infuse CAR T cells into patient**

CAR T-cell Therapy
What are the Responses to CAR T cell Therapy in CLL and Side Effects of Treatment?

• CAR T cell therapy can be dramatically effective for many patients with relapsed/refractory CLL who have run out of effective treatment options.

• The first 2 patients that we treated at the University of Pennsylvania remain in remission more than 10 years later, with no detectable evidence of CLL by any measure.

• In some patients, the CAR T cells eradicated 7 and a half pounds of tumor!

• Just over 50% of CLL patients respond, and between 25% and 35% of patients achieve a complete remission.

• Among these patients, the relapse rate is low.

• Most patients who respond to CAR T cell therapy develop some degree of cytokine release syndrome (CRS). It can be mild to severe and treatment options are available.

• Some patients experience neurologic toxicity that can lead to confusion, delirium, aphasia, seizures, etc.
  • In most cases, with supportive care, neurologic toxicity resolves spontaneously after a few days or up to a couple of weeks.
What is the Current Status of FDA-approved CAR T cell Therapy for CLL?

• Right now, the FDA has approved CAR T cell therapy for adult patients with certain types of lymphoma and for children and young adults with acute lymphoblastic leukemia that haven't responded to other forms of treatment.

• CAR T cell therapy is not yet FDA-approved for CLL, but ~30 clinical studies across the globe are currently recruiting patients (i.e., generally for treatment of relapsed/highly refractory disease).
How does CAR T cell Therapy Compare with other Treatments for CLL?

• Difficult to compare CAR T cell therapy with other treatments.

• Used primarily in patients with multiply relapsed or refractory disease, and there are not many treatments for CLL in that category.

• In contrast to other treatments in CLL, CAR T cell therapy is a one-time treatment. Repeated dosing is not required.

• When CAR T cells are effective, they can induce deep clinical remissions even as assessed by deep sequencing, which can detect 1 in 1,000,000 CLL cells.

• Few treatments for CLL can induce deep sustained complete remissions.
Is There Any New Promising Research in CAR T cell Therapy for CLL? What’s on the Immediate Horizon for this Approach?

- Rational Drug Combinations with CAR T cells for CLL
- Controllable CAR T cells for CLL
- Biomarker-driven CAR T cell Therapy for CLL
COVID-19 and CLL

Lindsey Roeker, MD
Memorial Sloan Kettering Cancer Center
Global impact of COVID-19
COVID-19 in patients with cancer

Cancer patients (especially hematologic cancer patients and older cancer patients) appear to have more severe COVID-19 (higher rates of ICU admission, requirement for mechanical ventilation, and death)

Risk of COVID-19 for patients with CLL

- Hypothesized that patients with CLL would be at higher risk
  - Immunocompromised from CLL and CLL therapies
  - Advanced age
- No high-quality studies of incidence are available
- This remains one of the major unanswered questions for patients with CLL
Symptoms for patients with CLL who get COVID-19

Table 3. COVID-19 signs and symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Proportion (%)</th>
<th>Number with available data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>88</td>
<td>196</td>
</tr>
<tr>
<td>Cough</td>
<td>85</td>
<td>193</td>
</tr>
<tr>
<td>Sputum production</td>
<td>25</td>
<td>183</td>
</tr>
<tr>
<td>Hemoptyis</td>
<td>2</td>
<td>190</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>74</td>
<td>197</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>18</td>
<td>183</td>
</tr>
<tr>
<td>Sore throat</td>
<td>16</td>
<td>184</td>
</tr>
<tr>
<td>Myalgias/artrhagias</td>
<td>36</td>
<td>176</td>
</tr>
<tr>
<td>Headache</td>
<td>16</td>
<td>179</td>
</tr>
<tr>
<td>Fatigue</td>
<td>72</td>
<td>192</td>
</tr>
<tr>
<td>Chills</td>
<td>34</td>
<td>185</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>29</td>
<td>190</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>14</td>
<td>192</td>
</tr>
<tr>
<td>Evidence of DIC</td>
<td>16</td>
<td>184</td>
</tr>
<tr>
<td>Lymphopenia (ALC &lt; 1.0 x 10^9/L)</td>
<td>25</td>
<td>185</td>
</tr>
</tbody>
</table>

Table 2. Clinical presentation and management of patients with COVID-19.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>No (%)</td>
</tr>
<tr>
<td>Fever</td>
<td>165 (87)</td>
</tr>
<tr>
<td>Cough</td>
<td>93 (49)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>92 (48)</td>
</tr>
<tr>
<td>Myalgias/artrhagias</td>
<td>29 (15)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22 (12)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>32 (17)</td>
</tr>
<tr>
<td>Anosmia/ageusia</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Nasal discharge</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>8 (4)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Management of COVID-19</td>
<td></td>
</tr>
<tr>
<td>Confinement at home</td>
<td>21 (11)</td>
</tr>
<tr>
<td>Hospitalization without need of oxygen</td>
<td>18 (10)</td>
</tr>
<tr>
<td>Hospitalization with need of oxygen</td>
<td>112 (59)</td>
</tr>
<tr>
<td>Intensive care</td>
<td>39 (20)</td>
</tr>
</tbody>
</table>

Outcomes for patients with CLL who get COVID-19

• Two large series of CLL patients suggest this is a serious problem for those patients who are sick enough to require hospitalization for COVID-19

• Factors that might increase chance of bad outcomes:
  • Older age
  • Other medical problems
    • Asthma
    • Chronic kidney disease
    • Smoking
  • CLL treatment (?? – found in one study, not the other)
    • BTK inhibitors are being studied as a treatment for COVID-19

Immune response to COVID-19

• Preliminary study: 30 patients with CLL who had COVID-19
  • 21 patients had SARS-CoV-2 antibody testing
  • Antibody testing 28 – 93 days after COVID-19 diagnosis
• 67% (14 of 21) tested positive for SARS-CoV-2 antibodies
• Low immunoglobulin levels predicted lack of SARS-CoV-2 antibody development
• Receiving CLL therapy was not associated with antibody development

Changes to CLL management in the setting of the COVID-19 pandemic

- Recommendations made by groups of CLL experts
  - Timing of Therapy
  - Choice of Therapy
  - Logistics of Clinic Visits versus Virtual Visit
  - When to test for COVID-19
  - Changes in therapy if a patient gets COVID-19

- Precautions for CLL patients
  - Hand washing, social distancing, mask wearing

This program was made possible by grant support from:

- AbbVie
- AstraZeneca
- Bristol Myers Squibb
- Genentech
- Foundation Medicine
- Janssen
- Phacemicals Companies of Johnson & Johnson
- CLL Society
THANK YOU FOR PARTICIPATING

Please take a moment to complete our event survey, your feedback is important to us.

Please register for our upcoming webinar “The Future of CAR-T Therapy: Can CAR-T Cure CLL?” on Tuesday, November 17 at our events page under Support Groups/Education.