

COVID-19
AND **CLL**

MAY 21, 2020

**Understanding the Impact of COVID-19 on the Care of Patients
with Chronic Lymphocytic Leukemia – A Live CME Webinar**

Moderator

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Faculty

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Anthony R Mato, MD, MSCE

Jeff Sharman, MD

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Exelixis Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Genomic Health Inc, Gilead Sciences Inc, GlaxoSmithKline, Guardant Health, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncoceptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seattle Genetics, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc and Tolero Pharmaceuticals.

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Dr Davids — Disclosures

Advisory Committee	AbbVie Inc, Ascentage Pharma, AstraZeneca Pharmaceuticals LP, Celgene Corporation, Genentech, a member of the Roche Group, Janssen Biotech Inc, Pharmacyclics LLC, an AbbVie Company, TG Therapeutics Inc
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Data and Safety Monitoring Board/Committee	Celgene Corporation, TG Therapeutics Inc

Dr Sharman — Disclosures

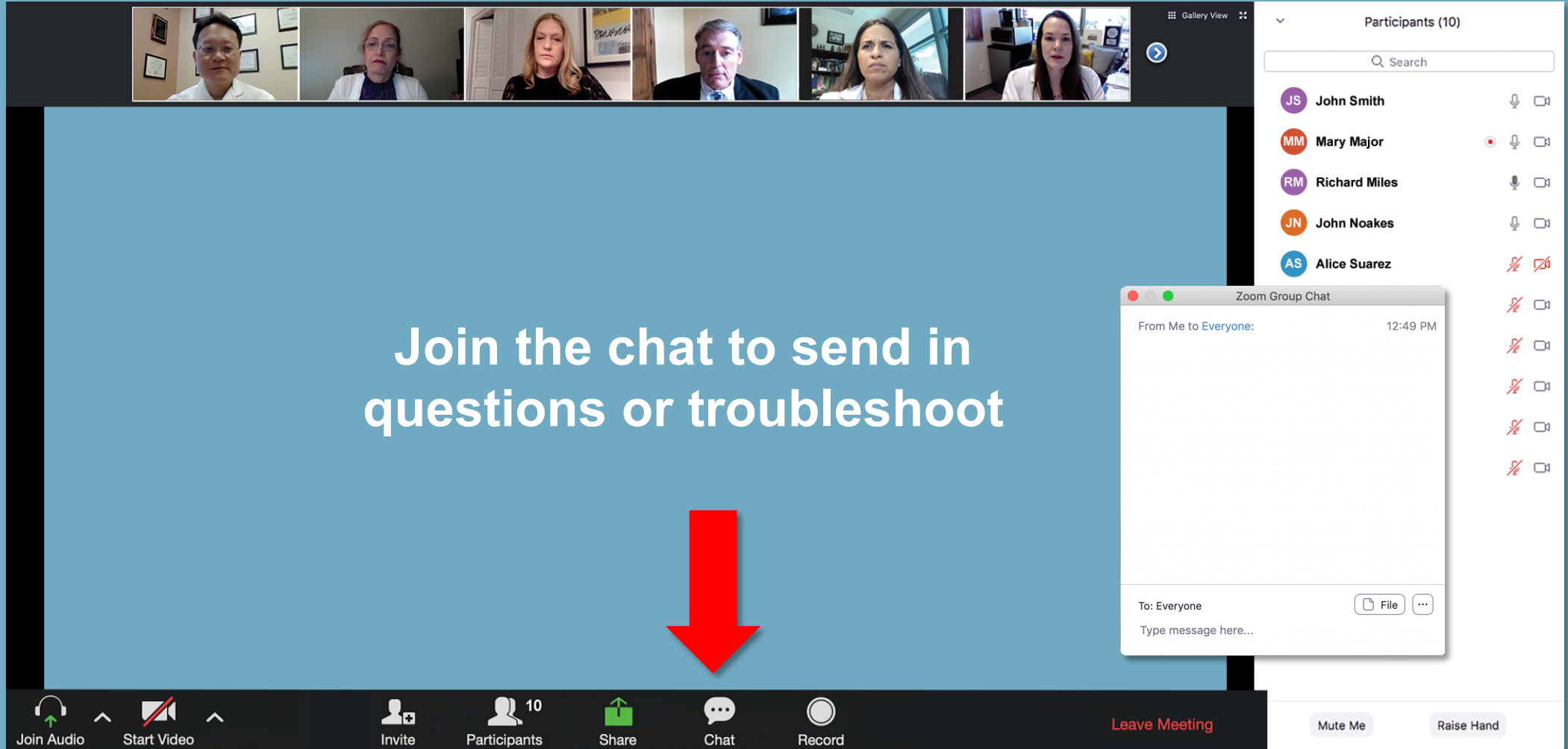
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Familiarizing yourself with the Zoom interface

How to participate in the chat

Join the chat to send in questions or troubleshoot



The screenshot illustrates the Zoom interface during a meeting. The top section shows a gallery view of six participants. On the right, the 'Participants (10)' list is visible, showing names and icons for audio and video. A 'Zoom Group Chat' window is open, displaying a message from 'Me' to 'Everyone' at 12:49 PM. The bottom toolbar includes icons for 'Join Audio', 'Start Video', 'Invite', 'Participants' (10), 'Share', 'Chat', and 'Record'. A large red arrow points down to the 'Chat' icon. The 'Leave Meeting' button is visible on the right side of the toolbar.

iTHREE AMIGOS!



Agenda

**MODULE 1: Management of CLL (without SARS-CoV-2)
in the Pandemic**

**MODULE 2: Evaluation of Patients with CLL and
Symptoms/Signs Suggestive of SARS-CoV-2**

MODULE 3: Management of CLL and SARS-CoV-2

MODULE 1: Management of CLL (without SARS-CoV-2) in the Pandemic

1. A 61-year-old patient with (del)11q CLL; IGVH unmutated. No (del)17p or P53 mutation. Patient is observed for 4 years; develops progressive lymphadenopathy and worsening fatigue, which makes it difficult for him to work. What would your likely treatment be?

- a. BTK inhibitor alone
- b. BTK inhibitor in combination with a CD20 antibody
- c. Venetoclax/obinutuzumab
- d. Other

Case: Dr Davids

59 y/o female hair stylist with a history of DCIS s/p surgery + radiation in 2000 followed by a couple of months of tamoxifen which was poorly tolerated and discontinued. CLL was originally diagnosed in 2009 and observed who soon thereafter was diagnosed with ER/PR/HER-2 positive stage 2 breast cancer s/p bilateral mastectomy and adjuvant chemotherapy with TAC. Referred to me in 2014 and prognostic markers revealed del(13q), mutated IGHV, wildtype TP53. Over the course of the next few years had slow progression, most prominently in the cervical lymph nodes and tonsils. Disease would flare in setting of URIs but then quiet down with short courses of steroids. By early April 2020, the nodes had become bulky enough that CLL treatment was indicated. Options that were considered included FCR, venetoclax + obinutuzumab, ibrutinib, and acalabrutinib. Given the prior chemotherapy, FCR was not preferred. Given the COVID-19 pandemic, the patient was hesitant about venetoclax + obinutuzuamb. Given the prior anthracycline chemotherapy and chest radiation, acalabrutinib was chosen over ibrutinib given the possibly better cardiac side effect profile. The patient started acalabrutinib about 1 month ago and is doing well so far.

COVID-19 and CLL: Frequently Asked Questions

Version 1.3; May 6, 2020

Hematology.org

Management of CLL Patients Early in the COVID-19 Pandemic: An International Survey of CLL Experts

Koffman B et al

***Am J Hematol* 2020;[Online ahead of print].**

Assuming the current SARS-CoV-2 test availability...

- What is your general SARS-CoV-2 testing strategy for patients with CLL who are not currently receiving treatment and do not have a history of multiple infections?
- What is your general SARS-CoV-2 testing strategy for patients with CLL who are not currently receiving treatment but have a history of multiple infections?

- For a patient receiving treatment for CLL who tested positive for SARS-CoV2, do you change or modify therapy?
- Will your approach be different based on the type of therapy (BTKi, PI3Li, venetoclax, antibodies, chemoimmunotherapy, et cetera) or the severity of viral infection?

CALAVI Clinical Trial with Acalabrutinib Against COVID-19

Press Release – April 14, 2020

“A randomised, global clinical trial [will be initiated] to assess the potential of acalabrutinib in the treatment of the exaggerated immune response (cytokine storm) associated with COVID-19 infection in severely ill patients.

The trial design is based upon strong scientific evidence supporting the role of the Bruton’s tyrosine kinase (BTK) pathway in the production of inflammatory cytokines and on encouraging early clinical data. *Acalabrutinib* is a next-generation, highly selective BTK inhibitor currently used to treat certain types of blood cancers.

The trial, called CALAVI, is based on early clinical data with *acalabrutinib* demonstrating that a decrease in inflammation caused by BTK inhibition appears to reduce the severity of COVID-19-induced respiratory distress. The goal of the trial is to evaluate the efficacy and safety of adding *acalabrutinib* to best supportive care (BSC) to reduce mortality and the need for assisted ventilation in patients with life-threatening COVID-19 symptoms.

This large, multicentre, global, randomised trial uses a two-part patient-centric design developed in record time to accelerate data capture and analysis. Part one evaluates the addition of *acalabrutinib* to BSC versus BSC alone in patients hospitalised with COVID-19 who are not in the intensive care unit (ICU). Part two evaluates the addition of *acalabrutinib* to BSC in a cohort of patients in the ICU.”

BTK inhibitors in cancer patients with COVID19: “The winner will be the one who controls that chaos” (Napoleon Bonaparte)

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Clin Cancer Res 2020;[Online ahead of print].

MODULE 2: Evaluation of Patients with CLL and Symptoms/Signs Suggestive of SARS-CoV-2

2. Have you had a patient with CLL with symptoms suggestive of SARS-CoV-2 who tested negative?

- a. No
- b. Yes, 1 patient
- c. Yes, more than 1 patient

Case: Dr Sharman

- 61-year-old woman with HTN, DM, COPD, hypercholesterolemia and social challenges
- 2004: Presented de novo with WBC > 300,000
- Bendamustine/rituximab
- 2017: Adenopathy, lymphocytosis
 - FISH: Del(13q)
- Obinutuzumab-based therapy on study (maintained remission)
- Follow-up CT scan: Widespread bilateral reticulonodular densities and patchy consolidation in inferior lungs concerning for multilobar atypical infection, onset of fever
 - Son being evaluated for COVID-19
- Referred to ER for COVID-19 testing and given antibiotics, with subsequent recovery
- Patient and son tested negative for COVID-19

Case: Dr Sharman

- 75-year-old man followed for years with IgHV-mutated, del(13q) CLL
- 2016: Disease progression
- Obinutuzumab/chlorambucil on UNITY-CLL trial
 - MRD-positive CR and in long-term follow-up
- Played bridge with asymptomatic friend, who shortly thereafter tested positive for COVID-19
- Patient developed cough and fever
 - Referred to ER for COVID-19 testing (negative)
 - Fever and cough persist for 2 weeks despite antibiotics
 - Wife became ill with similar symptoms
 - Tested negative for COVID-19

MODULE 3: Management of CLL and SARS-CoV-2

3. A patient tolerating ibrutinib well for more than 2 years has a spouse with SARS-CoV-2, which leads to the patient being tested and testing positive. The patient is asymptomatic. Would you...

- a. Continue the BTK inhibitor
- b. Hold the BTK inhibitor
- c. I don't know

4. The patient in the previous scenario (positive for SARS-CoV-2) is doing well on treatment but presents with moderate shortness of breath and cough. The patient is not admitted to the hospital. Would you...

- a. Continue the BTK inhibitor
- b. Hold the BTK inhibitor
- c. I don't know

Case: Dr Mato

- 71-year-old man with a history of autoimmune hemolytic anemia and PCP pneumonia
- Treatment for relapsed/refractory CLL on a clinical trial (Anti-CD20 antibody + PI3K inhibitor + ibrutinib)
- Presents with fever (102F), cough and dyspnea
- Study drugs held, ibrutinib continued
- Remained at home with persistent fevers x 10 days
- Admitted to a local hospital with increasing dyspnea
 - Hypoxemic, placed on oxygen
 - CT imaging: Diffuse ground glass / Beta-D glucan was negative
 - Oxygen demands increased (Currently on 50-90% face mask) but has not yet required mechanical ventilation
- COVID 19 treated with HCQ, convalescent plasma, IVIG, azithromycin and remdesivir without response
- Subsequent CT scans: Pulmonary fibrosis

Case: Dr Mato

- 49-year-old man with CLL receiving front-line venetoclax/obinutuzumab
- Presents with fevers to 103F and cough
- CT chest: Bilateral ground glass
- Venetoclax discontinued (MRD undetectable)
- Clinical course with SARS-CoV-2
 - 6 weeks with persistent fevers
 - Not yet required oxygen
 - Now evidence of transaminitis
- Admitted for observation 3 separate times
- Respiratory swab for SARS-CoV-2 is persistently positive (3 swabs over 6 weeks)
- Serum antibody testing for SARS-CoV-2 is negative
- Plans to begin convalescent plasma

5. A patient tolerating venetoclax/obinutuzumab well for more than 2 years has a spouse with SARS-CoV-2, which leads to the patient being tested and testing positive. The patient is asymptomatic. Would you...

- a. Continue treatment
- b. Hold treatment
- c. I don't know

Case: Dr Davids

71 y/o male taxi driver originally diagnosed with unmutated IGHV, del(11q) CLL in 2010. Initially observed and did well for several years but by 2014 had progressive disease and was treated on trial with idelalisib + ofatumumab and achieved PR. Upon subsequent progression, enrolled on trial with umbralisib + ibrutinib in 2016 and achieved CR. Ibrutinib was discontinued in 2018 after a CNS bleed. Since that time has been in CR on umbralisib monotherapy though has had intermittent pulmonary infections and chronic cough in the setting of active smoking. He and his wife had been quarantining since 3/13/19. On 4/30/19, his wife went to local ED due to respiratory symptoms and tested positive for COVID-19. Patient was told to isolate from his wife but on 5/7/19 he developed malaise and fatigue. Tested positive for COVID-19 on 5/8/19 and developed chills and low grade temps that evening. We decided to hold umbralisib at that time. Developed fevers over the next several days up to 101.9F, started on Tylenol around the clock. Wife pushed to take him to ED but no SOB so told him to stay at home. 5/19/19 is the first day he has been afebrile, though still taking Tylenol around the clock. Trying to decide when to resume umbralisib, fortunately his CLL appears to still be in remission at this time.

Case: Dr Mato

- 55-year-old man with a history of HTN who is under active observation for CLL
- Presents with persistent fevers to 103F and mild cough
- PCR testing: Positive for SARS-CoV-2
- Admitted and observed for 24 hours
 - Febrile without hypoxa
 - CXR: Mild infiltrates
- Discharged to home and observed for 2 weeks with fever
- Currently, in full recovery

6. The patient in the previous scenario (positive for SARS-CoV-2) is doing well on treatment but presents with moderate shortness of breath and cough. The patient is not admitted to the hospital. Would you...

- a. Continue treatment
- b. Hold treatment
- c. I don't know

Case: Dr Davids

66 y/o female property manager and former smoker from New Hampshire with Rai stage 0 CLL diagnosed in 11/2018 on observation with prognostic markers showing del(13q), trisomy 12, t(14;18) on FISH and complex karyotype with mutated IGHV (VH-4-39) but with wildtype *TP53* and *NOTCH1*. Developed fever, cough, dyspnea in mid-March and went to her local ED where she was found to have pneumonia on CXR and was admitted and started on cefpodoxime and doxycycline. COVID-19 testing came back positive on 3/22/20, and hydroxychloroquine and azithromycin were added. Patient improved and was discharged home after 4 days in the hospital and has now recovered from the infection.

Thank you for joining us!

**CME credit information will be emailed to
each participant tomorrow morning.**