



CLL SOCIETY

Webinar Transcript

Immunity and CLL: It's Complicated but Understandable

August 29, 2024

In science and medicine, information is constantly changing and may become out-of-date as new data emerge. All articles and interviews are informational only, should never be considered medical advice, and should never be acted on without review with your health care team.

This text is based off a computer-generated transcript and has been compiled and edited. However, it will not accurately capture everything that was said on the webinar. The complete recording of this webinar is available on-demand.

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Hello and welcome to today's webinar.

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I'm Robyn Brumble, a registered nurse and the CLL Society's Director of Scientific Affairs and Research.

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At the CLL Society, we are dedicated to bringing credible and up-to-date information to the CLL community...

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because we believe smart patients get smart care.

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As a reminder, you can re-watch all of our educational programs by going to this section of our website called Education On Demand.

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Prior to beginning our webinar today, we would like to mention a few items.

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All attendees in this webinar are muted and the only people on camera are our speakers.

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We ask that you please direct all questions to the Q&A section which is displayed at the bottom of the screen.

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Questions will be sent directly to our moderator, speakers and CLL staff...



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00:10:57.000 --> 00:11:00.000
and are not visible to the audience.

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After today's event you will receive a very brief survey that will help us plan for future events.

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We greatly appreciate your feedback.

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This session will be recorded and made available to everyone on our website.

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Closed captions are available.

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If you want to turn them on or off, please go to captions and then select show captions, or hide captions.

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At this time,...

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I would like to introduce our moderator. Thank you.

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Thank you, Robyn.

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I would like to welcome our audience to today's event.

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I'm Dr. Brian Koffman, the co-founder, Executive Vice President and Chief Medical Officer of the CLL Society...

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and we are joined today by Dr. Jacob Soumerai...

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An Assistant Professor at Harvard Medical School...



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and a clinical investigator in lymphoma at Mass General Cancer Center...

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and Dr. Andres Chang...

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who's an instructor at the Winship Cancer Institute of Emory University.

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We will be answering audience questions at the end of the event, so please take advantage of this opportunity...

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and ask your questions in the Q&A box.

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Before we begin,...

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there are a few important disclaimers I want to share.

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The information provided today is for educational purposes only, and should not be considered medical advice.

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For any personal health or treatment questions,...

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please consult with your healthcare team.

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Please note that while the CLL Society may have its own opinions and policies,...

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our speakers may offer differing viewpoints...

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especially regarding the management of CLL and its complications.

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Now it's my pleasure...



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to introduce and welcome Dr Jake Soumerai.

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So I'm Jake Soumerai and I'm a CLL doctor and Clinical Investigator at the Mass General Cancer Center, and many thanks to the CLL Society for inviting me to participate in this really important program.

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Today, I'm going to present on CLL and the immune system.

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And we're going to cover the following three learning objectives. First, how is the immune system affected by CLL.

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Second, how do CLL therapies impact immunity.

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And finally, what does this ultimately mean for patients. Right?

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So, we have long known that the immune system is abnormal in people living with CLL.

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Many years ago, before blood work to measure white blood cells was routinely performed,...

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many folks with CLL were actually diagnosed because they presented with recurring infections and they...

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went looking for underlying causes, and lo and behold they found...

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an elevated white blood cell count.

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These types of infections could be bacterial or fungal infections, including types of infections that only occur...



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when people have weakened immune systems suggesting that this wasn't...

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something that was, you know, maybe just a slight increase or uptick in the number of infections. But really there was more to it. There were some real abnormalities in the immune systems themselves.

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Later on we learn that greater CLL disease burden, this means...

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you know, how high is the white count, how...

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large are the lymph nodes, right? Greater disease burdens seem to be associated with higher infection, risk...

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suggesting that the disease itself contributed to this risk.

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So our immune system is actually comprised of two systems. Right? There's the more primitive and fast acting, the first responder, innate immune system...

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and the more specialized and longer acting adaptive immune system.

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These must be highly coordinated and they work together to protect against infections and actually cancers.

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Their powers must be kept in check...

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as excess immunity can actually cause harm when the immune system is off balance.

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It can attack our own organs and cells.

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This is called autoimmunity. And there's actually a whole field of medicine devoted to this group of diseases, these autoimmune diseases...

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where the immune system is attacked itself.

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Autoimmune diseases.

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The innate immune system is the most primitive part of our immune system...

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and includes numerous immune cells that are designed to prevent and kill infections and cancers.

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These are our first responders. Right? They have sensors that alert them to a wide range of invaders, from infections to chemicals to cancers.

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Things that are not supposed to be in our bodies.

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They are capable of clearing the intruders themselves, but they actually also recruit other parts of our immune system to mount a more coordinated attack.

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There are many types of first responder immune cells which often don't function properly and folks with CLL.

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which we know can contribute to infection risk.

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The adaptive immune system, meanwhile, is far more specialized. Right? And this includes an army of B cells and T cells...

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which are each designed to recognize very specific invaders, so unlike the innate, immune system where...

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they have sensors that say there's something that's not supposed to be here.

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These are all primed for very specific intruders.

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Now, B cells make antibodies to clear infections. Right? The antibodies are really critical to this process.

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T cells themselves, kill infections and prevent cancers.

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Now true to its name, this part of the immune system adapts to what it experiences. Right? And it produces memory of past invaders...

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such that it can be more efficient in clearing infections when they recur down the line. Right? So if you've...

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had an infection before and it took you some time to clear it,...

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you learn how to attack it, you sort of learn this infection, you're ready for the next time around...

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and you're better clearing it the second time that you encounter that bug.

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Now, in people with CLL, this part of the immune system is also abnormal...

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which contributes as well to infection risk.

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So let's focus a little bit on antibodies and specifically, IgG antibodies.

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B cells make antibodies such as IgG antibodies that can be measured in your blood. You may know this as your IgG level, something that your doctors...



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may have checked once when you were diagnosed or...

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may follow. There is some variability in how this is tracked.

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These are very important for clearing infections. These IgGs,..

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in particular, bacterial infections and the sinuses,..

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the respiratory system and the skin, but also other types of infections as well as viruses and others.

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IgG antibodies are low in about two-thirds of people living with CLL.

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Now, fortunately, only some of these patients will develop recurrent infections as a result of this.

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When people with low IgG levels...

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have severe or recurrent infections, we can increase the antibody levels with infusions or injections. This is often called IVIG...

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or intravenous immunoglobulin.

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Now,..

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I would argue that this reactive approach, where we wait for infections and then only intervene when they develop...

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leaves much to be desired. Right?



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I think we need a more proactive approach. But to accomplish this, we need to learn more about infection risk. Right? We need to better understand why some patients...

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have high infection risk despite relatively normal antibody levels which can happen,.

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while others can have extremely low antibody levels, yet never have infections. Right? So I think that there's really room for improvement and growth in this field...

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to better care for our patients in the future.

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Now, CLL treatments also impact the immune system.

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Now, chemotherapy really is no longer used in CLL here but many current patients were previously treated with chemotherapies.

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And many of these chemotherapies have kind of long lasting effects in the immune system. If you've received fludarabine or bendamustine even years ago,.

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we can still see effects of the chemotherapy...

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on the bone marrow or other types of immune cells that can influence infection risk.

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Antibody therapy, such as the CD20 antibodies, which target B cells, for example, obinutuzumab and rituximab...

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directly reduce B cells because that's their target and this can lead to lowering of antibody levels which, as we just discussed, can lead to certain types of infections.

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Now modern targeted therapies like BTK inhibitors, such as acalabrutinb,.

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and zanubrutinib, the B2 cell inhibitors and others...

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are much more complicated. Right? So these,

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in general, don't suppress the immune system as deeply as chemotherapies or as broadly. They tend to interact with the immune system in much more specific ways.

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But they interfere with many different types of immune cells.

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And we know that these drugs lead to increased infections in some ways, although it's possible that in other ways they might actually correct some abnormalities in the immune system. And so, there's many sort of complicated ways in which these novel therapies actually interact with the immune system and influence the risk of infections. Right? And so,..

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I would argue that with targeted therapies, that requires a much more detailed discussion based on the individual drug or medicine that you're taking.

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So going back...

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to thinking about how we actually estimate risk to guide our patients. You know most of what we know about infection risk and CLL either comes from the chemotherapy era or from the early phases of the COVID-19 pandemic.

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Right.

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Now this makes it very hard...

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to estimate infection risk for people with CLL...

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many people who are diagnosed now and only receive modern therapies. Right? Maybe they...



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had all their vaccines long before they're diagnosed, right? So, it's very hard to know...

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how the data that we have from many years ago, even from a few years ago,...

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can be applied to somebody who's diagnosed with this disease today.

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And, like all other aspects of caring for people living with CLL,...

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I would argue that we really should strive to estimate risk on an individual patient level. Right?

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You can see 10 different people living with CLL and you really have seen 10 different diseases. Right? There are no two patients who are completely alike.

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And I think that if you look at infection risk,...

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infection risk for two patients can range from near normal, right, to somebody with maybe minimal disease burden,...

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has never been treated, has been fully vaccinated, has normal antibody levels,...

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to very high risk. Say, somebody who's had a lot of prior therapies, including past chemotherapy, and so...

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these two patients are very different, and should be approached and counseled in different ways.

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So how do I estimate an individualized infection risk?

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Well, I consider a patient's age,...

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what comorbidities they have, what other medical problems they have, diseases...

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aside from the CLL that might impair their immunity or...

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lead to some particular risk, like, for example, emphysema or COPD...

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and pneumonia risk, something along those lines.

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How much CLL do they have?

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Do they have a very high white blood cell count? A lot of disease in the lymph nodes.

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What are their antibody levels or is their IgG very low, as we discussed before.

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And what treatments have they received either in the past or in the present? And when, right, because some treatments have a more durable effect, whereas others the effect really wanes once you stop it.

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Finally, we can learn a lot about a patient's personal infection history, right? That just because somebody is diagnosed with CLL today doesn't mean that it started today, right? It often has been present for years.

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And so, if we look back and ask a patient, well, how have you done with infections?

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And they say, "well, you know, I've had the flu and Covid, and this, that, and the other, and..."

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I actually do better than the rest of my family". You probably feel a little bit better about that patient than somebody who's telling you that they've had...



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many infections and really struggle to clear them.

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As I alluded to before, the immune system is also important for preventing cancers, which, like infections, present themselves as invaders. They're not...

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self, right? They're not supposed to be in your body...

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because these immune cells are often dysfunctional. They often don't work...

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totally normally in people with CLL. We do see higher rates of other cancers in particular, skin cancers in our patients.

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I encourage patients to have...

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routine age and risk factor guided cancer screening. And it's very important that all patients with CLL see dermatologists for routine skin checks at least annually to prevent skin cancers...

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as these can otherwise become more invasive and more troublesome and I consider...

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these to be really a never event, right? I mean, I think that if you continually monitor with a dermatologist,

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if they detect these early often at pre-skin cancer stages, or at least at early skin cancer stages,...

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they can really avoid serious trouble in the future.

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Finally, the immune system is off balance in people living with CLL as I've mentioned.



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And this can redirect the immune system against patients. This is actually called autoimmunity.

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And CLL autoimmunity most often results in decreased red blood cells or platelets.

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We call these complications autoimmune with red blood cells...

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or immune thrombocytopenia or ITP with the platelets.

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Other much less common autoimmune complications can also occur.

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We usually treat these conditions with steroids, things like prednisone or dexamethasone.

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Although sometimes only treating the underlying CLL is effective. And so it really depends on what specific complication it is.

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And oftentimes seeing how folks do with steroids, are we able to control it quickly? Or, do we need to add something to really control the CLL itself, which may be the motor underlying it.

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In summary,...

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the immune system can be dysregulated or imbalanced in people with CLL...

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and this may lead to infections, other cancers...

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and autoimmune complications.

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It is critically important that our patients take infections seriously.



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This means notifying...

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doctors, when infections occur as early diagnosis and treatment can improve how patients do...

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and can lead to faster recovery. In the case of right.

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and also notifying doctors if they experience...

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severe infections, as your doctors may be able to reduce infections with preventive measures. For example, if your IgG levels are low, this is something that we can fix and we can actually reduce infection risk.

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And finally, routine cancer screening should be performed. This is really important.

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And in particular, dermatology visits to conduct full skin exams to prevent skin cancers.

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I'd like to thank the CLL Society and all of you again...

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for this opportunity to participate in today's program.

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And I'd like to welcome Dr. Andres Chang to continue with his portion of the presentation.

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Good afternoon everyone, thank you for having me today. I'm going to talk about...

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how to prevent infections and what we know about immune reconstitution and CLL.

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And so the learning objectives for this talk is to provide you with an overview of the strategies to minimize the frequency and severity of infections...

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but also to discuss the potential strategies that might be available in order to reconstitute the immune system in patients with CLL.

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And so let's start with talking about infection prevention.

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Okay. And like Benjamin Franklin said, an ounce of prevention is worth a pound of cure, and that is definitely true when it comes to infections, especially in patients with CLL.

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I want to stress the fact that...

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things like what I call common sense, okay, the measures that we instituted during the pandemic, including sick contact, avoiding sick contacts,...

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performing proper hand hygiene, wearing a mask...

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but also improving air quality around our environment,...

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having good public health measures and community surveillance, and those kinds of things...

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actually do work.

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And I want to...

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use this graph here, on the right, as an example where...

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you see the different shades of blue. This is different,



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strains of influenza viruses...

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and you see, the higher the peak is, the higher the incidence or the prevalence of it.
That particular viruses are in the city of Seattle.

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And you can see, over here, over time that starting in 2019,..

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in the wintertime, we see a peak that corresponds to what we normally call the flu
season...

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and then over the summer, the amount of influenza infections is lower, and then over
the next blue season we see another peak.

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But I want to...

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point out what happened in April of 2020, right. This is at the beginning of the
pandemic...

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when we all had to...

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lockdown and people stopped eating out, people start wearing mask and all these
things. And look at what happened with again, influenza infections, and we see that...

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those dramatically went down and stayed down. And we really in 2021,..

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really didn't have any much of a flu season and even in '22 there isn't much of a flu
season either.

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And this just highlights how...

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instituting some of these measures can potentially help preventing infections.

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And this is true also if you look at influenza worldwide, here different colors depict again different viruses.

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And now remember, this is worldwide data. And so there's...

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also some influenza infections in the southern hemisphere during what..

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for us is in the summer. But you see a huge peak over here in the 2020...

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flu season, and then, come April, we have a dramatic reduction, and there's really not much activity in 2021 and it's not until 2022 where some countries..

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really start opening back up, where we see infection rates from influenza going back up again.

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These common sense measures...

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are in fact, so effective that throughout this period we were effectively able to eradicate one of the four influenza strains depicted here.

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So what about vaccines?

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Well, vaccines are not designed necessarily to prevent infections, but rather to...

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reduce the...

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reduce the risk of severe infections and hospitalizations.

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CLL SOCIETY

We know that that's true, for...

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many...

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people, most people in the general population. But we also know that patients with CLL among suboptimal antibody responses to vaccines.

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What that means is that the antibody titers, the amount of antibodies...

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that are produced after vaccination might be lower than in the general population.

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And so there are different ways in which we've tried to mitigate this, this deficit.

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Most commonly is through additional booster vaccines, and in some cases these might help.

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But also to try to better understand what happens to the other compartments of the immune system, such as...

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now, what happens to T cells...

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after vaccination and...

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and that sort of thing.

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I, in my...

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practice, I still tell people, and I still advise people that they should get vaccinated because some response is better than no response. Right? And so I still commonly recommend patients receive their annual influenza vaccine, Covid vaccines, ..



CLL SOCIETY

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RSV, if they haven't had the pneumococcal vaccines or shingle vaccines and so forth.

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And also to stress the importance of a vaccine in close contacts because if you vaccinate close contacts, then the risk of infection to the patient is reduced.

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I do want to point out that...

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we should avoid using live vaccines during periods of significant immunosuppression. Then significant immunosuppression happens...

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usually around or soon after the times of certain therapies...

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but those should be discussing more detail with the...

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patients provider.

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Now there is another strategy that we have employed historically to try to reduce...

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The incidence and the severity of infection and that is to administer some sort of a prophylactic medication or preventive medication ahead of time in order to reduce those potential complications.

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One of the best examples, and probably better known examples is this medication called AZD7442, which was branded as Evusheld...

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during the height of the pandemic...

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this was a...

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cocktail of monoclonal antibodies that aim to reduce the...



CLL SOCIETY

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risk of a severe infection in our immunocompromised patients or high risk patients.

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But, as you probably will know already, this medication is no longer effective, nor is it available for...

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our patients anymore.

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That said, there are new antibodies coming up.

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Pemivibart and sipavibart are two of these such monoclonal antibodies, one of them, the first one has received emergency use authorization but none of these medications have had their publications out yet, and so they're still allowed to be known about the true effectiveness of these medicines.

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Now,..

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even before the pandemic, we in the CLL community have used...

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this medication call IVIG or which is a essentially a mixture of polyclonal antibodies...

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in order to decrease or reduce the risk of recurrent...

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and severe infection.

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And in fact, there's on the figure on the right, this is a publication by Dr. Soumerai earlier this year where he looked at..

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a cohort of CLL patients and lymphoma patients...

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CLL SOCIETY

and determine...

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that patients who actually get...

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this IVIG treatment have a decreased rates of infection and decreased rates of...

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the use of antimicrobial medication.

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There is, in fact, ..

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currently undergoing a clinical trial called the pro-sid trial which is trying to look at this question of effectiveness, of this IVIG prophylaxis in a prospective manner. And hopefully, that will give us even better data...

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yeah, on how to best use this medication in order to protect our patient population.

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And then...

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depending on the circumstances, ..

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doctors might be prescribing medications such as acyclovir / valacyclovir to prevent herpes reactivation,

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and entecavir, which is used to prevent hepatitis B reactivation when we use with anti-20 monoclonal antibodies...

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in some cases we will use...

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trim sulfamethoxazole or brand name Bactrin , in order to prevent certain bacterial infections,



CLL SOCIETY

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anti-fungals and so forth.

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And all those things might need to be discussed...

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in more detail, depending on each person's particular...

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scenario and treatment.

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Now, what happens when somebody actually has an infection?

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How do we manage that for our patients?

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Well, one of the key things that we need to keep in mind is that...

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prompt initiation of therapy is key to a good outcome.

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I highly encourage our patients to seek care early when the signs of infection first manifest...

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and that is because it's a lot easier...

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to treat patients early in the infectious course.

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And sometimes,..

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in some cases, medicine's only really work...

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with infections when we start,..



CLL SOCIETY

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when we start treatment early, and that is in the case of influenza, with also time of year, brand name. Tamiflu.

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As well as with Covid, which we have several different medications most notably the combination of remdesivir, nirmatrelvir/ritonavir (Paxlovid) which is probably the preferred agent for most in most cases, and then, of course, for bacterial infections we have antibiotics and for fungal infections, we have antifungals.

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But again,...

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I cannot stress enough the importance of early initiation of therapy.

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So in the last couple of minutes I want to...

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talk about a little bit of data of what we know about immune deficiency in how we are able to revert this.

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And so there are now a few publications...

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that have come out that have shown that patients who are receiving BTK inhibitors as their treatment for CLL actually...

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might have better T cell function.

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And so that is...

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something that some people have kind of...

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try to...

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CLL SOCIETY

develop this further into a way to reverse immunodeficiency.

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But I do want to point out also that BTK inhibitors also have been shown to reduce antibody response which is the B cell side of things, and so...

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whether

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one has a net benefit from an improved T cell function or not because of the reduced antibody responses to be seen...

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PI3 kinase inhibitors, which are medications that we used to use a few years back for CLL,..

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may also improve T cell functions...

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but the reason why these medications are no longer used is actually because there is a higher risk of opportunistic infections.

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And so it's true role in terms of how much...

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the immune system is strengthened by these medications is really up in the air.

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And then there's some early data suggesting that...

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if we treat CLL, I mean, we can get them into an undetectable, measurable disease status...

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that in some cases the immune system actually does respond better. And there's some reversal on some of these markers associated with other immune system.

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All in all, though, I would say that this is an area that a lot more studies are needed...



CLL SOCIETY

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so that we can clarify the mechanisms of immunodeficiency in CLL, and so that we can also develop...

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better mechanisms and better methods in which we can reverse this immunodeficiency.

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And so to conclude, I want to stress again, that prevention is better than treatment.

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And so some of these common sense measures, I still educate my patients on them, trying to either wear a mask or avoid very crowded places, avoid contacts,..

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vaccinate patients and vaccinate their close contacts.

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In some cases,..

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antimicrobial prophylaxis might be prescribed by the...

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patient's provider.

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Pre-exposure prophylaxis, is coming for, at least for Covid, hopefully for some other diseases as well. And then IVIG, which I will say, is pre-exposure prophylaxis for more than just Covid or one disease...

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might also be beneficial for certain patients.

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All these measures should be discussed also in more detail with their particular provider.

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And then early treatment...

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CLL SOCIETY

is important for people who have confirmed infections.

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And then more studies are needed to understand the mechanisms of immunosuppression, and how to reverse this process.

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And so with that, I want to thank you for your attention, and we will turn into our question and answer section.

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I hope everybody enjoyed these presentations. I sure learned a lot, and it's certainly a hot topic, and I'm looking at the questions just keep pouring in so very, very exciting. I want to thank...

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doctors Chang and Soumerai...

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for these very informative talks on CLL.

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And please, we'll begin answering your questions, but we'll try to get to as many as possible. If we're not able to get to your questions for any reason,...

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please email them to Ask the Expert email after this event...

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and we will share that email in closing.

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So there are so many great questions. And I wanted to start...

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with one that has...

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different kinds of themes. And I'll throw this to both of you.

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We understand that CLL patients are immunocompromised. Is there anything that they can be doing? Are they taking...



CLL SOCIETY

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multivitamins , is exercising helpful...

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there's a lot of comments. The microbiome has got a lot of attention recently. Is there anything in terms of...

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probiotics, we've heard. Maybe CLL patients shouldn't take probiotics, you know, because it could be dangerous for them. Is it safe for them to take it? Does it make any difference? Is there anything...

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that they can do without going to their doctor, and then we'll talk about what you can do is position that...

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help improve immunity at different phases.

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Andres, do you want to start?

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Sure. Thank you very much, Dr. Koffman. So...

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I think you know, in general, there are no strong data that have been published, that either shows a conclusive benefit or a conclusive harm.

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Things like probiotics or doing, you know, certain diets and supplements and so forth.

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What I do counsel my patients and Doctor Soumerai alluded to, this, too, is that...

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the healthier the patient is, the better their immune system is going to work and...

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by that I mean...

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CLL SOCIETY

if somebody's active, somebody's eating healthy, somebody's having,...

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minimal what we call disabilities or other kinds of diseases that are piling up,...

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then, the chances of that particular patient having...

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a strong immune system, and therefore..

The fewer number of infections kind of improves.

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But,...

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Jake, do you want to add anything to that?

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Yeah, I couldn't agree more. I mean, I think that and you know that involves both. General, you know the,...

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general diet, exercise, health, all these other things that we do to keep ourselves healthy.

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Also sort of routine primary care.

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I think that I worry sometimes that, you know, primary care is sometimes difficult to...

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establish in this day and age, and...

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something that I like to ensure is that my patients, although we establish a relationship that goes on,...

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I tell all my patients that our goal is that they retire me right? Is this is a long relationship...



CLL SOCIETY

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but that they really should maintain a connection...

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With primary care docs to address any other major medical issue. For example, make sure that COPD is better controlled. You know address, anything else that might be...

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associated with infections that might...

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further increase the risk sort of just beyond the CLL itself.

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Both of you talk quite a lot about vaccines, and I think that they're the backbone of a lot of the prevention. But there are some questions about it. Here's a basic one. Dr. Chang.

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And then I'm going to follow-up with a couple of ones. What is Tdap you mentioned? What is Tdap? Can you remind patients what that vaccine is, and when they need that.

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And maybe you also mentioned live, not, get live vaccines. What vaccines are live that a CLL patient should not get?

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Yeah. So Tdap is a vaccine that is all based on toxins against tetanus and pertussis. Normally, this vaccine is recommended to be given to patients every 10 years, and so...

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given that...

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a lot of our patients will have CLL for over 10 years, then chances are that they will be due for one of those vaccines at some point while they are, have the diagnosis of CLL.

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In terms of live vaccines, really, for adults it's mainly there's a live, attenuated shingles, vaccine...

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that I usually counsel to stay away from, especially now that we have...



CLL SOCIETY

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a shingles vaccine that is not live.

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And so that will be really the main one. The other vaccine that has live

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viruses...

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is the measles/mumps/rubella vaccine, but that usually is a vaccine that is given to kids.

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And while we're on the vaccine question there was something about...

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after having a transplant, which is used less and less in CLL, you need to be vaccinated. I wonder if you could comment on the timing of that Dr. Soumerai and also...

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I'm hearing that people have CAR-T, which is becoming more important. When I had my CAR-T there wasn't a lot of talk about vaccinations, but friends who've had it subsequently, I had mine, you know, seven years ago, very early in the CAR-T story,...

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but people now are saying, "no, you've got to get vaccinated". So what's the story on that? And...

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do we have to...

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would some of these treatments require that we need to be revaccinated. So is there thinking about that? If you could share that with us, starting with the transplant, which I think has the most data on that.

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Yeah, thank you. That is a great question. So as you said, most of our data comes from the transplant setting...

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CLL SOCIETY

and there we're talking about a wide range of vaccines. Right? It's and these are really repeating all of our childhood vaccines because when you get...

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sort of when you have...

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either of the types of chemotherapy, that when you have the types of chemotherapy that can really remove...

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your bone marrow function such that you need to replace it, you need to retrain these immune cells to fight these childhood vaccines, and so...

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there are a number of different schedules, and these have actually evolved over the years.

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But in general, if you think back to, or if you think of family members,..

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who've as children have had all their childhood vaccines over the first several years of their life,..

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that's basically what we do. And over the first few years after a transplant, we do these vaccinations.

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Now CAR-T cells is another interesting question. So you know, I...

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was heavily involved in the early CAR-T cell studies...

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that led to the approval of Liso-cel, which is a type of CAR-T cell. Now, this is the type of treatment, right, that...

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sort of where your own T cells are re-engineered to go after a...

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CLL SOCIETY

protein or sort of a flag that we know is on CLL cells, typically such that the immune system these T cells can then...

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attempt to kill off the CLL.

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This involves a couple of very immunosuppressive things. First, things that involves fludarabine and cyclophosphamide. These are chemotherapy drugs that we used to use a lot in CLL...

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but we don't anymore.

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And these have a broad effect on many different types of immune cells. But it also involves the CAR-T cells which really bring down B cells and antibodies quite a bit.

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And so,...

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in the studies we didn't, this was not, this has never been a thing that we have really sort of done early on, but with Covid you know, I'd say that this has evolved a little bit. And so we, we do, typically we did...

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early on, and we do continue to suggest that people get vaccinated against Covid for example,...

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three months out from their CAR-Ts.

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The truth is that this is with very little data and...

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this is just based on sort of consensus and expert opinion rather than based on studies that show that this is really, unequivocally the right thing to do.

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Yeah. So a couple of other questions, there's a lot of questions on vaccines, and people have had,...



CLL SOCIETY

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let's talk about the Covid vaccines particularly.

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If people have had no response. People, you know, you can get tested to see if you have response to the spike protein...

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and you haven't responded to it,...

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are you still recommending that people get...

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the vaccine? And do we know anything about...

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T cell response in the absence of antibody response? Because I think you elegantly touched on these different aspects of the immune system. Do you want to take that?

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Sure, so like I mentioned you know some response is better than no response. And so...

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for testing for antibodies is something that we sometimes do. But it's not...

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routine practice for all the patients, and so...

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for most patients, I still say I, I still stand by that statement...

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that some response, is better than no response.

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Now there are papers and published data showing that people who do not have...

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an antibody response, they might still have a T cell response. Now...



CLL SOCIETY

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how effective that T cell response is, and how much of a protection that...

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that...

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confers clinically...

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it's a little bit up in the air, but I think that the fact that at least one branch of the immune system is responding...

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to the vaccine...

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it probably means that it gives some benefit and some protection. And so I think that...

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as long as one branch of the system responds, I will still recommend patients to get that but this is...

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as you know, it's a very...

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hot area of research right now.

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I'd maybe just add the, you know, we did some early work looking at the immune response to Covid vaccine. It was really interesting.

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That, you know, there were people, you know, most people did have a T cell response, but also...

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actually, even though there were patients where we...

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couldn't identify antibodies, using the tests that are available, say at Quest or in the clinic usually...



CLL SOCIETY

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we actually were able to identify antibodies using a more sensitive method in all patients and so...

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I think that...

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I actually recommend in general, outside of a study, I recommend against using that test. I think that...

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it causes potential harm. Because, if you don't have a positive result, you might think you're not protected...

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but you might be. And on the other hand, if you have a positive result antibody test...

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it's not a license to go and lick the subway, right? I mean, it doesn't tell us that you're clearly protected against Covid and I think that to me is the most important thing is what happened when the vaccines came out.

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Right.

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We were losing. It was devastating the number of patients that that we were losing in the clinic.

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Every week, and then the vaccines came out and there's, there's just dramatic reduction in severe illness and death.

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And it's actually it's been a couple of years now...

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since I've had a patient of mine pass away from Covid, and it's actually pretty uncommon now that my patients end up in the hospital with Covid. So I'm not saying this isn't a major issue and a real problem. There are patients who have...



CLL SOCIETY

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real trouble with this illness. We have to do all we can to protect it.

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But what this tells me is that we can't take our foot off the brakes right? That...

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vaccines were probably the most important thing that we did...

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to tackle this problem, and folks with...

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CLL and SLL and other lymphomas, but focusing really here in the patients that we care for mostly with CLL and SLL.

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And the, and so moving forward, it's just so critical that...

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we protect ourselves against changes that may develop, that make this more problematic. Again, if we don't, if we don't continue to vaccinate the community.

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Let me,...

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yeah. And, and again, I think, I think, you know, to underscore...

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we're not aiming at no infections after vaccination, right? Like, I mean, this is...

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just like common colds and flu. People can still get infected after vaccines. But the goal is to keep patients out of the hospital to keep patients...

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from dying from the disease, or even having...

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more severe illness, that...

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CLL SOCIETY

puts them in bed for like three to five days. Right? I mean, if it's a mild disease...

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then I think that the vaccines are doing their job.

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Let me..

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ask a question that's tangential to this. Because you both treat a lot of CLL out patients. But I think it's an important question that keeps coming up.

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Covid is not going away. We know that, and...

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protection is good, but it's far from perfect, and there is a risk...

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so how are you counselling your patients...

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about their life, because I know people...

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that are still locked at home,..

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that won't go out, that won't do anything.

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And then I know other people who say,..

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forget it. This is this, is it? I'm doing everything.

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And there's a lot of us in between, you know, and I'm...

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you know, on a personal level, I'm not going to big concerts. I'm...

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CLL SOCIETY

very nervous about eating indoors at a restaurant. Plane flights still make me nervous. I wear an N 95 mask. What are you counseling your patients...

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about doing this. Because there's a real psychological risk to staying locked down. So maybe I'll start with you. And how do you have that conversation, because this has got to be an ongoing patient, and does it vary during the course depending, if they've just gotten a transplant, obviously it's different than if they're in deep remission. But talk to me about that conversation.

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Yeah, thank you. I think this is so important, because I think there's risk on both sides. Right? I think that there's...

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on one hand, if somebody is particularly immune suppressed like, let's say, you know,...

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let's say I'm caring for somebody who's had a lot of chemotherapy and just got CAR-T cells. That's somebody I'm worried about.

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But and maybe their risk is more from, say, getting an infection.

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On the other hand, I have patients who, as you've pointed out, don't leave the house and have...

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disconnected from family. Don't see grandchildren, you know, like the...

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and I have patients that are depressed or who have had memory issues. Right? I mean, like, there's a there's a lot of downstream effects, of really...

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being so isolated. And so I think that...

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this is where we really need to do a better job of...

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trying to identify who's at greatest risk and trying to sort of match...



CLL SOCIETY

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our counseling to the person.

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But you know in general, I don't take a one size fits all approach. I do this in the clinic. I talk to people about their individual risks. What makes the risks higher, lower.

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I tell them that there's not a rule, right? Like they're allowed to travel. They're allowed to do things, and it's about sort of risk benefit...

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and just as a point of example, you know, in the clinic, we don't have a mandate for masks anymore. But if I have a patient who's wearing a mask, I wear a mask.

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Right, like I do it out of respect, because it's important to them.

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And if I have a patient who's not wearing a mask, I don't wear a mask, because...

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I asked them if they want me to, actually. But if, but I, I think that there's value in faces, and there's value in ...

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other types of communication. So I think that...

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counseling patients, and the way that I approach patient care really comes down to a...

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really a more involved discussion about this and understanding sort of the risks and benefits of sort of either extremes, and finding...

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where that person's comfort level is.

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Dr. Chang, you want to add, that was great. By the way, I totally agree. And it's, you know, we say, and you mentioned this, if you know one CLL patient, you know one CLL



CLL SOCIETY

patient, and you've got to customize everything, Dr. Chang. Anything you want to add to that.

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Yeah,..

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I think..

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Dr. Soumerai, and my approach is very similar that we highly counseling, and we spent quite a bit of time talking about this particular subject because of its importance. And many people have kind of...

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alluded to, you know, the world has moved on, but...

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still around and I'm still immune. What do I do?

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And I think that the other thing to keep in mind is,...

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you know, we...

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still know when there is a disease prevalence or an uptake in certain infections versus when things are kind of at a very low baseline, and...

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I think that the risk of it not only depends on the individual patients, but also on the circumstance.

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Both of the society level as well as...

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the, you know, the people around them, right, the immediate people around them, and what they want to do. And so...

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if it is you know, late spring, early summer,...



CLL SOCIETY

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Covid cases are very, very low.

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That probably means that the risk is much lower to patients than you know when cases are really high, and so...

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there is that aspect of it, too, that I counsel patients on.

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I'm going to move off vaccines soon. But there's a couple other quick questions.

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Yellow fever vaccine. Dr. Chang. That's a live vaccine. If you've got patients who want to go on a safari in Africa, what are you advising them?

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Yeah, that's an interesting one that we normally don't give a lot of. Don't give this particular vaccines to a lot of patients.

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I think that it...

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also kind of depends on what kind of underlying CLL status we're talking about for that particular patient where they have...

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treatments, where they've had infections recurring infections in the past. I think that...

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that also, as Dr. Soumerai mentioned,..

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tells you a lot about what CLL in of itself is doing...

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to that particular patient's immune system. And so,..

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there's not a straightforward answer. I think that it really depends...



CLL SOCIETY

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on the patient, whether...

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you'll be comfortable...

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recommending such a vaccine or not.

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Yeah, and I, I think there's,...

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there are no data, if I'm correct, about the live vaccines being risky, it's just...

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we assume that they're risky.

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And there are case reports of them being risky and people getting disseminated disease from the attenuated or weakened vaccines. We know that, and we know that from a smallpox history and other things like that. But...

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I don't think we have...

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data. And I think it's something that may at some point, if there's an ethical way to reassess, that needs to be reassessed.

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Remind us of the...

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Protocol for RSV vaccination. Is that a onetime shot? And I'll send that to you again, Dr. Chang, if you want. Is that a onetime shot, or does it get repeated?

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And is that something that you're recommending for all your CLL patients?

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Yeah, I do recommend it for my CLL patients. It is a new vaccine. And so the frequency of how often this will be administered...



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is to be determined, just like when Covid, the Covid vaccines first came out.

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But I think that...

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in general, I would say...

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that most patients...

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will benefit from getting the RSV vaccine...

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compared to not getting it, and I think that I saw one person saying, "you know, sometimes...

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if you don't fall in the category you might get a pushback". But I think that if you really want the RSV vaccine...

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being by just, the virtue of having CLL,...

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it should be approved...

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for you to receive the RSV vaccine.

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You do have to push sometimes, if you're not in the age group, but you, you can get it. You can push for that.

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Okay, I'm going to move off...

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of vaccines and move to an another area, just a big, broad area.



CLL SOCIETY

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So...

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Jake, you discuss this. Should every CLL patient consider themselves immunocompromised to some greater or lesser extent, like I mean...

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the minute you get that diagnosis you've had no treatment.

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You're feeling great. You went in for a hernia repair, the CBC showed your blood count showed that you had lymphocytes. You were shocked that you were told that you have...

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this blood cancer that's incurable.

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And now you're immunocompromised, too, and at high risk so talk me through that, is everyone immunocompromised, or

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I've got venetoclax and obinutuzumab and it's three years later. They can't find a trace of CLL. I'm undetectable, measurable residuals. I feel great. Am I still immunocompromised?

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Yeah. Those, I think, are, and I'll address, I think those both of those are really good questions, and I'll address them, maybe one then the other.

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So is everybody immunocompromised?

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I think the answer is probably not. There's probably some people who have a level of immunity that's similar to their neighbors. And...

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who are those people? It's that's part of the problem is that we don't have the best test to identify that.

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CLL SOCIETY

But if I had to venture a guess,..

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and again, this is just hypothesis,..

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then, it's probably those people that are most likely to be in that category are probably people who have...

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the tiniest amount of disease that have never been treated.

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And probably without other like major comorbidities, although we could maybe separate that out from this discussion.

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But, and we know the reason that I say that is, that we have some earlier evidence, right that the amount of CLL is associated with infection risk and so...

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is somebody who has, you know, one cell over the cutoff, and other it to be called...

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a person living with CLL as opposed to a monoclonal B cell lymphocytosis? Are they,

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do they suddenly have a major deficit?

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I don't know. I think that's, that's not known. But those folks probably are at a lower risk.

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What I counsel patients is that...

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their risk is probably...

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more than it would be if they didn't have CLL.

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CLL SOCIETY

But to what extent we don't know, and we sort of then go into the different factors, that sort of guide us. But all the data we have is on a more of a population level.

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And it doesn't really give us such specificity that allows us to...

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say, every, every single patient has that immune dysfunction.

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The treatment effect after time, limited therapies, I think, is a really great question. I'm actually, we're very passionately interested in this right now, and a lot of...

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my interest is in developing these time limited treatments. Right? So you know, most of my clinical trials, for example, are combinations of therapies to try to achieve deeper remissions, to try to stop therapy, and more people, maybe even sooner, so that we can have more time off there, because I just think in general, my patients might like me, but they don't want to see me as much right, so I think it's better to try to be off there. Some people,...

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right...

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that...

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and so the question is...

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if we remove CLL from the equation with a medicine, if I get down to the point that...

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I can no longer detect any CLL say, even like one in a million cells,...

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and let's say that we're now out three, four years, as you've just said, and we're...

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at a point where we still maybe can't detect it, although often we can, but at a very low level, often...



CLL SOCIETY

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and we've had recovery of B cells, right? Maybe even globulins or these antibodies that often go down with some of the therapies that achieve these kinds of remissions.

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Where are we, then? What is our infection risk, then, and does it return to normal? This is just a complete unknown. You know this is an area where...

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I think that we need to do, you know, we're going to get this data, we're going to get a lot more information in the coming years.

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I would expect that the risk is, I'm sure, lower in time. But how much lower and how close does this get to normal, I think, is unknown.

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Dr. Chang, you talked a little about immunoglobulins and IgG replacement.

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Can you just review a little bit about that? The indications for that? And could you also touch on, we can give the immunoglobulin as subcutaneous does that work as well as by giving it by intravenous is that something patients can do at home?

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Do we do? We have data on that.

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And just talk in, ..

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and talk a little bit about the, you know, people have had low IgG but...

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also low IgA and IgM and that's not replaced with the IgG that you get in the immune globulins. So if you could just...

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walk, I know this was covered, but people had some...

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questions on it still, yeah.



CLL SOCIETY

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Yeah, you touched on a lot of important questions. And I think...

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yeah,..

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it probably involves a whole new hour talking about this, but in general, what I will say is...

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IVIG or immunoglobulin replacement...

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is like you said, only replacing IgG.

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Does not replace IgA or IgM, which are also immunoglobulins, are important for protection for other types of diseases. But in general, we think of, the protection that is conferred...

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for...

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most viral infections to be IgG.

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IgA tends to block infections at the mucosal level, or meaning right at the site where viruses come in...

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and so definitely has an important role. But we...

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don't have any sort of medication that addresses that. At this point,..

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the data that we have in terms of immunoglobulin,..

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and I,..



CLL SOCIETY

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show that figure from Dr. Soumerai's paper,...

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it does seem like we have good data, at least, you know, in the, in a retrospective manner that it works for our patient population.

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I alluded to the pro sid trial which is trying to evaluate the same question in a prospective manner.

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And we're hoping that that will read out sometime next year.

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But those are probably the best data that we're going to have in terms of...

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the benefit of IVIG replacement.

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To my knowledge, there's not as much data in terms of efficacy of infusion versus a spontaneous administration.

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There is...

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some changes in terms of how well it is distributed in the body and how quickly it gets distributed throughout the body...

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and therefore probably how quickly gets clear from the body...

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depending on which route...

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the antibodies can administer it. But I'm not sure that there is any...

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clinical difference...



CLL SOCIETY

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that will be noticeable between the different methods of administration.

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Talking a little bit about therapies and their effect.

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One of the...

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therapies that are commonly used are these antibodies and the antibodies killed off the cancer's B cells but the good B-cells, too.

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Remind us, Dr. Soumerai, how long? If you take rituximab or obinutuzumab...

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How long afterwards does it take the immune system to recover from this? I understand it can be very prolonged before you see your antibodies yet again, and you have advice about vaccinations like coming back to vaccinations again here.

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But about how long you should wait after getting Gazyva – Obinutuzumab and rituxin....

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before you advise your...

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patient to get vaccinated?

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Yeah, so I generally tell folks that in obinutuzumab has, you know it, this is cross trial sort of anecdotally, but has a...

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more prolonged effect on...

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B cell depletion, or this reduction and lymphocytes or B cells. These types of like blood cells that it targets...

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and a consequence of that is that the effect on antibodies can be a little longer, too.



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Ah,..

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I usually tell folks a year or two is sort of, the sort of a general and the end and but then some people who have pre-existing drops in the remaining lot in their antibody levels.

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I'm a little bit more worried that it could be longer and that sometimes we can see...

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more sustained reductions in these antibodies.

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Now, I think there's a lot of, there are many different messages out there about what to do. Right? Should we, should we only vaccinate after we're done? Should we vaccinate during? Should we wait three weeks after the obinutuzumab is done?

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You know, there's a lot out there. I, in general, I...

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follow the same thing that Dr. Chang said that that the drugs like obinutuzumab, which is really my antibody of choice in CLL,..

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the...

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have such a prolonged they're there for so long. Right? They're even in the, they're in the body for many months that waiting to vaccinate is not something I typically do. I just do the vaccinations on treatment off treatment early off...

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and, and I do them at the schedule I otherwise would be planning...

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with a caveat that I tell...

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folks that that I'm recommending this to...



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that the efficacy, the effect of their vaccines might not be...

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and probably are not up to what they would be, without these therapies. Also, I'd point out that the same is true with other therapies. So it's not just...

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antibodies but...

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acalabrutinib, zanubrutinib, pirtobrutinib, you know, all these therapies reduce B cells. That's why we want them to reduce B cells. They reduce cancer B cells, but they also reduce normal B cells to some extent, and even...

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have effects on other components of the immune system, as well.

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And we've seen some data that holding the BTK inhibitors for a few weeks might increase vaccine response.

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They were just small studies is,

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Dr. Chang, is that part of your practice, or is that still kind of considered to hold them for a vaccine? Do you have a...

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did you have an approach to that question?

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Yeah. So I think in general, my approach is just exactly what Dr. Soumerai says with the...

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caveat of maybe the,

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yeah,...

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CLL SOCIETY

the person who is about to get off of venetoclax that I might tell them, you know, and flu season's coming, then I might tell them...

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well, maybe wait a month after you finish with your venetoclax and then, and then get the vaccine.

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I typically do not ask patients to hold their acalabrutinib or the, or whatever BTK inhibitor the patient's on.

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I know the data that you're talking about, and I still consider that experimental...

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because I don't,..

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the data is on, on antibody efficacy.

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In terms of how well the vaccine is able to elicit an antibody response. But there's not a direct translation in terms of whether patients do better, live better, live longer, have less risk of infections, and so forth.

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And, and I think that if you're treating...

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CLL with a BTK inhibitor for a reason, I would try to...

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avoid doing...

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those kinds of things...

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unless it's absolutely necessary.

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And I would just add, on one other thing is, there is a, as I think, in what's informing Dr. Chang's recommendation, that there is, too, that there's a risk of a flare. So if you...



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hold these drugs, there's a risk that the CLL can worsen.

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And you know ,what you know,..

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we think we're pretty good at identifying who's at greater risk.

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Right, so I worry a little bit more about somebody where I just started treatment a few weeks ago. You know that their disease is not yet under deep,..

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in durable control, probably.

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But we're not always perfect at this, and there are folks who have been on therapy for years where we hold therapy for one reason or the other, and they can actually have a pretty significant, even symptomatic flaring of their disease.

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It's not a reason not to do it. We have to hold it for procedures, all sorts of things, and usually this is very safe.

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But it's a risk. And so I think that...

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the anytime we're thinking about holding for something, we've got to really be sure that it's with good reason, and that our comfort level with the risk...

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is, is, okay.

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I had a friend who's been on a BTK inhibitor for more than seven years...

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and got Covid went on Paxlovid that had to go off the BTK inhibitor.

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CLL SOCIETY

Her counts were completely normal and she had a symptomatic flare.

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I mean, yeah, symptomatic.

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So I mean it, it is an issue. And that's another thing. You can't take Paxlovid and a BTK i together. Is that correct?

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You can with so..

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I always talk to the pharmacist. So, for example, with...

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I just did this today, somebody on zanubrutinib, you can drop it to 80 milligrams a day...

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in combination with Paxlovid.

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Assuming no other interactions. Right? There's a lot of things that can interfere with this, so that it is not, as Dr. Koffman said, not a recommendation. But it, but it's, but there are ways sometimes to continue on therapy.

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We ran a randomized trial of zanubrutinib vs placebo in treating Covid. It turns out it doesn't, doesn't work.

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But at least it showed that you could do it. It was safe in some in, so I mean, I have no problem, and somebody who's not critically ill...

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which is thankfully very rare,..

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but continuing on sort of dose, modified zanubrutinib in combination with Paxlovid.

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Look.



CLL SOCIETY

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Yes.

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Is much harder to do with acalabrutinib because of the limited dosing that we have. But yeah, that is definitely something that...

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you can discuss with your provider...

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if need be.

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Up.

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Jake talked to us a little bit about the role of lymphocytes and neutrophils, and some patients are neutropenic from their CLL or from its treatment. And are there special guidelines, I know, after my transplant there was very strict...

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guidelines if when you're neutropenic. But I think those of loosened up a little bit now, so can you talk about because there are patients who are neutropenic.

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Yeah, yeah, so neu...

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Neutropenic means low neutrophils. I'm sorry I should, you know point that out. Yeah.

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Yeah. So you know, lymphocytes and neutrophils are different types of white blood cells. They have different roles. You know, neutrophils are, in fact, probably just infection fighting white blood cells. They...

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are important for a whole wide range of infections, but when they're very low...

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CLL SOCIETY

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thresholds that sometimes are used.

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And usually more for a more prolonged period of time. If it's low for a day, we don't worry quite as much, but if it's low for a very prolonged period of time, it's more, more problematic.

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You know, the bugs we worry about the most are things like bacterial infections. and fungal infections.

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And these are bugs that don't have to come from elsewhere. They can come from our own body, right, like they can come from our, our gut. They can come from us.

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Now the good news is that with...

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whereas, you know, years ago, when we were using things like FCR or bendamustine, these are chemotherapies.

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Fludarabine and bendamustine caused a lot of neutropenia, lowering of these infection fighting neutrophils or white blood cells...

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that could be quite prolonged and these folks had a pretty serious risk, long term of it, of infections, while they remain low.

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With modern therapies, it's much less so. We can definitely see this. Still, with CAR-t cells...

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where we can have fairly prolonged drops in these counts.

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But whereas we see them go down with drugs like venetoclax or BTK inhibitors or obinutuzumab,...

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CLL SOCIETY

we can get on it pretty quickly and boost them up. And usually this is not a prolonged issue.

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But if they are low, you know, I don't, is maybe not the day for sushi. It's not the day for raw meat. Beyond that I, I you know, a salad bar is probably never a good idea, but if you wash your vegetables it's okay,...

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you know.

01:20:25.000 --> 01:20:35.000

But if they're low, I mean, this is a reason, really more importantly, to see your doctor and make sure you understand why and is there some other thing that needs to be addressed.

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The lymphocytes being low is a much more complicated issue. And the reason is that there's many different types of lymphocytes. There's the...

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the lymphocytes, the B lymphocytes, the T lymphocytes. These are, these other types of immune cells that many, as I mentioned, many different responsibilities.

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They're often low after drugs like CLL therapies, including drugs like obinutuzumab, and they can be low for a while, and, and we...

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and...

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in many cases without a significant, you know,...

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risk of infection, right? There is an increased risk. But without, you know, life altering risk of infection for a majority of patients, right.

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And so it's more important to look at, sort of the why and the what type? And is it the T cells that are low, and that has very special risks or is it...

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CLL SOCIETY

the anti or the B cells that are low and the antibodies are low that has different risks, and...

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that's really a more case by case, by patient discussion, and it depends really on what therapy, when it was...

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and further evaluation.

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Let's talk about pre-exposure prophylaxis. We had Evusheld in the past. We have Pemgarda now.

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And there was just a paper that came out...

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this week, I think, or last week, that showed an 80 plus efficacy in reducing hospitalization and serious problems.

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But there was also something that came out that said, it may not be active against the newest FLiRT variant.

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And I'm going to mess it up, KP 3.1.1., I think it was.

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Maybe I messed that up. But it's, it's growing 25-30 percent.

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So what is your counsel on Pemgarda, Dr. Chang? You want to take that, or are you giving that to your patients?

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Are you getting a lot? It doesn't seem that there's as much buzz about it as there was about Evusheld.

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Yeah, I think, I think part of the reason why there's not as much is twofold. One is that, or threefold. One is that...



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society has kind of moved on. That's one.

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The second is that the current strains, although present and still cause,...

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can cause significant infection, they...

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are not as...

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deadly as the prior strains were, and I think that probably has to do with some with the strains, but also with how much...

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what we call herd immunity, or how much...

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immunity there is in the society against these viruses that kind of dampens...

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the severity of the infections.

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And then also...

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there's not as much data forthcoming as there was initially with Evusheld. And so...

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this medication has been, you know, out and received emergency use authorization...

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for a few months now and the paper still kind of lingering. And if you ask the manufacturers, they still don't quite have the actual clinical significance. They use something calling a bridging strategy, meaning...

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that they took numbers from a different study, and then they did some equivalence in labs, and say, well there, because this one exceeds that equivalent number, therefore it



CLL SOCIETY

must be protective. And I think that those calculations really need to happen with each strain, if they're going to do it that way, and with the newest strain, the KP. 3.1.1,...

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that data still, kind of not quite out there yet. And so there's some hesitancy on that regard, I think you know in my practice...

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as an institution, Winship has not adopted that yet as a routine practice, and so...

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and we find that not many of our patients have...

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really inquired about it either.

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And so we haven't been routinely giving it to our patients.

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I'll point out I'm going for Pemgarda. I'm going to Europe for three weeks, and I'm going to get Pemgarda. I'm going to take the risk. There's also the anaphylaxis risk 0.6 associated with it, but I think it's worth it for the extra protection, because I'll be in Europe for three weeks for meetings. Let's talk about...

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a couple of other things along that line. What do you think about...

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when your patients travel, and I'll give this to you to Dr Soumerai.

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Having them have, and especially if they're going out of the country,...

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a prescription of Paxlovid in their bag with them, a Z pack in their bag with them, Tamiflu in their bag with them.

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Can you,...

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CLL SOCIETY

how do you feel about that? Do you have any advice for patients? I know some docs don't want to do it because there's potential drug interactions and patients might use them inappropriately.

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And also, are there any other diseases we use...

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antibiotics...

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on an ongoing basis. You know, people with certain kinds of fever and stuff get penicillin and stuff like that on an ongoing basis. We use...

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antibiotics on a long term basis, urinary tract infection, sometimes we suppress those with low doses of antibiotics. Is there any role for low dose long term antibiotics in CLL, so they're two different questions. One is for the acute, you know. I will tell you personally when I travel...

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in my carry-on my Paxlovid. Paxlovid has been X-rayed so many times, it's got to start to glow, you know, because it's been through that scanner. So many plane flights. Yeah, yeah.

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Yeah, it's, it's a great question. So I, I it...

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so, yes, so I do send patients who travel to places that don't have easy access to Paxlovid.

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I will send Paxlovid with my patients, but under very, very strict rules.

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That I say, never open this package without speaking with me, and even if I know what their med list is today,...

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I, you know, we I,...

01:26:41.000 --> 01:26:42.000



CLL SOCIETY

things happen,..

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right, like maybe another doctor told them to start something and...

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maybe it's an anti-hypertensive. And you take the Paxlovid a bit and it drops her blood pressure, right, like they're, they're real issues with...

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drug interaction. So the rule is, and that's why it has to be somebody where I know that they're...

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they're going to call me. They're not, going to you know, play cowboy and just take the drug.

01:27:03.000 --> 01:27:11.000

Which is most of my patients, but like, but I give them the drug. But I say, if you test, I want you to test for it.

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Bring a test with you, and if you test positive for Covid, I want you to page me day or night, it could be three in the morning. I want a conversation before you take your first dose so that we can review your medications.

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I don't do the same thing with antibiotics. And with antibiotics, I'm a little bit more careful, and there's, there's a few reasons for that.

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But you know one of them is that there's just so many different infections out there. I worry that I could not only be over treating something that's not a bacterial infection, which is a worry. But I think the bigger worry is that somebody might have a different bacterial infection and they assume that the antibiotic works for everything.

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And, and it doesn't work right? So I, I don't want to, you know, augment and might be a great antibiotic for something in their in their sinuses or their mouth right? But it's, it's going to be a pretty cruddy antibiotic for some other things. And so,..

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there's always an urgent care in the vast majority of places, and so I tell patients that...



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if there's concern for bacterial infection, go to an urgent care and have them, have them, page me, and let me know in advance.

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I don't do the same thing with Tamiflu as I do with Paxlovid for better or worse. I generally have them go to an urgent care. There's some wiggle room with timing. They can go...

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within a couple of days, and it, it really...

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that's a readily available just about everywhere.

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That prophylactic antibiotics is not something we typically do. And again, the worry is that we're going to...

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create resistance...

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and that's something we, we know happens if you take these antibiotics, there are exceptions. And so there are rare exceptions where somebody's had certain types of recurrent infections, where, in careful, careful...

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consultation with my specialized infectious disease doctors only, we consider doing that I would never do prophylactic antibiotics without an infectious disease doctor...

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being involved.

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Prophylactic antiviral is something I do, though somebody's had recurrent, for example, I'll give acyclovir on an ongoing basis, or valacyclovir sometimes as well.

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Sometimes the same thing with CMV which is another type of...

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CLL SOCIETY

viral infection. If somebody's had an infection,..

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oftentimes they remain on some antiviral treatment to prevent recurrence as well.

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And let me, while we're on the antivirals, do you also recommend the...

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vaccine, the shingles vaccine, so would you, it's sort of belt and suspenders you would do both, you know. Patients would take the antiviral pills and get the vaccine. Is that what you recommend? Or if you get the shot, can you stop the antivirals?

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Yeah, I think it depends. If somebody hasn't had the shot before, I mean the shingles vaccine, we, we actually have prospective data showing that it works...

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on people with CLL,..

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including in folks on BTK inhibitors, although it works a little bit less well than folks without them. But we have data, you know, and, and...

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so if, if somebody hasn't been vaccinated before, and they've had a couple of bouts of shingles...

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and they're on a prophylactic anti-shingles medicine...

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then down the road they, they get the new vaccine, you know, it's I look at sort of what's happened? I look at the severity of their illness. I look at all these things, and we have a discussion whether it makes sense to stop it...

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but I think of I, it's, it's one thing that adds to the discussion. It's, I don't just stop it just because I did the...

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did the vaccine.



CLL SOCIETY

01:31:04.000 --> 01:31:20.000

And Dr. Koffman, if I, if I may, I think you know all the questions about what kind of prophylaxis even, you know, pre-exposure prophylaxis with Pemgarda and whether you have Paxlovid or Tamiflu, or things in the bag you travel is.

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It's quite personalized, because it depends on where you go. And you know, if you're going...

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to the middle of nowhere and there's really, ..

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you know, ..

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nothing.

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Right then even a Z-pack might actually be useful under certain circumstances, whereas if you're going...

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from...

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New York to California, then you might not be as much of a big deal because access is still there, and so...

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and same thing with, you know whether you're going to a high risk area versus not. And...

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so there's, there's a lot of things that I think patients should definitely...

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talk to their providers before going...

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to places so that those kinds of discussions can take place, and the decision can be individualized.



CLL SOCIETY

01:32:08.000 --> 01:32:17.000

I'm going to, we hardly have any time left, but there's a couple of things. Here's a real quick one, Dr. Chang, you can take everything you're saying about CLL also applies to SLLL correct.

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Yes.

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Okay.

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Cancers. We know that skin cancer is a big issue in CLL.

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Do one. Do we know why? And two? Are there other particular cancers that CLL patients are at high risk for? And is there any particular special screenings? Or what do you recommend for cancer screenings for your CLL patients? Because we know they're at higher risk for second cancers, any particular ones? And do we know anything about why skin? And then I'm just going to give you a heads up.

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Jake, I'm going to ask you about bug bites, because there's at least 10 questions on exaggerated responses to bug bites. So you can prepare for that. Yeah.

01:32:57.000 --> 01:33:11.000

Yeah, I think the question of secondary cancers, the reason again, I think, is mainly because of the aberrant dysfunctional immune and so people who have a more dysfunctional system will probably have...

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higher risk of secondary cancers.

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Again, it's hard to know the degree of dysfunction, and so in general, I do recommend all my patients to go to dermatologist for...

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skin cancer, because that tends to be the most prevalent one. And that's true across several studies.

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Doesn't mean that other cancers...



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don't happen. And in fact, I think...

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at the end of the day, some of the things that I tell my patients is, you know, the fact that you have...

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CLL or SLL doesn't protect you from...

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having other things that otherwise people will have. And so...

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for the most part, you know, age appropriate breast cancer screening, colonoscopies. For smokers, first I counsel them to stop smoking. But then there's also recommendations for lung cancer screening and so forth. And I would just follow those. And that, and the trend has been that...

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the age at which people start screening has kind of gone...

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younger and younger, and I think that for CLL, because of that, I don't make any necessarily...

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modifications for...

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our patients because by the time they get diagnosed...

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will be due already for these types of cancer screening.

01:34:31.000 --> 01:34:33.000
Yeah.

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Jake, you want to talk about bug bites, you know the risk of getting secondary infections, even scratches. This seems to be a real problem. This exaggerated response to bug bites, well documented.



CLL SOCIETY

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Yeah, it's and it oftentimes predates the CLL. Even, even in cases where we can look back at laboratories and see that...

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the CLL numbers were low and weren't even detectable at some point.

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Oftentimes even back then we can see that there were these sort of exaggerated responses to bugs.

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This is a very well described phenomenon, as you say,...

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you know, it's thought that this is, you know, the immune system is not just universally suppressed, as I mentioned in, in the discussion.

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But it, you know it's up and down. It's a little bit dysregulated or off kilter, off balance, and...

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so when you get a bug, we can see these like welts. I mean, it can be really quite problematic.

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You know, it, they often do fairly well if you put some topical steroid on these and as you say,...

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scratching them can be a real problem. So you know, put on your best oven mitts and talk to your doctor about things to reduce the itch, and reduce the, the symptoms of the bites.

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But really, trying not to go after them, because secondary infections...

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again, can be, really, you know, pretty problematic. One other thing about this. It doesn't, . when you see these, sometimes they get better with treatments, or sometimes patients...



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receive CLL therapies, and then, these just, it doesn't happen as much.

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But sometimes it doesn't go away at all right and so and so, don't assume that...

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the fact that they're still happening means that the CLL is still active. But similarly, don't assume...

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we shouldn't assume that it's going to go away with therapy. It's, it can be sort of a separate phenomenon that...

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sort of as a little bit off out of sync with the CLL activity.

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I'm going to give...

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Dr. Chang the last question here, and then I'll ask you both to do a quick summary, and that is...

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Both of you mentioned autoimmune issues in the low platelets from that called ITP and low hemoglobin, called autoimmune hemolytic anemia.

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Is there anything that can be done? Is there anything that we know about this that can mitigate that risk? And there's also other rare autoimmune problems, too, like people get thyroid things and other weird things as there. And what do we know about that? Does it tell us anything about the patient's disease, their prognosis. Just give us a little bit.

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Fill out a little bit more on the autoimmune complications, and in CLL.

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Yeah, I think,...

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CLL SOCIETY

you know it, it is again another manifestation of how the immune system isn't working the way it should be, and...

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and...

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to my knowledge, there's not much in terms of not much data in terms of...

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you know, people who have autoimmune disease or not have autoimmune disease, whether their disease is in any different way. I think that the..

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the main thing is, if you, if the disease, if the CLL...

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does manifest with an autoimmune condition that is something in addition that I keep an eye on, and I keep track of.

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Sometimes I can,...

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I can even see,..

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I'm on a monoclonal protein kind of floating around, and that kind of tracks with their disease and, and...

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with the autoimmune complications.

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And so, for the most part, I think...

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with treating the disease, meaning the CLL often times these conditions get better. And so that's really kind of the main way in which we manage these complications,..

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aside from trying to manage it with steroids. For example, at the beginning,..



CLL SOCIETY

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I don't think that there is anything in particular that we...

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what that I'm aware of, that can prevent these complications from happening...

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or that we can actually predict these complications on any particular person.

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Thank you. And yeah, I had...

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ITP from hell, single digit. And it's how my CLL essentially...

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presented, you know, is a problem, and it was very difficult to treat.

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Dr. Soumerai, any final words of wisdom, any takeaway messages, and then I'll, I'll turn to you, Dr. Chang.

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Yeah, I mean, I'd say that my takeaway is that the field is changing and that outcomes are improving dramatically and quickly in this disease.

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And that the therapies have changed a lot over the last several years, and the...

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I've...

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I was speaking with a colleague recently who...

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has never given chemotherapy, CLL doctors never given chemotherapy. I found that amazing right like that speaks to the...

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where we've come and...

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CLL SOCIETY

a lot of the data we have comes from the chemotherapy era. And this is not to minimize the risk. There's a, there's clearly a serious risk still...

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with CLL and with the modern therapies. But we've only sort of scratched the surface of where we're going to come in terms of a reducing infection risk, I think, ..

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as a whole for all patients, by just having better therapies.

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But I think we, you know, acknowledging that we really don't know everything.

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That patients are different, and that their diseases are different and their infection risk is different, and...

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that I'm optimistic that in the coming years that we're going to be able to better identify who's at...

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greater risk depending on various clinical factors like...

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based on their person and their disease and their, their history...

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and also hopefully, things that we can measure.

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But just remembering that this is not a one size fits all approach, that everybody's very different, and that and that I would really counsel you to...

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not, not be just, generally afraid of all infections, but to really...

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think about your own history. Think about sort of what you've received, and sort of talk to your...

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CLL SOCIETY

doctors and, and care providers and families, and everything about sort of your unique risks.

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Dr. Chang.

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I want to stress the importance of you know, having a good communication with your treatment team...

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because...

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there are a lot of these issues that...

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that we raised today, that...

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are highly personalized and...

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and many people can give you many different advice. But I think that, having a good discussion with...

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your provider risk versus benefit whatever particular situation you might be encountering is really of importance. And so that you can actually make the best informed decision in your particular case.

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And then, of course, you know, being proactive at taking care of your own health...

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by...

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identifying,..

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CLL SOCIETY

you know, your, your whether you have an infection and notifying your providers early so that you can start treatment early, by trying to stay up on top of vaccinations, by encouraging patients around you or individuals around you...

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to vaccinate as well, and to be aware of your surroundings and what's going on in terms of infections and...

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and so forth, because that also affects,

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you know, the risk that each individual patient might encounter at that particular situation.

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Well,..

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I think this was an amazing...

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presentation. And I'm extraordinarily grateful to you. And I think it's also interesting how we've shifted because it used to be, how are you going to keep me alive. What's my next therapy?

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And now we're saying I'm alive and...

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prevent me from getting these...

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infections, prevent me from getting these,..

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you know,..

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secondary cancers, you know, with survivorship issues that were...

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shifting to and the...



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and the, I think the only silver lining of the pandemic is that the immunity issues have been really pushed to the forefront.

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And we're really glad the CLL Society is supporting research in that area. And we're really glad about that.

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Maybe we could move to the slides and...

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thank our, our generous donors, who made events like this possible.

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We're so grateful. I thank you all for joining us today.

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Our speakers were just great. I think this is amazing. There is an event survey.

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Please provide your feedback. We really pay very careful attention to it...

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and it does inform how we move forward.

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This was recorded. There will be a written transcript and the slide decks will all be available to you. It's usually within a week.

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I did not get to some really great questions. We didn't even talk about masks, for example, I mean, which is, you know, there was a bunch of questions about that. So I mean it. I just couldn't get to all the questions, so, please, you know, send them off to Ask the Expert ask at CLLSociety.org.

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But we have a really important webinar coming up the beginning of September 9th on Medicare.

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CLL SOCIETY

Understanding what the benefits are, the new changes with the inflation act. How that's going to affect you.

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Out of pocket caps on copayments. All of this stuff.

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It's extraordinarily complicated. And we actually have a legal team because it's really complicated. I highly recommend that you and your care partner attend this because it's important to understand the differences and the different kinds of Medicare.

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Please do remember CLL Society has invested in your long life.

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And you can invest in the long life of the CLL Society by supporting our work.

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Stay strong!

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We are all in this together. Thank you for your attention, and thanks for staying a few minutes late.

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Thank you.

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Thanks. Everyone.