



Facebook Live Event Transcript

Ask Me Anything – Featuring Dr. Deborah Stephens and Doreen Zetterlund

April 11, 2024

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Welcome everyone. I'm Doreen Zetterlund, a CLL and SLL patient and advocate and a member of the CLL Society's Patient Advisory Board.

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We're here with CLL Society's Facebook Live event, ask me anything. Where we're going to spend the next 60 minutes answering your questions with the CLL expert.

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We're so lucky to have Dr. Deborah Stephens joining us today. There are no presentations, and we encourage you to ask your questions on the Facebook page if that's how you're joining us...

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or through the Zoom platform. The event is dedicated to your questions, so ask them early so we can get to as many as possible.

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Before we begin, I have a few important disclaimers to share. Nothing said today should be taken as medical advice.

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Any questions about your health and treatment should be discussed with your health care provider. The information you post on Facebook will be shared on a public forum.

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So please, do not post or share any confidential information. So, without further ado, Dr. Stephens, would you please introduce yourself to our audience.

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Hi, everybody. Thanks for joining today and thanks for the introduction. I'm Deborah Stephens.

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I'm a CL doctor and expert at the University of North Carolina at Chapel Hill and I'm the Director of the CLLL and Richter's Program here.

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And I'm also a member of the Medical Advisory Board for the CLL Society, which has been really a great group to work with.

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I am so very excited to be here today and answer some questions.

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Wonderful. We so appreciate your support. So, let's go ahead and get started. What is your standard first line therapy for someone who has never been treated before?

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So, the standard is not a specific therapy. It is really, actually tailored to every patient. And so I would say my standard of care is to work with each patient for their best treatment.

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I don't use any standard chemotherapy agents anymore and I considered standard chemotherapy agents to be drugs like fludarabine, cyclophosphamide, you know, pentostatin, chlorambucil, just because they're, they're not very specific and they have a chance for toxicity and they don't work as well...

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as our newer agents. And so usually when I'm talking to somebody about front line treatment, I usually present one of three options.

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Number one is a combination of venetoclax and obinutuzumab. Venetoclax is an oral pill that's taken for a year and obinutuzumab is an intravenous therapy.

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It's an immune therapy and obinutuzumab is an intravenous therapy.

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It's an immune therapy, a monoclonal antibody that's given over a six month period of time in combination with venetoclax.



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Alternatively, I recommend a BTK inhibitor and those are oral pills. The ones I typically recommend now are acalabrutinib and zanubrutinib.

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Those are taken orally and they're taken continuously, meaning they are taken as long as they're working and not causing side effects.

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And I usually have a third option which is a clinical trial. And those clinical trials change over time. So, you know, if you're approaching your first treatment...

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definitely ask your doctor if there's a clinical trial available. And you know, if not, maybe there's a center close by that might have one.

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It's worth hearing about it. If you're willing to travel to a center that has one.

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Great. And, leading off of that, are you recommending that CLL patients receiving ibrutinib as a first line treatment, consider changing medications to one of the newer drugs just because?

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No, I actually am not recommending that for everyone. I will say there are certain patients that might benefit from that.

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So, for those of you, I think a lot of you probably know and have read, there's been a couple of clinical trials that have compared ibrutinib to the other newer BTK inhibitors...

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acalabrutinib, and, and kind of the overall findings of these studies is that they're, you know, at least as effective so at least as good at keeping the CLL under control, potentially better and the newer drugs have less toxicities. However, I will say the majority of toxicities with...

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ibrutinib and any of these drugs are going to happen during the first couple of months that you're on the treatment.



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And so if you've made it past that and say you're doing really well, you know, two years out and things are going well...

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I wouldn't necessarily recommend switching over to the new drug. For one, you'll get their side effects kind of unique to each of those drugs.

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And when you switch over to the new drug, you are going to get some additional side effects, at least during that initial period that you switch over to the drug.

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You know, there are some concerns and I think valid concerns about long term toxicity of ibrutinib and those are things like heart arrhythmia or an increase in your blood pressure.

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And those are real things that can be monitored by your doctor and can be managed and you know if they're becoming unmanageable or becoming a problem they're certainly things that you can switch off the ibrutinib to another drug.

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You know, one thing that I have done with some patients if they're in a very, if their CLL is in very good remission, sometimes I actually give them a break off of therapy altogether.

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Typically, just because I think it's written up as a very good drug and we actually have the longest amount of follow-up on clinical trials with ibrutinib...

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to demonstrate the safety of these drugs. I, you know, I typically would try to reduce the dose of ibrutinib first before I would discontinue it altogether.

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Now, if somebody has a bad side effect of ibrutinib, like, inflammation of the lungs or, you know, really severe, abnormal heart rhythm, then I might just switch directly.

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But usually if it's kind of milder side effects that are, you know, bothersome but not life-threatening, I, I usually try to reduce the dose of ibrutinib first.



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And so it's still kind of a decision that's going to be, you know, among the patient and their doctor.

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And both, you know, staying on the ibrutinib could be the best route or changing could be the best route, but it depends on, you know, the reasons for changing, you know, how good of a remission this CLL is in at the time.

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You know, there's a lot of factors that go into that. But I have it, you know, when these studies first came out, I did have, some patients that I talked to about them and they said, you know, absolutely I want to change over to these new drugs.

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And I had people change over to these new drugs.

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And I had people change over and they did, they had people change over and they did they got the side effects,...

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those initial side effects with the new drugs and almost every single one of them called me and said, hey, Dr...

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Stephens, can I actually just go back on the ibrutinib because I was doing fine with that.

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And so, you know, just keep in mind if you do decide to switch that you're still going to have that initial period where your body is still getting used to the drug.

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Sure. Now, when you mentioned high blood pressure on ibrutinib, are those things that happen early on or is it that happens more as, you're on the ibrutinib for a longer time.

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They typically they can happen over time. So the longer you're on it, those are side effects that can build up.

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Now, those things were also compared in those clinical trials that compared to the new drugs.



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And I will say that zanubrutinib has a pretty similar rate of high blood pressure when compared to ibrutinib.

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And so if the reason why you're switching is because of high blood pressure, I'd probably choose to switch to acalabrutinib instead of zanubrutinib or just do a break in drug therapy.

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Of course, under the guidance of your doctor. So yeah, so over time it can develop.

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And so it's not just something that gets better over time. Which is some of the side effects we see with these drugs like diarrhea, headaches, things like that.

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Those usually get better. But the high blood pressure and the risk of atrial fibrillation, it can accumulate over time.

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Okay. Are there going to be trials comparing the newer available treatments like aacalabrutinib and zanubrutinib to each other instead of just comparing them to older treatments like ibrutinib.

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Yeah.

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And I also just want to clarify acalabrutinib is also called Calquence and zanubrutinib is also called Brukinsa, so if you're new to the CLL world, you get a lot of these names and you don't know that you're talking about the same medication.

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Yes, thanks. Thanks for clarifying that. And I think that that's such a smart question and I think that would be such a smart trial to do.

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But I think, the reality is I do not think that, acalabrutinib and zanubrutinib will be compared head to head.

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And there's several reasons for that, most of which just get into complicated relationships between, you know, drug companies and funding sources for the trial.

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You know, the companies have both kind of done some basically after the fact analyses of the clinical trials to try to, you know, take...

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similar patients from both of the trials that received acalabrutinib and zanubrutinib and then compare those data to each other.

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You know to try to give people an idea and I think you know I just don't think it's something that is realistic in terms of, you know, the cost the study would be and, you know, like I said, just, you know, having the drugs provided for the study would be, I think really, just really logistically difficult.

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Okay. We'll go to some questions that are just coming in. What are the criteria for either treatment and or participating in a trial with CLL, particularly the BOVen trial.

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So the question was for participation in a trial, what are the criteria?

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Yes.

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So those are going to be very different and very specific for every clinical trial. And so, you know, there's clinical trials for people who are, you know, just starting their first treatment for CLL.

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There's clinical trials that, you know, they require you to have had two or more prior treatments for CLL.

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There's clinical trials for, you know, complications of CLL or, you know, early intervention so people on watch and wait and so the criteria for each trial is a lot different. And you know, the initial BOVen trial was, you know, there we already have published results of that but you know, there's like follow-ups that are similar and BOVen is basically zanubrutinib and ...



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obinutuzumab and venetoclax combination.

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And so most of those, you know, these drug clinical trials, you have to meet criteria for you to start.

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So you have to have, you know, one of the things your doctor probably asks you about all the time.

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So either, you know, drenching night sweats, you know, fatigue that's really impacting your day-to-day activities.

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Weight loss, which is a significant amount of weight loss. You know, or your other labs like you're becoming more anemic or your platelets, which are the cells that help your blood clot are getting low.

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So you might just need to meet a criteria and then, you know, again, each trial has their own. So you might just need to meet a criteria.

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And then, you know, again, each trial has their own criteria. And then, you know, again, each trial has their own criteria, some of which are age.

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You know, and of course we can't do anything to change that as much as we would want.

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You know, and of course we can't do anything to change our age, and of course we can't do anything to change that as much as we would want.

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And you know, other factors like things will be looked at like your kidney function, your liver function, and just making sure that it's going to be safe for you to receive the treatment on clinical trial.

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And so, you know, each trial is pretty specific and what it requires. So, if you're interested in a specific one, I would have you ask your doctor about it...

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so that they can tell you whether you'd be a good candidate or not.

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Okay, something I'm going to interject here for our SLLers when I was being considered or considering some clinical trials back in 2015, SLLers were excluded.

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Has that changed? Have you found that that has changed? I mean, I eventually did progress to CLL and was on a trial, but...

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Huh. Yeah, yeah, that's so unfortunate and I've heard that, that story a lot and I, you know, I, I really don't even like the term SLL because I think it gets confusing to people and you know for those of you who don't know SLL is small lymphocytic lymphoma and CLL is chronic...

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lymphocytic leukemia. And so I think people get confused because they're thinking, well gosh, do I have lymphoma or do I have leukemia and, you know, the staging systems are different.

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So if you are staged as a lymphoma, a patient with lymphoma, it's called this Ann Arbor staging system and it's different.

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If you're staged like you have CLL, you usually use the RAI or Binet staging system and so it leads to confusion because people can say well, you know my doctor told me I was stage 3 SLL staged under, you know, non-Hodgkin lymphoma staging.

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And then they come to me and I'm like, well, you know, actually, I would say your stage one because I'm using this RAI staging.

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And so when I explain it to patients is, you know, the cancer is basically the same.

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They're cancer cells and it just depends on what part of your body they're in. So, you know, if there are more in your blood, it's typically called CLL and by definition you have to have more than 5,000 of these cells circulating around when you check your blood to be considered.

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And if it's SLL, it's more in your lymph nodes or in the spleen.

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But when I think about it, I tell people, you know, think about if you have a couch.

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And your couch is in the living room and you decide to move your couch to the basement.

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It is still the same couch. And so that's why I think, you know, even though it's in a different location, there's, you know, maybe a little bit different signaling to make sure which location it goes to.

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It's treated the same. And so I hate to hear when SLL patients are excluded from clinical trials.

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And so I think that is changing a lot. And so, you know, a lot of times you'll see, you know, especially like for example, when I write trials, I try to put in your CLL/SLL so everybody's included and then put a little caveat because usually people are like, well, how do you even stage SLL?

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And I just say, you know, if you have SLL, you just automatically started at least stage one.

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And try to get, you know, as many patients able to participate in the trial as possible because, you know, I think the trials are going to benefit people with classic SLL just as much as CLL and so I do think it's changing and we try to catch that and make sure, you know, that that's clear that patients with SLL can participate but, you know, in some cases they are just excluded and, you know, maybe it's...

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a trial that like some of the science that's being done around it, you need to be able to pull a certain amount of cells out of the blood...

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in order to do the research on it and that's a place where maybe it would be appropriate to exclude patients with SLL. But I think in general, more and more you'll find the SLL, people with SLL are included as opposed to excluded like it was in the past.

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Well, it's like you say, we want more and more people to participate, so why exclude anyone?

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Okay.

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And I can say that I kind of barked aloud when that happened to me because it was like, it's the same being treated the same, but I do understand that there imaging you need more you need more scans to see what's happening with the lymph nodes than just pulling blood.

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So I understand the complication, but as an SLL, I'm always pushing, pushing my people in there to be included.

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Yes.

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I don't, we don't, we don't like to be, you know, not included.

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I love that. I love that and you shouldn't be excluded.

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Okay. All right. Let's go to the next question. Can one lose your MRD status without the CLL progressing?

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As that term is used in the studies. If so, what constitutes progression?

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Alright, so this is a good question. And for those of you who don't know what MRD is, that basically stands for undetectable measurable residual disease.

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And this is something that's not checked in all patients and so if you're thinking, gosh, I was on a treatment and I have no idea what my MRD,...

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MRD levels are, it's just because it's not actually standard of care to check in all patients and with all treatment.

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For this measurable level of residual disease, that's usually checked by a lab test and basically it's generally reserved for somebody who looks like they're in remission so their lymph nodes have shrunk down to less than one and a half centimeters.

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You know their other blood counts are totally normal, maybe you can't find any CLL in the bone marrow but when you do a test to look deep enough to look in the smallest amount of cells that you can, you might be able to detect a little bit of residual CLL.

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And you, you mentioned the term MRD, and that stands for undetected.

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And that's exactly what it is. It's undetected but that doesn't mean it's not there.

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It's just not, we're not able to, there's such a small amount that we're not able to detect it with our current technology.

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And so, when you're using the term, I think the question asked, can you lose undetectable MRD?

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Absolutely, because basically, you know, what generally happens just because none of our treatments are known to be curative for CLL yet.

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And usually there's going to be a small amount of disease that starts to come back. And when you're checking at such small levels, you'll see that disease start to come back.



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Earlier than you would with our just standard, you know, clinical labs. Like you might not even see an increase in your white blood cell count, but you might see, you know, oh, I think I had a point 5 percentage increase in how many of these you know these MRD cells that we're looking at.

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And I would say that that's, that's pretty common and that happens. Probably the best studies that have been done on this or after the regimen that I talked about obinutuzumab and venetoclax.

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And there was a big clinical trial called the CLL14 study. And they did some tests looking specifically at minimal residual disease after the treatment.

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And basically they saw, about on average from when you can detect the minimal residual disease, it takes about two years to actually see what we term clinical progression and clinical progression would mean your white blood cell count has gone up, your lymph nodes have gotten bigger.

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But even when we say clinical progression, that might mean you still feel fine. And so, you know, sometimes, you know, when I talk to people about checking MRD, I say, I just want to be sure that you really want to know.

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Because we're talking about, you know, two years between knowing that the CLL is back and even being counted as technically clinically progressive disease and even at that time point, if people don't have any symptoms related to CLL, I wouldn't just jump right back in and start another treatment.

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And so this minimal residual disease or measurable residual disease, we can detect the CLL coming back way earlier than I would say that it is clinically meaningful. Meaning you wouldn't, you know, you would be walking down the street...

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you wouldn't know if you have, you know, 5% MRD or 8% MRD.

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But you know, you need to know yourself and if you're somebody who are, you know, that's going to really make your wheels start turning and think.



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Yeah.

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Oh gosh, I got this disease here. The CLL is coming back, why aren't we doing anything about it?

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You might be somebody that says, you know, hey, just don't tell me what my numbers are or don't check it.

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You know, it isn't standard of care yet to check, but there's a lot of clinical trials going on.

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To look at that now.

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Right.

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So, moving forward with a little bit of progression does not mean that it's time to treat and as many of us know when we were diagnosed, we probably had CLL/SLL for years before it ever manifested into something.

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Yes.

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So it's sort of the same thing all over again.

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Yeah, exactly. I describe it like when you're deciding on the next treatment for CLL, I say, you know, think of it as we've gone back to watch and wait.

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So, we're still kind of doing the same thing we were before we decided to do treatment the first time.

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Same criteria apply for needing treatment.



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Okay. What medical precautions or dental procedures, would you suggest, that we, as immunocompromised people, what precautions do we need to take?

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Where should we ask? Do we need to prophylactically treat with antibiotics or go off our medications?

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That's a good question. And there's several parts to it. So I don't routinely recommend antibiotic prophylaxis when you get dental work done.

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So just routine dental work, you're going in for cleaning, even you know you're getting a tooth pulled.

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Now that might be different if one, you've had infections before. If you've had a bad dental infection before, that might be applicable...

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or if there's something unique about you, like you've had a new heart valve placed or there's some, you know, you had a joint replaced and you have a history of having an infection there, you know, that that might be kind of an individual one-off.

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And I found even, you know, in the time that I've been practicing medicine, there were a lot more guidelines for, hey, let's put people, all of these people on antibiotics.

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And then now they're a little bit less, you know, less people are recommended to go on antibiotics, but then you have the people that, you know, have been told for 10 years...

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hey, I need antibiotics every time I go to the dentist. And so there's just been a little bit of a change in the philosophy.

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Now, the other question is should I go off my medications and probably that person is thinking about drugs like ibrutinib, acalabrutinib, and zanubrutinib, you know, Brukinsa, because they are ones that can increase the risk of bleeding.



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And so, you know, let's say you need a tooth pulled, you know, do you need to go off of your medications?

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Now, if your CLL is under good control, always consult with your CLL specialist or your cancer doctor,...

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I generally recommend those come off three days before and three days after doing a procedure like that. However, the risk of bleeding is minimal.

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And so if you're kind of right in the throes of your CLL treatment, maybe your CLL isn't under quite perfect control yet...

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you might talk with your doctor and just, you know, have your doctor and your dentist, you know, talk with each other and say, "hey, I think the risk of coming off the medication is too great.

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We think the risk of bleeding is low. So maybe let's just continue your cancer treatment and if a bleed arises we can deal with the side effects."

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Isn't that, isn't it true also early on in your treatment that you don't want to come off and on as much as possible until you're sort of stable?

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Yeah. Yeah. I would say in general, you know, not taking a lot of breaks is a good idea.

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Can you tell us in lay person terms how CAR-T cell therapy works in CLL patients and will it become a standard therapy for CLL and thank you for being here today, that person says.

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Oh, that's very nice. You're welcome. Great question and great timing. Because it actually did, there's a CAR-T therapy called liso-cel or Breyanzi that just actually got approved for patients with CLL.

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It got approved around March 15, so it's pretty new. It's just been approved for about a month.

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Now, the approval has come through for people who have had two prior treatments for CLL and one of those treatments should be a BTK inhibitor like ibrutinib, acalabrutinib, zanubrutinib, and the other should be venetoclax.

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Now of course, if you've had like five prior treatments, as long as one of them was a BTK inhibitor and one of them was venetoclax, you would qualify.

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So this is something that can, you know, quote unquote be prescribed it's not really a pill, but it's something that will be sent through your insurance for authorization.

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Now it is available off clinical trials. Now what a CAR-T is basically what it looks like for the patient is you would come in, you would have your blood drawn out.

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It's a process called leukapheresis. It's almost like a dialysis for blood.

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Basically, you pull the blood out, separating out specific part of your white blood cells called T cells; so a specific part of the immune system. And then, the rest of the blood goes back in because we're just really looking for the T cells.

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Those T cells get sent to a lab. And that lab might be at your local institution. It might be at a manufacturing place, a little bit different from person to person.

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In the lab, there are viral vectors inserted and basically what that means is the cells are trained to take up these things that make them want to go after a specific target.

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And, and a liso-cel, the one that's approved, it goes after a target called....

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CD19, which lives on the surface of CLL cells. Basically, we train ourselves to go after this target.



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Then we grow up kind of like an army of these cells. And then coming back to the patient, we give them some chemotherapy to reduce your immune system a little bit so you can accept the cells to come back.

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And then we infuse those cells. Basically, you know, just looks like an IV infusion going in.

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And to come back in. When those trained army of T cells get into your body, they are supposed to go out through the blood and the tissues and find any cells with CD19...

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on them and kill them. And so that should, you know, eliminate, the CLL cells because they generally all have CD19 on the surface.

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During that process, you know, when the cells are, you're basically just ramping up your immune system...

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so you can get a couple of side effects that are important to know about.

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You can get something called cytokine release and that basically looks like, you know, you have a really bad flu, you could get fevers, low blood pressure, you can get really sick with it, so your doctors are really going to be watching for that.

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Or, you can get something called neurotoxicity, which basically means these T cells do go into the brain and spinal cord and it can cause things like confusion, when there's inflammation in that area.

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Those are short-lived. Usually longer live than anybody wants them to be, but you know, it's usually, you know, that is compressed within, you know, a week's time.

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Sometimes it can get a little bit longer but it's usually getting better over time and it resolves with treatment that your doctor can get.

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But so when you get the CAR T cells back in, you should make sure that you're very close to whatever center is infusing.

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And usually, like for example, if you live really far away from the center, most places will help set up housing or there's some sort of system to set up patient housing.

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So you know you can have a family member come with you and you can stay there, usually for a month after just to make sure everything is going smoothly, no side effects.

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So it's really kind of a unique treatment. It works a lot differently than most of our treatments and that it's basically training your own...

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system to remember how to fight...

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and that is still not going to be one of the first things that we treat with that's still further down.

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Okay.

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Yeah, just I know I described that process so logistically, it's a bit complicated. It usually requires being seen at a transplant center.

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So usually the same doctors that supervise bone marrow transplants supervise this kind of procedure just because, you know, there's a lot of steps and it takes, you know, from the time when you get your T cells collected until when they're ready, it's usually about a month.

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And so, you know, there's just a lot of things happening so it's logistically a little bit complicated. And then the other part is that, the clinical trial, that helped to approve this, this treatment for CLL, shared some data about when we saw responses.

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So the response rate was 44%. And what that means is, 44% of the people enrolled on the trial, were able to get response to therapy and these are specifically the people who had these two prior therapies. a BTK inhibitor and venetoclax.

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So it's kind of close to like a 50:50 chance of getting a response and so of course you know if you're in that 50% that doesn't get a response, you're pretty, you're really bummed out.

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I mean you've just gone through a kind of a big procedure. You just got chemotherapy and then you know maybe the chemotherapy's made you sick.

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You have side effects still but you didn't get the benefit of getting the response. And so that's, you know, that's what I, that's the part that's really tough.

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On the other hand, the 44% of people who get a response do really, generally pretty well.

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I mean, they're still side effects with the treatment, but you know, you kind of always weigh, are the side effects worth what benefit you get?

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About 20% of people, so half the people who got a response got something called a complete remission.

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So can't find CLL at all. And those people, at least with our follow-up, which we have about three years of follow-up on the trial now, none of those people have had a relapse yet.

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And so you know, that's at least three years off any sort of treatment which is great.

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And so, you know, you've got kind of both ends. You've got people who have a great response and can have a really long response.

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You get people who have no response but have side effects. And if I could, you know, if you were a patient walking into my clinic and if I could very accurately tell you, you were going to be that 20% that gets a complete remission...

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that would be so helpful to me. But I don't have that information I need, yet to say that.

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So I can't say, you know, you know, people with purple hair and green toenail polish...

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those are the people who they're going to really get a response. But I mean, really, you know, there's a lot of studies going on now in the background now that we have all the data from the trial to say, what is it?

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Is there a marker like trisomy 12 or you know unmutated IGHV or something that we can say, okay, you're most likely going to be in the people who are going to respond.

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So it is, in my opinion, worth it for you to go through and say, okay, you're most likely going to be in the people who are going to respond?

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Yeah.

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So it is, in my opinion, worth it for you to go through any possible toxicity because you could get to the state where you're not on any treatment for CLL so it's still that's why it's not, you know, just recommended for everybody yet, because they're still a little bit to be, to be worked out.

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But I think it's a great treatment. It's really unique how it uses the immune system and you know, all the time research is being done trying to figure out how do we make it have less side effects and how do we make it last longer or work better for more people?

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Sure, sure. That's great information. Thank you so much, Doctor. Alright, let's please explain the benefits for a CLL patient to work with the CLL specialist in addition to a more local hematologist or oncologist.



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Can they work in tandem?

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Well, first of all, this is the question to a biased person so I'm just going to throw that out there as a caveat so you can take everything that I say with a grain of salt because I am a CLL specialist.

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You know, I selfishly find that I, you know, for example, it was my family member,...

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I would want them to have a CLL specialist on their team. And just because, you know, really I have the really great benefit and the joy to be able to focus on CLL.

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So, you know, any kind of research that's coming out that involves CLL, I'm just, I'm digging into it.

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I'm trying to figure out, does this apply to my patients or not. You know, I'm constantly attending conferences to try to, you know, figure out what's the next best thing.

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You know, making sure that there's clinical trials available, something that you might not have otherwise have access to.

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So I think it's always good to get a consultation. And I know the CLL society is very good about there's actually a spot on the CLL Society's website that you can look and see, you know, in what area, you know, what state you live in, where the closest expert might be.

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And so they make it easy for you to find it. But what I say is I really think it's important to actually still work with your local hematologist or our oncologists too.

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You know these people are so smart because they have to see you know 12 different kinds of cancer in a day and they have to keep up on all of this information.

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So they're very, very smart. They're just not specialized. And so what's often helpful, you know, some of the treatments that's easy to recommend, you know, there's a lot of good treatments out there.

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But what might be nice is, you know, let's say you need a new treatment is just to check in with the CLL specialists and say, "hey, you know, my doctor recommends treatment..."

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Do you think this is a good one?" Because there might be a clinical trial that might have something, you know, the latest and greatest that you might be able to enroll in and, you know, what I typically do is I say, "You know, come see me, we'll talk about what the, what I think is the best option."

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Then I'll talk to your doc back at home. And if the best option is like acalabrutinib and your doc could just write a prescription for it and can manage you at home,...

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perfect. If you know that you have already had your CLL progress through a lot of different treatments and maybe none of the standard ones are great...

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then you know, come here and we'll do a clinical trial. And so I really like to work with the local docs because I think it's so helpful and, you know, hopefully we're providing a good service to them too so we can like really pull apart all the logistics of the CLL and just, you know, give them a recommendation.

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But I think it's important because, you know, what if you have a side effect of the treatment and you, you know, your oncologist is like hours away.

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It's really good to have somebody close that can help with side effects or you know maybe there's just something you need like blood transfusions or antibiotics or something like that.

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It's really good to keep a good relationship with your local doc at the same time.

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Okay, good. Good. Thank you. This questioner says I'm a 68 year old male recently diagnosed as CLL.

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Full blood testing verified and working with a good hematologist. I'm on watch and wait.

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No symptoms. Anything in lifestyle changes that I may want to consider?

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Great question and it's an area that I'm particularly interested in. For one, I'll just kind of put in a little plug depending on the risk factors.

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There is an early intervention, clinical trial going on. So if your doctor did risk factors in your blood and found out that you have high risk disease, you might actually qualify for an early treatment trial.

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It's called S1925. It's a clinical trial going on across the country...

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and that trial randomizes patients to either venetoclax and obinutuzumab right up front or waiting until a time when treatment is needed.

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Now this is only for people who have been diagnosed within the last 18 months. And again, with the caveats every trial has, the few little, you know, things that, you know, you have to make sure that you do to qualify.

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So that that's one option saying, you know, "hey, do I have high risk disease"? Should I go on this early intervention clinical trial and it's available at most...

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I think, most states have an open site across the country. Now, otherwise, you know, if watching and waiting is appropriate, I think there's a few things to consider.

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Of course, your doctors probably talked with you about risk of infection and so, that plays into making sure you're up-to-date on appropriate vaccinations.

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You know, just to name a few, influenza vaccine every year, making sure you've had the shingle vaccine every year, making sure you've had the shingle series, which is a two shot series.

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There's a new pneumonia vaccine called the Prevnar 20 vaccine, which I think is very good.

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And then there is a new RSV vaccine which you know still is a little bit new and I think potentially it could be very helpful for patients with CLL, although admittedly hasn't been tested specifically for CLL.

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And then COVID, prevention or, vaccination is usually kind of a personal decision you can talk with your doctor about but the FDA has approved COVID vaccines to be taken essentially as frequently as every 2 months...

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for folks who need it. Now, I don't typically recommend my patients get vaccines every two months because I think that might be just a little too frequent, but, of course, a lot of you may have heard that there's another method for preventing COVID that just got an emergency approval which is called pemgarda.

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This is basically an antibody, it's an IV infusion that can be given every 3 months as a pre-exposure prophylaxis so it's not a vaccine.

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It's basically just putting those antibodies right into you and that's something, it is a very new approval so most centers don't have it yet.

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We actually don't quite yet have it at my center and I don't know the details for insurance coverage for everybody yet...

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so that's kind of the caveat of that. So I would say, infection prevention is one thing to consider when you're in watch and wait.

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The other thing to consider is you are at a little bit higher risk of second cancer when you're in watch and wait.



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The other thing to consider is you are at risk of a little bit higher risk of second cancers...

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and so making sure you're doing what you can to protect yourself from getting skin cancer so, protection from the sun, and doing skin checks.

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At least once a year, you know, doing your age appropriate colon cancer screenings, mammograms, things like that.

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Just make sure you're up-to-date on that. Otherwise, there are not, you know, there have been...

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some studies done with supplements because I know a lot of people are usually saying, you know, there is there some kind of supplement I can take that would help me.

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And I haven't been fully sold on any of the supplements. There was a little bit of data with green tea extract and curcumin...

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but you have to take really high doses of it and those can cause their own side effects and I don't think it really impacts the natural course, you know, like it doesn't cause your CLL to go into remission or anything like that.

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And so, you know, just be wary. I don't want people to get taken advantage of spending a lot of money on supplements that haven't totally been proven.

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One thing I will often do for people is, you know, check vitamin D levels because I think vitamin D supplementation for one, can make people feel better.

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And for two, folks who have CLL are a bit higher risk for osteoporosis and so that is something that can help you to build bone density, you know. Just making sure that you're getting your standard screenings, like DEXA scans and things like that to look at your bone density.



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And I generally, I mean, again, I'm probably biased, but, you know, the CLL Society has support groups that are really across the country.

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And there's even, you know, there's local support groups and most of these are still online.

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They went online during COVID and they're still on line but there's also like specialty groups.

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Like I know they have a group for doctors who have CLL and some other groups. So it's something you can check out on the website.

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I just, I feel like I can tell how beneficial it is for my patients to have met somebody else that has CLL and maybe they're also in watch and wait and it makes you, you know, you have somebody to come to talk about your symptoms with.

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It's not a medical professional, so you can kind of, you know, is this something you've experienced and, you know, just have somebody to really kind of commiserate with on a common experience.

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And I find that it's also even helpful for significant others or family members, you know, whoever would be considered, you know, your primary caregiver, you know, whether that's a, you know, significant other sibling or, child or whatever.

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A lot of those people actually participate in the care group or the support groups. It's nice for them to have other caregivers that they can connect with because they know, you know, I mean it's very hard.

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For all the folks in the CLL community to go through something like a pandemic where you're at increased risk of infection.

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And then you also have, you know, this other group of like people who aren't immune compromised, but they're at CLLse contact with a loved one that does.

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And so, you know, I think there's something to be said about support groups. Exercise, physical activity.

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Yes. Do it as much as you can. It helps. I think that's the one thing I found that helps the most with CLL related fatigue is exercise, it releases good endorphins so hormones that make you feel better.

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It also helps your sleep to be better because you've fatigued your body and your muscles.

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And so make sure that you're getting out there and exercising and I know I think COVID through a wrench in a lot of people's plans too because maybe people like to go to the pool and do water aerobics they like to go to the gym and lift weights or whatever aerobics or...

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And then, you know, COVID came and everything shut down and you had to come up with a whole new plan and you know people's level of comfort for getting back into their old...

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routine is, you know, people's level of comfort for getting back into their old routine is definitely variable.

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Make sure you're getting out, getting regular exercise. I think it is really important for watch and wait, especially for that fatigue that comes along with it.

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Sure, yeah, I was a pool person. And during the pandemic I started marching. I just went marching.

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I mean, just find something else and what you were saying about the support groups is true. We have some for veterans.



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We have people who are just in watch and wait. We have caregivers support groups. So check out the CLL Society website for any specific support groups.

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But, and I think the idea of support groups ,people sometimes have a preconceived notion of what support groups are.

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And I think you should just try it because especially in the CLL Society, it is very much about educating yourself and I think that really helps with the anxiety level of this diagnosis, especially watch and wait is hard for people to get their minds around.

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I have cancer and you're not going to do anything. I think that's really helpful, to talk with others, as you said, that are in the same boat that you are.

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Okay, our next question is, are there drugs which are currently undergoing or about to undergo clinical trial that are showing promise and significant advances?

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Beyond the current therapies, specifically for those with genetic abnormalities of IGHV mutations and TP 53 aberrations.

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Great question. There are tons of drugs that are, there's always drugs under investigation in the lab and then clinical trials.

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You know, I would say just to mention a few that I think right now in clinical trials that are really showing some good promise.

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There's a group of drugs called BTK degraders. And so basically, you know, you might have heard me say that these drugs like ibrutinib, acalabrutinib, and zanubrutinib they are BTK inhibitors.

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And so BTK is something that's really important to CLL survival. And so sometimes when like, for example, when ibrutinib stops working...

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it's because it's mutated and the drug can't bind in the right spot anymore.

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Well, this BTK degrader is another way to come in and get rid of that BTK protein...

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and so it's showing some good promise in patients, especially if they've had prior BTK inhibitors even, and showing some good results.

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There's quite a few of them out there. And so, you know, make sure you're looking out for clinical trials.

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I mean, there's one by Nurix and Accutar and BeiGene so, you know, and other companies are making them.

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So, beyond pirtobrutinib, Doctor, that was a question, someone wanted.

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Yes, I mean, these are people, sometimes these are people that have also had pirtobrutinib, because when the mutations happen, it's a different way that the CLL becomes resistant to treatment...

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and so it can still be used even after pirtobrutinib. The other thing I'm kind of interested in are these drugs called bispecific antibodies...

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and basically what that means is they're antibodies that they go in and they have a target that's on the CLL cell...

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A lot of them right now are CD 20 targeted and then they have something called CD3 that they target which is on your own T cells.

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So again, it's working on bringing your T cell over to the CLL cell to kill it.

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It's basically kind of an immune therapy. And what's nice about that is a lot of the, you know, let's say you, your CLL has become resistant to ibrutinib or pirtobrutinib, or venetoclax.

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The resistance is different and so that means that these drugs can still work because it's targeting something else and it's targeting an immune response as opposed to you know something,...

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a mechanism in the CLL. So there's a drug called . There's a few called epcoritamab, one called glofitamab, and mosunetuzumab.

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These are all drugs that are showing good promise in clinical trials and they're at various stages.

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And then of course, you know, once we figure out a good drug, we end up combining it with another good drug and figuring out does it make sense to combine it because maybe we can have even more success...

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or does it not make sense to combine it because we've just caused a whole bunch of side effects.

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And so those are the classes I'm probably the most excited about, the furthest along that are coming through clinical trials, but there's always a lot of other drugs that are kind of, you know, in various stages.

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We're very fortunate. I know when I was diagnosed in 2015. The BTK inhibitors were just new.

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Ibrutinib wasn't even FDA approved yet. It just seems like it's a bouquet of flowers blooming for us with all of these options.

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I love that analogy. Yeah, and I mean even in the last six months we've had two new treatments approved for CLL with pirtobrutinib and liso-cel, the CAR-T therapy.



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So, right, you know, moving fast.

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Yes. Okay, next question. I'm 3 weeks post treatment after being treated for 13 months. I'm extremely fatigued.

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Is this normal?

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Yeah, I mean, I think fatigue is one of the hardest parts about CLL because I think, you know, it comes if you're not treating it, it comes when you're treating it, and it comes after you're done being treated.

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And so I would say it's normal and depending on how far out you are from treatment generally, I feel like if the fatigue was from the treatment,...

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it will get better over time. It's just, it's not overnight. Like I think a lot of people think like, "oh well, I'm done with treatment, shouldn't I just feel better" because you know, it's not necessarily the case it will, you know, take time.

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Now if the fatigue is severe, definitely talk with your doctor about it because, you know, who knows maybe it could be the CLL, you know, coming back quicker than expected.

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Is there something else, has there been a side effect to like, you know, kidney function or liver function or something that's causing that level of fatigue.

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But again, as much as you can, you know, exercise and be active, even though I know that sounds silly when you're saying I'm tired and I can't do those things.

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Those things really do help. And so again, if it's severe fatigue, I would talk to your doctor about it because after treatment shouldn't have it start, you know, I can understand if like the fatigue has been going on all during treatment and maybe it's getting worse with the, you know, cumulative effect of treatment but then to just have it start, you know, kind of suddenly after treatment that's a little bit strange and I would...



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want them to talk to their doctor about it just to make sure there's not something...

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else going on.

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Okay, another question, should valacyclovir be taken for life and maybe you can explain why someone would be prescribed that?

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Yeah, this is a great question. I don't know that anybody has a hundred percent the right answer to.

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Valacyclovir is a drug that would be used to prevent a cold source in the mouth or shingles...

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and I would say people who have a tendency to get these and are not having a side effects from Valtrex or valacyclovir, I would say maybe you should take the valacyclovir indefinitely.

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I often put people on it during treatment, just because people are a lot more prone to these infections when they're on treatment.

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Maybe, you know, if you finish treatment or maybe you're doing well, maybe, you know, you feel good about you've had your shingles vaccine, you don't have a history of oral source or, you know, cold source, things like that...

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you can come off of those, valacyclovir. In general, I find that people tolerate the medication pretty well and if it prevents you from having a bad case of shingles,...

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it's probably worth it. So, I think it just depends on the person's history, you know, have they been vaccinated...

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for shingles, do you have a big history of, you know, oral or, you know, vaginal genital ulcers, anything like that?



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So kind of depends on the person. But some people, yes, I do think it's appropriate kind of to take it indefinitely.

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Okay, what are the risk factors for Richter's transformation in those with CLL/SLL?

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A good question. All Richter's is not created equal. And now what Richter's is, Richter's is the transformation of CLL into a more aggressive lymphoma...

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and it's often really aggressive. I mean, people are sick. And this only happens in about, you know, 5 to 10% of folks who have CLL and maybe that factor will change over time as people are living longer.

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I would say classically, this is something that comes up after people have had multiple treatments for their CLL, so you know a high number of prior treatments might be a risk factor for Richter's.

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And there are certain mutations and there's a lot of data out there on a lot of different...

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mutations like TP53. There's a mutation called a MYC mutation.

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You know, there's a slightly higher risk with, I know your doctor probably just told you, if you had mutated or unmutated IGHV...

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but there's certain subtypes of that that can be associated with Richter's...

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and so the hard part is every now and again we see a patient they don't even know they have CLL and they come in directly with this Richter's Transformation and so you know it's not always related to a higher number of treatments.

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And so I think it's just something that they should be aware that it exists. Usually when it happens, people are sick.



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It's usually a really quick growing lymph node, you know, maybe drenching night sweats, maybe fevers, people generally don't feel very good.

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There's something that has changed with your CLL especially that fast growing lymph node or if the lymph nodes feel like harder or more firm than they did before, that's something you should definitely have your doctor check out.

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Okay. Is it normal for CLL patients to experience increasing sinus and ear issues? If so, what do you recommend to address these issues and provide more comfort?

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Yeah. Oh gosh, it totally is. And I'm sorry. It seems to be very bothersome.

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Because a lot of people with CLA get kind of recurrent sinus infections,...

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you know, which can lead to problems with their ears, things like that. The first thing I usually do when I hear people saying they have frequent sinus infections or maybe they have a sinus infection that they had to go through like three different rounds of antibiotics or something to get rid of,...

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I'll check their levels of immunoglobulin. Because with CLL, you can get low levels of this antibody called IGG and if it is low, so like less than 500, you might benefit from getting an infusion called intravenous immunoglobulin or IVIG and that's a monthly infusion that can help to prevent, you know, just help to boost the immune...

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system enough to prevent these sinus infections. Usually when people have issues, I make sure that they have an ear nose and throat doctor that they can go and see because occasionally there's, you know, something structurally like the surgeon needs to go in and like clear out a sinus or, you know, maybe they have a nasal passage that's blocked that that can be fixed surgically...

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and then that can prevent that, you know. Occasionally people just have to be on preventive antibiotics...

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so like a low dose of antibiotic to keep them from doing it, but you know...

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it's definitely a really bothersome thing that happens to folks with CLL. So you're not alone out there if you're suffering from this.

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For sure. Dr. Stephens, this has been great, but we had so many questions that we didn't have time to get to, but we covered the ones we did really well.

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So I hope you'll come back and join us again. But before we close, do you have any last thoughts for our audience?

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No, I just want to say thanks to everybody for joining. And I really think it's, it's very empowering to learn more about CLL, the more you know the more educated care that you can get and you know what questions to ask.

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When you're working with your doctor and, you know, just again I think we've talked about lots of new treatments. I just want to give everybody hope that, you know, that these treatments just keep getting better and better and, you know, even if, you know, someone's told you something discouraging like, you know, this is the last treatment I can think of to give you, you know, just wait a couple months there will be another treatment or there'll be a...

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clinical trial and so, you know, I just want people to have hope about that and there's lots of folks out there like me that are still working hard doing research trying to make things better for you guys.

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Well, thank you so much for your time and expertise, Doctor. We're very grateful for your participation.

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And thank you to everyone who joined us today. We'd also like to thank our generous donors Astra Zeneca, BeiGene and Genentech for making this event possible.

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A few brief reminders. If you're a Facebook user, please remember to like and subscribe to the CLL Society Facebook page.



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Please complete the short survey that's linked to the comment section on Facebook and will be shared with everyone who registered.

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We really need your feedback. Please join us on May 16 for our next webinar, COVID...

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19 in 2024. Recommendations and strategies for those with CLL and SLL with Dr...

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Shazad Mustafa. So a lot of those COVID questions that we didn't get to, catch us next time.

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If your question was not answered today, please send it to our Ask the Expert email service. This is a free service and can be found on the website...

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under programs and support. Remember to follow CLL Society on Facebook and other social media platforms. And lastly, CLL Society is 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. So thank you.

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Thanks everybody.