

Transcript | The Current CLL Treatment Landscape & Advocating for Your Care

Part 1: Introduction to CLL and Overview of Disease Staging

Andrew Schorr: Greetings. Thank you so much for joining us. I'm Andrew Schorr in San Diego. Welcome to this Patient Power Town Hall meeting, and it is "The Current CLL Treatment Landscape and Advocating for Your Care." I've been living with [CLL](#) 25 years. We have almost 400 people living with CLL around the world joining us. Thank you so much. We hope that what you get out of this is the latest information and confidence in living, hopefully, a very long, full life with CLL. We'd like to thank our partner, the Robert H. Lurie Comprehensive Cancer Center of Northwestern University in Chicago. They are a true center of excellence and they've been great as we've planned this event. I'm joined by two of my dear CLL friends. There is Michele Nadeem-Baker in Boston. Hi, Michele. Thank you so much for being with us. And then in Rockville, Maryland, Carol Preston. Carol, thank you so much for being with us.

And we have some wonderful guests who will be with us now over the next three hours. And I want you to see them. There's Jenny Boyer from Northwestern. She's a nurse practitioner in hematology. Jane Dabney is a senior oncology social worker at the Cleveland Clinic and certainly very knowledgeable in all the issues that affect us. As we go on, we have Dr. Deborah Stephens from the Huntsman Cancer Institute and she's in Utah. And then Dr. Shuo Ma, also from Northwestern and the Robert H. Lurie Cancer Center. Thank you all for being with us. And, of course, you'll be able to hear from them and ask questions along the way. We want this to be an interactive program. So, if you're with us on Zoom, as most people are, at the bottom of your screen, use the Q&A button and send in a question. And we have wonderful producers behind the scenes, and they will look at your question.

If you can tell us your first name and where you're from, that makes it a little more personal, but don't ask a personal question. "Here's my blood counts. What should I do?" That's not appropriate for our medical experts to practice medicine over the internet. Discuss your personal situation and what you learned here with your own doctor. That's how you get the care that's right for you. I want to thank our financial supporters, our sponsors for this program, and that is AbbVie and Genentech and Adaptive Biotechnologies. Remember though that our sponsors in all Patient Power events have no editorial control. And I also want to thank the CLL Society, our dear friends there who do such great work and who helped raise awareness for this

event. And we work in partnership with them regularly. A couple of ground rules. Remember send in your questions, not too personal. We'll have a whole [Q&A](#) section at the end.

If you're with us on Facebook, you can just put your question, first name, where you're from, in the comments on Facebook. People are joining us in many different ways. Okay. So now let's move on. So, Michele, you're going to kick us off with our first section for people newly diagnosed. For me, 25 years ago, terror. And you, a few years ago. Let's take it away.

Michele Nadeem-Baker: Thank you, Andrew. And I'm so excited to be here with everyone who's with us. 400 people. That is fabulous. And I'm excited to be here with you, Andrew, and with Carol, the co-host team today, and also with our panel. I'm Michele Nadeem-Baker and for Andrew, it may seem like a few years that I've had CLL, but for me it seems like a lot longer. And it's been since 2012, how time flies, huh? And so much has changed in the treatment landscape since then. And we'll be learning a lot about that today. But I'd love to welcome our experts for this section of the program, Dr. Ma and Jennifer Boyer, starting with Dr. Ma. Can you please introduce yourselves when we get to the end of my introduction here? I want to just jump right in.

This is like a primer to CLL. It's great if you're a newly diagnosed patient. Let's call it CLL 101. And also, it's a great refresher to those of us who have had CLL a while. Perhaps we're back in watch and wait, or we've continued our remission for a while, but it's great to refresh all of this information for us and see what else is happening out there. So, we want to make this as interactive as possible for you all. And we're going to start with a poll, just jump right into a poll and find out where you all are in your CLL journeys. If we could have the poll, Jordan, please? So, our poll starts with "How long ago were you diagnosed with CLL? Less than 6 months, less than 1 year, less than 5 years, less than 10 years," that's where I would be, "more than 10 years." Andrew, that one would be yours. So, these polls are pretty fast and we'll be getting those results in quickly. So, if all of you out there can just fill in which one you're with.

And while those questions are being tabulated, Dr. Ma, can you help us here? Let's say I'm in your office. Oh, here are the results. Let's just go with them, just so we know who's with us. So less than six months, we have 9% of who's watching. Less than a year, 6%. Sorry, 9% are less than six months. Less than five years, 35%. Less than 10 years, we have 26%. And I'm sorry, I finally have to admit, I need to put on my glasses. And more than 10 years, wow, 24%. So we

have an audience that's from newbies all the way through people who have been living with CLL for more than 10 years.

Andrew Schorr: And, Michele, I think I might mention, the people even less than five years may have had no treatment. I had no treatment for four and a half years. So, I was still newly diagnosed at four and a half years in my mind, and I was wondering which way we were going to go.

Michele Nadeem-Baker: Yeah. And that's very true. I was three and a half years before I was treated. So, Dr. Ma, in your office. I really don't know what's happening. I've just been told I have CLL. What would you tell a patient CLL is?

Dr. Ma: Yeah. Well, first of all, good morning, everyone. It's very nice to have this opportunity to talk to all of you. And know this has been a very tough year with the [COVID](#) and all of that. And you probably have not seen my face or Jenny's. Jenny is my nurse practitioner partner at our practice for over a year, so it was very nice to say hello to everyone. Blast off. Yes. So, when we have a patient in the office, especially with the newly diagnosed CLL, we often see the patient being very anxious, of course. So, anyone who's labeled with a new leukemia diagnosis is very nerve-wracking. But I think that the most important thing I hope the patient will get after walking out of our office after the visit is that they can understand that CLL is not the typical picture that you think of as acute leukemia. This is a completely different disease.

And also understand it as a chronic condition. So, it's really a chronic condition, even though we cannot cure it, but we do have very good ways to treat it. And oftentimes we may not need treatment, but periodically we might need treatment. So, think of it as a chronic condition that will make the patient feel more reassured that this is not a cure for leukemia, but this is a very manageable disease.

Andrew Schorr: And it is a cancer. That was one thing I didn't know at the beginning, because it's not breast cancer, lung cancer. It's leukemia. What is that? And my understanding is it's part of your immune system, your B cells that have sort of gone haywire. Is that right?

Dr. Ma: Yes. Yeah. So CLL is really a disease that is caused by the slow accumulation that the abnormal population of lymphocytes. So, for people who are not very familiar with blood cells, we know that in the blood there are three major types of blood cells. There are the white blood cells, which is really making up our immune system. And there are the red blood cells, which are

carrying oxygen, deliver oxygen to the tissue. And then there are the little platelets, which are the tiny cells that help to form blood clots in case of bleeding. So, all of those cells are made from the bone marrow and among the white blood cells, there's many different types. So, for example, the major groups are neutrophils, lymphocytes, and then there's some minor groups, like monocytes, basophils, eosinophils, et cetera. So, among the lymphocytes, so these are really our immune cells, there are B cells and T cells. So CLL is a disease of the B cells. So, during the B cell development, there are some genetic changes that make the B cells not going through the cell death that they usually should go through the life cycle.

Instead, they just keep on living and their gradual accumulation of those abnormal B cells. And they're all from a single clone. That's what we call monoclonal B cell population. So that's really what's making CLL, is the slow accumulation of the monoclonal B cell population in the blood, in the bone marrow and in the lymphatic tissue.

Michele Nadeem-Baker: So, Dr. Ma, and I also want to mention that Dr. Ma is with Northwestern at the Lurie Cancer Center and seeing CLL patients all the time. And with these patients, what tests are necessary for them? Someone is suspecting, a PCP or a general oncologist. When patients come to you, what tests are necessary for those CLL patients for you to help determine where they are? And within that, what are the different stages of CLL once they have these [different tests](#)?

Dr. Ma: So I think I can throw this question to Jenny who will be very well equipped to answer that, because we have seen patients all the time, and many times the patient really was initially referred to us because their primary care physician just happened to detect an elevated white blood cell count. And there [are] important tests we need to do to determine what is the etiology of that. Jen, you want to take over?

Jennifer Boyer: Yeah. So as Dr. Ma was saying, a lot of times our patients come to us initially with an abnormal white cell count that was found by accident based on annual blood draw. And so, it's very important to get a differential on that blood count to see the actual lymphocyte population. Dr. Ma mentioned when she was discussing what CLL is, we want to see if it is the lymphocytes that are growing too much or proliferating. And then beyond that, there's also a test called flow cytometry that can be run, where it does look at not only the lymphocytes, but whether those lymphocytes are actually coming from a single clone, a factor Ma mentioned.

CLL is where a single clone is proliferating too much. So that helps us to find the monoclonal B cell population, which can help us to diagnose the CLL.

Andrew Schorr: Hey, Jenny, I have a question. Over the years, Michele and I, we've been in [clinical trials](#), which we'll talk about later. We've had bone marrow biopsies. Do most CLL patients need a bone marrow biopsy, or can you really get a good picture of the CLL from these blood tests?

Jennifer Boyer: Well, it depends. At least, initially, you don't necessarily need a bone marrow biopsy, because we can get a pretty good picture from the peripheral blood. But if we have other questions where we're not getting the whole picture and we need to make sure we are finding out the amount of bone marrow involvement in your disease, then a bone marrow biopsy would be necessary.

Dr. Ma: Right. So actually, for a diagnosis of CLL, it's not required to have bone marrow biopsy. As long as you can do a flow cytometry of the peripheral blood to detect the monoclonal B cell population with the correct combination of surface markers, we can make a diagnosis of CLL. So, bone marrow biopsy is not required for CLL diagnosis, but rather we use that to investigate if a patient has low blood counts. For example, if they have a low red blood cell count called anemia, if they have a low platelet counts, then we want to see is it the bone marrow production problem that is causing that. And, if so, is it caused by CLL over-proliferation in the bone marrow?

Michele Nadeem-Baker: So as we're speaking about all this and we're talking about these tests, what would be some of the prognostic indicators that these tests would show? Because I know a lot of patients are asking questions about "What are they? Which ones should I be checking out on my tests?" So, what are the ones and are some worse than others? For instance, I have 11q and I'm mutated. But not everyone knows these things or what it is that they need.

Dr. Ma: Right. Jenny, do you want to touch on the staging, first of all? And then I can talk about the other prognostic factors?

Jennifer Boyer: Sure. Yeah. So still the most important prognostic indicator for CLL is the staging. And the main system that's used in the United States is called Rai, R-A-I. And so, it mainly focuses on the total lymphocytosis. So, your count of your lymphocytes, which we

already touched on. And then it also takes into account lymphadenopathy, which refers to enlarged lymph nodes around your body, which can be detected on an exam or on imaging, such as CT. And then it takes into account any low blood concept you might have, as Dr. Ma mentioned. If you have a low hemoglobin, low platelets, low neutrophils. And then, finally, another something that can happen in CLL is your liver and [spleen](#) can become enlarged from the lymphocytes gathering. So that is also another part of the staging and for the Rai staging system.

Andrew Schorr: Okay. So, all these mutations, though, and mutated, unmutated, it's like crazy making when you're newly diagnosed.

Dr. Ma: Right. Right. Yeah. So besides what Jenny was talking about, the clinical staging, as in the old times, before we had the molecular techniques, the clinical staging was the most important prognostic factor. But in recent 10 years or so, as we're becoming more advanced in detecting the genetic abnormalities in leukemia, so now they're emerging some even more important prognostic factors. So, for example, the one that's most commonly done is a chromosomal study called FISH analysis. So, a FISH analysis is that we know among CLL patients there are several commonly occurring chromosomal abnormalities in the CLL cells. Remember this is only in the leukemia cells. Doesn't mean that it's in your normal cells. And it seems we know that these are commonly occurring abnormalities. We design a panel to fish out whether or not this particular patient has any of those abnormalities.

So this is a panel designed to specifically look at those few chromosome abnormalities. So that's a FISH analysis. So the common ones are, for example, chromosome 13q deletion. When we talk about q, it means the long arm of the chromosome. So, the long arm of chromosome 13 was missing, 13q deletion. And 11q deletion occurs in about a quarter of patients. And then there's also the trisomy 12, meaning there's one extra copy of the chromosome 12. Make it three copies. There's also the [17p deletion](#), which means our short arm of chromosome 17 is missing. So, over the years, there have been many studies confirming the finding that certain chromosomes are really correlating significantly with the overall prognosis of CLL patients. For example, a 13q deletion, if you only have 13q deletion, that itself is considered in most favorable prognostic factor. Patients with 13q deletion tend to have a more slow process of the disease, or we call it indolent process of the disease.

And then it's really a whole spectrum. So, on the other end of the spectrum, the one that has the highest risk is the 17p deletion. A patient with a 17p deletion is typically having a more aggressive course, relatively speaking. Even though CLL, in general, is an indolent disease, but relatively speaking, some patients progress faster at a faster pace. And also, they tend to not respond very well to the conventional chemotherapy, which is very important to know. And in the old times, before we had the more novel therapies and other core therapies, when we only had chemotherapy as our treatment options, then those patients tend not to do very well. But, fortunately, in the recent years, six, seven years, actually, with the emerging of the novel targeted therapy, which we're going to talk more in the next section, we are definitely seeing much more improved overall clinical outcome, even for a patient with 17p deletion.

And then the other high-risk feature is 11q deletion, which Michele, you said you had that in your CLL. So 11q deletion is also an indicator of a relatively faster pace of the disease. And those tend to occur, actually, in younger patients. And they can present more with bigger lymph nodes, especially in the abdomen. But those patients, despite the faster pace, they actually do respond fairly well even to conventional immunochemotherapy, as far as the novel therapies. And then somewhere in between, we will call intermediate risk, is the patient who has trisomy 12. And those who actually do not have any of those abnormality are what we call normal FISH panel. So that's the FISH chromosome study. The second... Michele, do you have a question?

Michele Nadeem-Baker: I was just going to say thank you so much. No one has ever actually explained to me about the 11q deletion. These are wonderful correlations for patients to understand, and this is terrific. And so, it helps us all understand what symptoms should we all be looking out for, like what you just said. So that's great to understand all this. And I'd love to hear more about symptoms along with what you're saying that the patients should be looking out for. And maybe Jenny can jump in about when it's time for treatment.

Dr. Ma: Right. Right.

Andrew Schorr: Yeah, Jen, what do you tell people? When they, you've been watching them for a while, whatever numbers they have, when is it time? For me, four and a half years, swollen lymph nodes, enlarged spleen, night sweats – what is it you look for?

Jennifer Boyer: Yeah. I think you bring up a good point, because we definitely do want to look at the whole picture. We always tell, especially newly diagnosed patients, there's not one

number with the lymphocytes that that's the day we're going to start treatment. We want to look at the whole patient and overall health. So, we do monitor for, as you mentioned, Andrew, the so-called, the B [symptoms](#), which are things like fever, unexplained weight loss, and night sweats, mainly drenching nights sweats. So, any of those things, definitely alert your doctor about that. And then in addition, we see if there are swollen lymph nodes that the patient's experiencing, we see the pace of those and how fast they are growing and how they are affecting the patient's overall health and how uncomfortable they are.

Michele Nadeem-Baker: And at what point do you know it's time, then? When you look at this whole picture, is there anything that signals "Okay, it's time"? Because I know you're saying you look at the whole patient, so we're seeing maybe some of these, maybe we're seeing night sweats, maybe you're seeing some swollen lymph nodes, but their white blood count is lower. Their platelets are high. I don't know. How do you determine?

Jennifer Boyer: Yeah. So definitely if we're seeing low blood counts. So low hemoglobin, platelets, neutrophils, things that we believe is caused by the CLL. Then if that starts to get to the point where it's progressive and it may become dangerous to the patient, that would certainly be an indicator for treatment. And then we can do imaging, which gives us a better idea of the internal lymph nodes. And it's because there's lymph nodes all over your body, so it's impossible to feel all of them on exam. So, we can do imaging, which gives us an idea of exactly how big those lymph nodes are and maybe how big it's getting. So, when all of those factors come together, it may be time for treatment.

Andrew Schorr: Dr. Ma, I'm sure you get asked this question a zillion times. "Did we do anything to get CLL? Was it hereditary? Did we get exposed to some chemical? What we do to deserve this?"

Dr. Ma: Right. Yeah. I know. I think that's a question that probably will come to anyone's mind. Many of my patients are living a very healthy lifestyle, so they don't understand why they're having this condition. So, unfortunately, we don't know exactly how CLL occurs and what exactly is the underlying cause of it. Even though we know it's a B cell clonal expansion, but what started it? The common thoughts are actually, for the majority of the patients, this is not a hereditary condition. It's not a genetic condition that pass on your family. But there is a small population, probably 10-15% of patient, who has a strong family history of either a CLL lymphoma or other blood cancer. So those patients, they might have some kind of genetic

predisposition then, make them more likely to develop CLL. Even though there's not a one-gene mutation that can test for. Unlike for breast cancer, for example, you can test for a BRCA mutation.

In CLL, there's not one gene mutation can test for. We just know that patient who has strong family history has a stronger tendency, but 80% of the patients do not have any family history. So, I will say probably the strongest factor is [aging](#), because CLL is really a disease that's mostly in older patients. The median age of diagnosis is about early seventies. So, the majority of the patients in their sixties, seventies, eighties, or older. There are some rare younger patients, like Michele. But if you look at the age curve, so with each age group, as the age are increasing, the incidence of the CLL significant increases. And so, we think during the aging process, there could be some genetic mistakes occurring as this B cells that going through this differentiation and growth. So that might have triggered the chromo B cell population.

Michele Nadeem-Baker: Another question, Dr. Ma, you are a [CLL specialist](#). Oftentimes they're diagnosed by their community PCP and go on to their community oncologist. When should they be seeing a CLL specialist? And do you work with a general oncologist in helping treat patients that don't live nearby?

Dr. Ma: Right. So, I think any patient can benefit from seeing a CLL expert, especially at diagnosis and especially when the disease is progressing and you're thinking about treatment. So those are the critical time that a CLL expert can really give you maybe some additional insights that might help you to make an important decision. And we do work a lot with our community oncologist and I believe that's very important, because not all patient has the luxury of living close by to us. And if they live very far, it would be convenient for them to see their oncologist. So sometimes we see patients periodically and then in between they see their local oncologist, so we can maintain a relationship and we can help to follow the patient along. And some patient who live extremely far can choose to come to us as needed. So, there are all different ways we can collaborate.

Michele Nadeem-Baker: So this is a long-term relationship for patients? It's not just a courtship. You're partners for life, basically, when you have CLL. So, what do you suggest for patients on how to build a relationship with their team, of which it would be, potentially, their community doctor, and oncologist, and a field specialist, like yourself? How do they build that?

Andrew Schorr: Jenny, maybe you can start on that one.

Jennifer Boyer: Yeah. I think it's important to look at if it is a team. So, Dr. Ma and I work together. We have nurse coordinators that also help us. And then, yeah, if we're collaborating with community oncologists, we all need to work together. So, I think definitely when a new patient comes to establish a relationship that will, hopefully, be very long, just to be upfront about expectations and to discuss your understanding of what's going on. And we can help to shed some light on that.

Dr. Ma: And I often tell patients that "We are your team. We are all working together with you. We're all one team to help you to handle this disease." And we have many, many patients who I think, really, it's a long-term relationship, because CLL is such a chronic disease. And we have patients we've been following for many years and even decades. And some I inherited from my predecessors. So, I do have patients that have been with us at Northwestern General for decades with their CLL, many of them. So, this is going to be a long-term relationship and we're all going to know each other very well. Many of my patients know my family and my kids. So, I think it's really great. I really appreciate this great relationship with my patients.

Andrew Schorr: You become friends. That's cool.

Dr. Ma: I do. Yes.

Andrew Schorr: Very cool.

Michele Nadeem-Baker: Thank you for all of this very helpful information. And we're going to transition to our next section now, with Carol Preston, our host. Dr. Ma will be staying on with us, as well as an oncology social worker, Jane Dabney.

Carol Preston: Hi, everyone. Carol Preston here again. I've been living with CLL since 2006. But before we transfer directly to CLL and COVID, I do want to offer some great hope for anyone who's been diagnosed with 17p deletion, because that was my diagnosis when I relapsed. And while these oral medications were not yet available, it was my CLL specialist at MD Anderson who interpreted the pathology to say it was only a small number of cells that were the 17p deletion, which meant that I was a candidate for the gold standard of care at that time, which was FCR. So that is another plug for CLL specialists, because they, oftentimes, are light years ahead of the community oncologist. And even if you see a specialist once for an outside

consult, it's well worth the time and the energy. But I want to welcome back Dr. Ma. Michele is joining me as co-host for this segment. And we are also joined by Jane Dabney, who's an oncology social worker from the Cleveland Clinic.

Welcome Jane Dabney. And, boy, do I wish I had had access to an oncology social worker when I was originally diagnosed in 2006. There's a lot of information on the Patient Power website, patientpower.info, about COVID because it has become the umbrella of our lives this past year, plus. And we'll also take any COVID questions during Q&A. And by the way, speaking of Q&A, don't forget that Q&A button at the bottom of your Zoom screen and our producer will be reviewing it, and we'll make sure that we cover as many questions as we can. So, the \$64,000 question is "We get our vaccines, I've gotten my vaccines, what do we do after those vaccines?" And maybe more important, "What can we do?" Who wants to kick us off with that? Dr. Ma or Jane Dabney?

Dr. Ma: Jane, do you want to start?

Jane Dabney: Well, I can't speak to the medical aspect of it, but at my center, we're all encouraged to still take precautions and wear a face mask, and until, really, we know that herd immunity is really happening, 'til more people get [vaccinated](#). But the specific medical part, I will let Dr. Ma respond to and I can speak more to coping with the uncertainty.

Dr. Ma: I think I get this question a lot. Obviously, it's really on the top of everyone's mind, "When can we start to be free and do things?" So, I think, first of all, the challenge is that we really don't know how our immunocompromised patients are responding to the vaccine. That's a big unknown, because none of the vaccine trials actually included immunocompromised patient. So, we really don't have any data. We know these are great vaccines. I think we can say that these are very safe vaccines, and they're very effective in the general population. They're over 90% effective, most of them. And, eventually, I think for the large society as a whole, from the public health perspective, I think this will help us to get over this pandemic. But when it comes to individual patients, since we don't have any data, it's very hard for us to say that it will be safe for you to let down the guard just because you had the vaccine.

And so we are actually doing some studies, trying to understand more about how our patients are responding to it. But I think the safest to do is, like Jane said, that even if you had the vaccine, I will still recommend you to take all of the standard precautions as you have been

doing for the past year plus, until the general population have had herd immunity and other incidents is really very, very low. I think that's the point that we can start to gradually let down our guards.

Carol Preston: So in full disclosure, I am a grandmother. I had completed my series of vaccines February 20th. And for the first time in a year, I was able, and I got the okay from my son, who's a physician, so every circumstance is different, to hold my grandchildren. I had never held the one-year-old. It was his birthday, Sunday.

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Carol Preston: And I stayed back, and unexpectedly and happily got the okay sign from my son. So, I felt that was a fairly good endorsement, but every circumstance is different. In the meantime, I'm always, and Michele is the same way, we're out and about wearing masks and social distancing. But we do want to find out before we go any further about what our audience is doing and has been doing, so we have another poll. And the question is as follows, if Jordan you could throw up the poll, have you gotten one or both doses of the [COVID vaccine](#)? This is a simple one. Yes, or no? And so, we would really like to hear how people are doing. As we know throughout the country, the vaccine rollout has been uneven, and every State seems to be handling it differently. So that's another reason.

And here we go, wow. We have an audience who has been very adept on their computers, very adept. Signing up for those vaccines. We have 81% of those watching and listening today who have gotten at least one vaccine, and upwards of 20, upwards of a fifth who have not yet accessed it. And of course, one of the issues that we're facing, and I'll address this to both of you is vaccine hesitancy including healthcare workers. Some people have access to it but aren't quite sure. So, have you confronted this with your patients? Let me start with you Jane, have there been questions about whether I should even take this vaccine, especially as an immune-compromised patient?

Jane Dabney: Right. Many patients have questions and I always recommend starting with the treatment team and talking to the team about when it is most appropriate for you to get the [vaccine](#), and also to gain more information about the vaccines. So, we know exactly what's in these vaccines. So sometimes it's a matter of sitting down with the doctor or the infectious disease specialist and learning what the ingredients are and how they are designed to work

within your body and with your immune system. And sometimes with more education, patients become more comfortable in getting the vaccine. Also, in seeing more and more people getting vaccinated and understanding many of us have had side effects, especially with getting the second dose of the vaccine, but realizing that those last maybe a few hours to a day, and then you're back to your usual self. I think with more information, patients are becoming more and more comfortable getting the vaccine when it's appropriate for them.

Carol Preston: And Jane, if I can follow-up with you in terms of coping with the emotional part of navigating the process. I mentioned that some people are very adept and other people don't know where to start.

Jane Dabney: Right. From the beginning of all of this, COVID has been a moving target that, just when you think you have a handle on it, something changes, and you feel like you've lost your grasp of it. So, all I can say is, take a deep breath, try to settle in. Now I think things are getting more organized, at least in my state they are, so the information on the website of your state health department should be probably your starting place to determine where you can get your vaccine and also to getting general information about the vaccine. And sometimes patients are overwhelmed with competing responsibilities in addition to their health, family, employment. So sometimes enlisting the help of a close family member or friend to help you navigate that process, also talking it over, you can ask at your... If you don't know who your oncology social worker is, ask your team for a referral to an oncology social worker and they can help you problem solve and work through some of the frustration around the process.

Michele Nadeem-Baker: So Dr. Ma, how do you deal with this uncertainty about how effective the vaccine is? It was a huge struggle for me, I have to tell you, when we first learned of the vaccines, I was hoping, hoping, hoping for so long that we'd get a vaccine, every night at dinner, we'd talk about it. There's a vaccine and then when we find out that for [CLL patients](#), it's probably not as effective for us due to our immune systems. So, I had originally envisioned, I'm getting this vaccine and I've only gotten my first shot, I'm like, "The heavens will open. Everyone will be singing, and I'll be singing myself about it," and I got it, solely anticlimactic. How do we move forward? I'm so uncertain. I have been more protective of not going out. I still continue to mask. I am not seeing anyone still. I'm not having dinner with anyone. And even when I get my second shot next week, I don't think I will just because of this uncertainty, and I know a lot of CLL patients are dealing with this. What do you suggest for us?

Dr. Ma: Yeah, I think the vaccine responses are likely going to be very variable among different CLL patients, so there's probably not one standard answer. But we can say that, for healthy individuals who do not have immuno-compromised condition, the vaccines can be very effective in preventing symptomatic disease. We're awaiting information on whether the vaccine can prevent asymptomatic infection, that's really the key. Because if it can prevent asymptomatic infection in your surroundings, right, in your friends or family friends, then it might be safe for you to have interaction with them if they're also careful out there.

I think for the small environment, if your family had always been very careful and they are vaccinated, then I think it's probably safe. Although I would like to see more data to say about the asymptomatic infection, whether they can still be a carrier, that can expose you. So hopefully with more time, we will have more data. But I think for now, and to the bigger population at least in public, I would still, will say you should do all the same that you've been doing for the past year.

Carol Preston: We could talk about this subject for the rest of our time together, but please send your questions because we can address more COVID/CLL questions during our Q&A time. We're going to move along now, Andrew and I are going to talk about combination treatments, and that means continuous versus fixed duration therapy. Before we get to that though, Jordan let's hear from another patient.

Jennifer Abraham: My name is Jennifer Abraham, and I am currently 55 years old tomorrow. I was diagnosed with CLL six and a half years ago, and it was my third cancer [diagnosis](#). I think I cried for 30 straight days. I was inconsolable, I think. It was a ton of emotions I felt. And then I put my big girl panties on and started educating myself. I got online, I found doctors, I found Patient Power. I told them my story, they connected me with doctors that they thought I needed to see. I ended up finding the terrific doctor here in Boston, and she works today still with a doctor in Houston and a doctor in New York. I really created a team for myself.

At the time I was in watch and wait, my lymph nodes were very big and swollen and I was unable to put my arms down. I wasn't able to cross my legs. I looked like the elephant man, and it was very uncomfortable. My skin was very enlarged. I was always in stomach pain, and we decided that we would start treatment. I'm still not MDR negative, but I have a life which is beyond my wildest dreams. Arm yourself with knowledge, find places like Patient Power, talk to people because this is really the best time to get CLL. We have doctors all over the world just

concentrating on CLL, and we are living, we're not dying anymore. We're living really long lives and I never thought I'd feel good enough to exercise, I'd feel good enough to work out again, I'd feel good enough to work. And I'm a mother to my girls, my daughter went off to college. So, I'm living an amazing life.

Carol Preston: Another wonderful story.

Andrew Schorr: I love her. I love her.

Carol Preston: She's fantastic and spoke so beautifully about it. First of all, welcome back Dr. Ma. Dr. Ma is still with us, and now we are joined by Dr. Debbie Stephens from Utah. And Dr. Stephens, can you briefly introduce yourself? Tell us a little bit about yourself?

Dr. Stephens: Sure. Thanks for having me here today. I'm a CLL expert. I am the director of the CLL program at the University of Utah Huntsman Cancer Institute. And my research focuses on developing new therapies for patients with CLL.

Carol Preston: Terrific. We're so grateful and glad that you're here today, and that's just what we want to talk about now, treatments. Many approve one, some used alone, some in combination, and I just have to hold this up. You really won't be able to see it very well, but in the communications biz, this is what we call an eye chart. Although for CLL treatment, we're not necessarily picking one from column A and more from column...

Andrew Schorr: This is the approved therapies.

Carol Preston: ... yeah, exactly. For B. So, before we dive into treatments, continuous versus fixed, let's do another poll because we want to find out where you all, in our audience, are in your CLL. Are you in treatment or not? So, if we could throw out the next poll to see where you are in your experience. Obviously four categories; watch and wait, or I think now they call it watchful waiting.

Andrew Schorr: Or watch and worry.

Carol Preston: Or watch and worry, which Andrew, you certainly had the honor of doing for many years. Initial therapy, in remission with no treatment now, or on treatment again. And I

have to say that I think in the last five years, the [CLL treatment](#) landscape has exploded. We can bring our poll up anytime. So here we are.

Andrew Schorr: Oh.

Carol Preston: Wow! Almost two thirds of our audience today are in watchful waiting. Which well, I don't know if it's a testament to how well and how much we can parse a nuance, but that's wonderful. Initial therapy, 16%, in remission, 8%, and on treatment again, which indicates to me that there's been a relapse, about 14%, but so many on watchful waiting. If I could just ask that before we get into the treatments themselves, Dr. Stephens first and then Dr. Ma, are you finding increasingly with your patients that you are able, as a specialist, to keep them in watchful waiting longer than the old days when I was diagnosed, for example, or Andrew?

Dr. Stephens: Well, this is a great question. And again, I think every patient with CLL is different, and people have different tolerance levels of symptoms related to CLL. And as you just mentioned, the treatment landscape has changed very significantly in the last five years. And the reason why we do watch and wait is because there were studies done that show there was no benefit to doing early treatment. Well, all of those studies were done with our old chemotherapy drugs. And so, there are several ongoing studies right now actually looking at watch and wait folks to determine whether they may have some benefit by being treated earlier by the early targeted agents.

There's a large study going on in Germany right now looking at ibrutinib (Imbruvica) and early intervention, and we just opened up a big study here in the United States looking at venetoclax (Venclexta) oral pill and obinutuzumab (Gazyva), which is an IV infusion of it and immunotherapy, if looking at high-risk patients who are on watch and wait to see if they might benefit from having early therapy. So, I think this is still really a changing field, and I think as of now, as for standard of care, people who do not meet criteria to be treated for CLL should fall into this watch and wait category, but just know that there are a lot of [clinical trials](#) that are going on to see if we need to change that.

Carol Preston: And we're going to talk about clinical trials.

Andrew Schorr: We will talk a lot more about trials.

Carol Preston: A little bit later, yeah. So, Dr. Ma, I held up that eye chart, can you highlight what the current treatment options are? We know watchful waiting is a non-treatment option, but once you've decided or the team has decided that a patient needs treatment, what's your go-to?

Dr. Ma: Right. So, I think we're really having a longer and longer list of treatment options for the frontline treatment, which is really a great luxury to have, I'll say. Because six, seven years ago, what we have is really just even a chemotherapy. So, several our hosts have had the chemotherapy such as FCR, the chemotherapy plus a monoclonal antibody or some version of that, so that had been the past gold standard. However, in the past five, six years, the standard is shifting, now we have at least two classes of what we call oral targeted therapies. So those are oral pills, which are targeting particular molecular enzymes, and which are important for the lymphoma cell and leukemia cell survival and proliferation. So, by blocking this enzyme, you can really induce the death of those leukemia cells as a treatment.

So the two classes are, one was called BTK inhibitor, so BTK is the target. And in that class, we currently have two of the approved drugs, the first one is ibrutinib or Imbruvica, which is really the very first part of a therapy we have for CLL, and which has already been there for six, seven years now. And then the newer comer is called acalabrutinib, or Calquence. They both work the same way, they're both what's called BTK inhibitors that you take orally once a day or twice a day continuously. And this is a continuous chronic treatment, we don't stop unless, if the disease is no longer responding or if the patient has an unusual side effect, so that's one class of target therapy we'll have available. And both drugs can be used either by itself or combined with a monoclonal antibody such as obinutuzumab, which Dr. Stephens mentioned previously. But previously, we'd combine the monoclonal antibody immunotherapy with chemo, now we can combine it with the targeted therapy. So that's the one class.

The second class of targeted oral therapy is what's called [Bcl-2 inhibitor](#). So Bcl-2 is a protective protein that's in the CLL machinery. So, once you inhibit this protein using a Bcl-2 inhibitor, then you can actually induce cell death in leukemia cells very rapidly. So, the drug in this class is called venetoclax, starts with a V. Venetoclax is always used in combination with monoclonal antibody immunotherapy. So, in the frontline, it's combined with again obinutuzumab. And so, this treatment, the current of the approval is for one year of venetoclax, class standard six months of immunotherapy. So, these are the standard options that are available including immunochemotherapy, the BTK inhibitor or the venetoclax-based therapies.

But then the more exciting is the clinical trials, which we're going to talk more. But I think a lot of patients probably have heard about a combination of the two classes of targeted therapies, by combining [BTK inhibitor](#) and the Bcl-2 inhibitor. And there are actually several very important ongoing large number of trials, that we have a lot of patients who decided to participate, and we can talk more about that in the later stage.

Andrew Schorr: Right. Because one plus one equals three. We'll get to that. Dr. Stephens, so there you have a patient in front of you and they're saying, "Okay, help me. How do I work through this choice? Take pills for a long time or take pills and maybe an infused monoclonal antibody for a short time, and then take nothing for some length of time?" How do you have that conversation when it seems like both directions are good depending upon side effect profile and I guess the way somebody wants to live. Maybe they aren't sure.

Dr. Stephens: Yeah. I think these are really great questions. And when I start a patient on a new treatment, I find that they have the longest discussions with people, because it's nice now that patients get to participate in shared decision-making about what is the best treatment option for them. As a physician, we can make recommendations about what we think is going to work the best, meaning what do we think is most likely to put them into remission. Based on other medical problems, what is least likely to give them side effects. And we can make a recommendation, but in the end, it does sometimes come down to, "Would you rather do this continuous therapy with drugs?" Like Dr. Ma mentioned, the BTK inhibitors like ibrutinib and acalabrutinib, or a shorter therapy with venetoclax.

Sometimes when people say, "Gosh, if I start ibrutinib, does that mean I'm going to be on this drug forever?" And forever just sounds like a really long time, right? But to be honest, it's not always forever because some people can't tolerate the drug, they have side effects and some people will end up relapsing on the drug. And as you've just heard, our field is moving forward so quickly that who's to say that in two or three years from now, maybe we find a new drug that we add to ibrutinib, and then you are able to stop ibrutinib therapy. And so, I don't want people to be intimidated by the thought of, "I'm going to be on this drug forever," because things change a lot over the course of years. Plus, the drugs, ibrutinib and acalabrutinib are really great drugs. We have the longest follow-up on clinical trials of the drug called ibrutinib just because it's the first one that was introduced.

And so, we know a lot about long-term side effects or what happens after eight years when you've been on ibrutinib for eight years. Whereas venetoclax is very good and very exciting, but we just don't have quite as long a follow-up on that. So, if you asked me what happens eight years after you've been on venetoclax, I don't really have a lot of data to support that just because it's a newer drug. But in the end, they're both really great drugs, they both cause really deep responses in patients. And for the most part, you heard the patient video, it's all about getting the patient back to their normal life. Having a treatment that's really effective that relieves the symptoms of the CLL and also trying to tailor it to make sure that the side effects are tolerable so people can go on living their lives.

Andrew Schorr: Jennifer Abraham was on that video a couple of minutes ago. She mentioned MRD, either minimal residual disease testing or measurable residual disease testing. Where does that come in, particularly with the venetoclax course, and what does that mean for patients and for you as a practitioner?

Dr. Stephens: So this is a relatively new concept just because when we really introduce ibrutinib and acalabrutinib, we know that actually there is still some level of small disease in some patients, but as long as people keep continuing the drug, that's not a problem. Where it comes into play is with venetoclax, when we're trying to do these limited courses of therapy, our goal is to get people into the deepest response possible. And so, this MRD or minimal residual disease are essentially laboratory-based tests that are used to detect the smallest amount that we can detect with our machines of CLL. And so obviously, if we can't detect any of that, that indicates a really deep response. That doesn't mean that the CLL is cured necessarily, but it means that we can tell people who have achieved no detectable or minimal residual disease that we expect them to have the longest remissions.

Now to be honest, it's very new and we don't use it a lot outside of trials right now and I think we'll talk more about how it's being used in clinical trials. One way it can be used in a clinical setting is when you're at the end of your venetoclax therapy, either one year in the frontline setting or two years in the subsequent line settings, we can check and see how deep is the [remission](#), and then have a discussion. Some people might say, "If you still have minimal residual disease there, maybe we shouldn't stop venetoclax." And so, I think that's still an area of flux, and these tests are not always available at all centers. And so, they're not always available to all patients yet. So again, I think this is still a bit of an evolving concept, which I think we're going to hear a lot more about and in the upcoming years.

Carol Preston: Yeah, I think this is where the art comes in when we talk about the science and we talk about the art. Dr. Ma, I don't know if this is more science or art, but let's say I relapsed, and we saw in our poll that some people are in treatment again, can I return to a treatment that I've used before? I was on ibrutinib, I went off, can I go back to it? Or I was on venetoclax, I've been on it for one year, can I go back? What is the science telling you?

Dr. Ma: Right. So, in the past when we only had immunochemotherapy, we used the same agent or similar agents when patients relapse, especially if the first treatment gives you a very long remission. So that means that this is a very effective treatment. If you relapsed very quickly after the first line treatment, then that's probably not a good thing to be reused again, that's the general principle. When it comes to the two classes of the targeted therapy, if you relapse while taking ibrutinib for example, then of course that means that is not, no longer responding because you've never stopped ibrutinib. If you stopped ibrutinib due to side effects, then if the disease progress, you could consider using an alternative BTK inhibitor such as the acalabrutinib.

And so, people who stopped treatment BTK inhibitor for side effects can still respond to another BTK inhibitor. If you were treated with the venetoclax-based therapy upfront, for example for a year, and then a few years later, the disease comes back. Then again, if you had a long remission after the frontline treatment, there has been data, even though it's not a standard yet, but there has been data, we actually participate in clinical trials that showed, for patients who relapsed after a deep remission like venetoclax can still be treated with venetoclax and potentially have response. We don't have a lot of data on how good the response will last and how long it will last, but you can still potentially respond to it. So, retreatment with venetoclax is a potential option.

Carol Preston: Yeah, that's actually very, very good news because it's such a powerful, effective drug.

Dr. Ma: And of course, if you've a had BTK inhibitor, you can always be treated with a venetoclax and vice versa. You can switch to a different class of [targeted therapy](#).

Carol Preston: Well, as we discussed, a bit of an eye chart there, but so many wonderful options. But I do want to find out a little bit about quality of life and this is maybe where the art comes in, when you're talking about treatments for the patient, I'm sitting in front of you and I

say, "Well, I'm very active. I'm old but I do a lot of fitness. I enjoy riding a bike. I love to travel when travel opens up again." So, is that going to be a driver for what you prescribe for a patient or really looking through the tunnel and saying, "This is what you need to get into remission."? It sounds a little bit tricky to me.

Dr. Stephens: Well, I think the big difference is, as far as administration of these targeted agents, is drugs like the BTK inhibitors, ibrutinib and acalabrutinib, they're pills, so they're taken by mouth, so patients don't need to come into the infusion center to get an infusion. And so, especially during this COVID pandemic, a lot of patients have preferred doing something like that, just because they don't need to come in and be exposed to that infusion center. Whereas with the venetoclax and obinutuzumab, the obinutuzumab does involve intravenous infusions. During the first month, there's four infusions, and in the next five months, there's one infusion per month. These hopefully are not too disruptive to people's lives, and so either one are very good options for people who are active or are traveling. We often can rearrange the infusions of obinutuzumab around if people are doing a prolonged trip, just so it can accommodate for a person's lifestyle.

But really, either of these options, patients should be able to go on living their lives and that's the goal of it. And I experience this a lot. I practice in Utah and people like to play here. There's a lot of outdoor activities and I often see patients who are 80 years or older who are still out skiing every day. And so, it is a consideration of how to keep people active and make sure that these medications are not interfering with their day-to-day life, because the point of the medication is to help them.

Carol Preston: Yeah, thank you. And I'd like to clarify something, I've made references on how to refer to this eye chart, and one of them perhaps I shouldn't have given, with what's going on lately in our country. But I just simply meant to say the metaphor really is, you pick up a menu in some restaurants and it's overwhelming, the choices and the combinations of items that you can order. So really, that was my reference for this very wonderful, active chart of medications. I'm sorry, Andrew, you were about to say?

Andrew Schorr: I was just going to say one thing we should just take a couple of minutes on, Dr. Ma, is related to side effects. So, for instance, I've had some friends who've been on ibrutinib and had muscle problems and things like that, or joint problems. I know there's a concern there about if people have atrial fibrillation, it might not be indicated and I don't know

where that comes up, whether with Calquence, acalabrutinib, or are there some contra-indications or side effects related to the venetoclax regime. So, there's no free lunch in cancer drugs, they're powerful medicines, could you just tell us about side effects that patients and their doctors should watch out for with the different medicines you've been talking about?

Dr. Ma: Yeah, certainly. So, I think it really comes down to when we're selecting a treatment and we'll have to look at the patient's other medical condition, and because we're concerned about certain side effects, it might be more likely in patients with other medical issues. So, I'll break it up to the two classes of drugs. So, the BTK inhibitors, really the common side effects are early on some gastrointestinal side effects, generally pretty mild, some might have said a mild diarrhea that you can usually get over in a few weeks. But for the long-term, there are several important things to keep in mind, one is the bleeding risk. So, because this class of drug does have some anti-platelet properties, so similar to baby Aspirin that a lot of people are taking. If you're taking this medication, you might notice more easy bruising and if you're planning on doing any invasive procedures, it's very important to remember you have to hold the medication for a few days before and after the procedure, so you need to let your doctor know. So that's one bleeding risk.

The other thing is the effect on the cardiovascular system. So, hypertension is something that we can observe in some patients, especially with the long-term follow-up. So, we do need to monitor a patient's blood pressure, but these are very treatable, we may need to tweak their medications to control the blood pressure. And then you mentioned the cardiac risk. So, the most common thing that we watch out for, with the atrial fibrillation, is a form of the irregular heartbeat where patients will be feeling computation lightheadedness when the heart is not beating regularly. So, this definitely has been a very well recognized effect in the BTK inhibitors and perhaps more so in the first generation ibrutinib and tends to happen more in patients who have underlying heart conditions. So generally, before I start a patient on BTK inhibitor, I'll take a look at their cardiac profile, maybe do a baseline EKG and echocardiogram to assess their cardiac risk to see if they're appropriate candidates for this class of drugs.

Carol Preston: I was just going to ask to both of you, and maybe you can segue from what you were about to say. I hate to leave the treatment section without talking about the C-word, which is cure. Are you looking at any of these treatments as a potential cure for CLL? And Dr. Ma, I didn't mean to step on you, but if you want to start with that one?

Dr. Stephens: I know. Eventually ultimately, right?

Part 3: The Current CLL Treatment Landscape

Dr. Ma: That's all of our research, are trying to see if we can find a cure. For now, we have a really good treatment that can control the disease for many years, so we're getting close. However, I don't think we have a treatment yet. I don't think any of the targeted therapy we've talked about here has the potential of cure yet, but maybe perhaps down the line when we're talking about other clinical trials and maybe some of this cellular immunotherapy might have some potential, which we'll still have to wait and see. So that's something we're still working out.

I just want to bring back, since we're kind of halfway through talking about the target therapy – side effects of venetoclax. So, we talked about the BTK inhibitors, but venetoclax, really the most important side effects is what's called Tumor Lysis Syndrome, which I wouldn't call it a side effect, I'll say it's a treatment effect because venetoclax can kill leukemia cells very rapidly. So, whenever you kill leukemia cells rapidly, the dead cells release the waste products that needs to be handled by your kidneys. But if the buildup of the waste product happened too quickly, then it's overwhelming your kidney's ability to clear them. And those can cause accumulation in the blood and electrolyte abnormality we can detect in the laboratory test. So, when we see that that's called Tumor Lysis Syndrome. So that's really a fact of the very potent drug. So because of that, we have to give patients venetoclax, using various stringent regimens to gradually build out those over five-week period and then to monitor through lab multiple times and make sure they have lots of hydrations to help to manage the Tumor Lysis Syndrome.

Once you get over the Tumor Lysis Syndrome risk period, the first several weeks, then ongoing treatment with venetoclax is really just sometimes mild, there's intestinal side effects like diarrhea, but generally mild and is otherwise very well tolerated.

Andrew Schorr: I think we've covered a lot, but we should mention, there are other approved therapies. Carol and I both had the old standby years ago, FCR/FNC being. So, these chemo drugs that Debbie Stephens was talking about heading are rituximab (Rituxan), which continues to be used broadly. And then some people had BR, bendamustine (Bendeka or Treanda) and rituximab, but just quickly, Dr. Stephens, just in a few seconds, are you using those at all anymore?

Dr. Stephens: I would say I rarely use those drugs, the people who I choose to use the FCR regimen on, are people who are less than 65 years of age and very good health and have low risk CLL. And we define low risk as in a mutated IGVH and a deletion 13q, and so only people who I think can tolerate it and have the best chance of having a really long remission.

Andrew Schorr: Okay. Okay. And I'll just mention Carol, you and I both developed [second cancers](#). You, sarcoma, and me, some myeloid condition called myelofibrosis. We don't know whether that earlier treatment had led to a second cancer. I know cancer patients can develop second cancers anyway. And Dr. Ma, just briefly with you, do you use the FCR or BR at all?

Dr. Ma: To be honest, I have not used any of those in the past year, especially with the pandemic. I'm really concerned about the immunosuppression with the immuno/chemo combination. But if we're not in the pandemic I'll agree with Dr. Stephens, that those patients who are the low risk CLL can still consider immunochemotherapy as a potential option, although most patients opted to use the private therapy and exactly because of the potential concern for long-term side effects.

Andrew Schorr: We've covered a lot of ground, Carol, and our doctors. Let's go on and talk about clinical trials. We have so much to talk about. Dr. Ma is back with us, Dr. Stephens. I hope everybody had a good break. Did you walk the dog? Did you get a sandwich, wherever you were? Michele, you and I have both been in clinical trials and that's what we're going to discuss now, first of all, are you glad you did it?

Michele Nadeem-Baker: I am very glad I did it. And you know what? I would do it again. What about you?

Andrew Schorr: Yes. I mean, I was in the phase two trial in 2000, long time ago for FCR, we talked about, and had a 17-year remission. 17 years without any CLL treatment. Wow.

Michele Nadeem-Baker: That is incredible. I am hoping I will be able to say the same, but any number of years is great, right? To be in remission or partial remission before you have to go back on treatment. And even in this short time, there were so many new drugs out there that have been approved. And also, those in research. I was amazed.

Andrew Schorr: They wouldn't be approved if people hadn't been in trials. So, I bet Dr. Stephens and Dr. Ma would give all of you who've been in a trial a big hug for doing it, because

they can't develop new medicines unless you consider being in the trial. Michele, let's do a quick poll. So, Jordan, pop up the poll to find out whether our audience here, are you interested in participating in a trial, have you been in one? And let's see what people say, you and I have been in them. Some people are hesitant. Let's see. Yes, no. Are you in one now? Have you been in one in the past? I'd be curious to see.

Michele Nadeem-Baker: I'd love to find out how many others have been on them.

Andrew Schorr: Yeah, let's see. All right. Do we have any results there yet, Jordan? Everybody's thinking about it. There we go. Okay. Yes. Are you interested in being in a trial? The doctors are cheering. Okay. That's how they advanced their research and you and I have been in one in the past. And 16%, no, I know we've been flooded with questions, folks, about trials. So, we have a lot to talk about. So first of all, you mentioned that... I think it was you Dr. Ma, I can't remember. We talked about those two groups, the BTK inhibitors. And we talked about the venetoclax direction or maybe you mentioned it Dr. Stephens, but about, can you, if you take one from column A and one from column B, stick them together, is that better? So, who wants to talk about combo therapy combining the classes first? Debbie, do you want to do that first?

Dr. Stephens: Sure. A lot of the clinical trials that are ongoing right now are looking at the fact, we have these great drugs, BTK inhibitors, we have these great drugs, Bcl-2 inhibitors, like venetoclax. And if we put them together, are we going to do even better? Meaning can we get even deeper remissions or maybe is this one of those ways that we can make those continuous therapies? Like ibrutinib or acalabrutinib, not a continuous therapy. Meaning if we add venetoclax to it for a certain period of time and get you into a deeper remission, is it possible, maybe we then can stop the ibrutinib or acalabrutinib altogether. There're also some other combinations, just newer drugs, looking at, can we add drug B to ibrutinib, and then maybe it causes a deformation so we can stop it. So just as we talked about, right now, these drugs are meant to be taken continuously, but there's so much research going on to find ways around that. So, you can still get the benefit from the drug, but maybe not have to take it forever. And that benefit could be in side effects or costs out of your pocket, or out of your [insurance](#) pocket.

Andrew Schorr: Dr. Ma, I have a question about BTK inhibitors. So, you mentioned earlier, we have a lot of experience with ibrutinib or Imbruvica, then came Calquence or acalabrutinib. So that's kind of earlier BTK inhibitors. I know that there are two companies, both Merck and Lilly

that have a new generation of BTK inhibitors. I don't get it between covalent, non-covalent. We don't have to get into that, but would these have fewer side effects? And where do they stand in trials? A new generation of BTKs.

Dr. Ma: Hi, thanks. So, the ibrutinib and the acalabrutinib, and there's another one, zanubrutinib (Brukinsa). So those are first and second generation BTK inhibitors. They work very similarly, a little bit different in the side effect profile. However, as some patients have been on it for a number of years, they could develop resistance to that treatment. And the resistance are commonly associated with a mutation in the BTK molecule that are making the finding of those inhibitors not effective anymore. So, the third generation BTK inhibitors are designed to try to overcome resistance to the earlier BTK inhibitors. And currently there's no the approved drug yet, but they're all ongoing clinical trials. So, for example, one of them that looks very promising is called LOXO-305, which you called non-covalent BTK inhibitor, that has been shown they have already treated over 300 patients and there's a recent publication that's shown that it could potentially overcome resistance.

So even for patients who failed prior BTK inhibitors, they might still able to respond to that. So, there's the very exciting next generation treatment.

Michele Nadeem-Baker:

I have a question on that doctor, what about the side effects that you're seeing with LOXO-305? Are they more profound? Are they the same or are there less side effects?

Dr. Ma: So even though these agents are not designed to minimize side effects, but the data actually looks very promising. So, so far, the published data is showing that the side effect profile are very mild, even for the ones that are very typical for other BTK inhibitors. We're not seeing nearly as much. So potentially hopefully it has a potential to become a very effective alternative treatment, but also well-tolerated treatment.

Dr. Stephens: And I, sorry to interrupt you, we have a clinical trial with the Merck compound going that's called ARQ 531. And I can say from my experience of my patients, it's very well tolerated, and head-to-head studies yet with the other BTK inhibitors. But I would say in my experience, it's better tolerated.

Andrew Schorr: And we could get to the same place where you say with a new BTK inhibitor, can we combine that with a venetoclax regime, to get a fixed duration? And one of the things we

haven't talked about and we'll talk about later on is about cost. So that was very attractive. When I had FCR, I went through my treatment, and I was done, and I didn't have any expenditure for medicine. And so, with these oral medicines ongoing, depending upon your insurance, that's copays, et cetera, something to think about. So fixed duration in this age of expensive medicines is important. We're getting lots of questions about even participating in the trial. So, Michele, you have a wonderful doctor, two wonderful doctors at Dana Farber, Matt Davids and Jennifer Brown. I have a lot of confidence in them. I had my MD Anderson doctor, Dr. Keating, and I felt I trusted them, but all of us in the back of our mind are concerned about the safety. Efficacy, of course and safety. So, Dr. Stephens, when I'm in a clinical trial and I'm on the fence, what do you talk to me about, monitoring and safety so that I am protected? Because the last thing I want to do is open a Pandora's box of problems.

Michele Nadeem-Baker: And before starting, one other thing on those concerns that I know some of us have, on a clinical trial there is this viewpoint sometimes, does that mean if I'm on a trial on a placebo or the drug that's being tested, and how does that work? So, that we can know...

Andrews Schorr: ... Am I getting the good stuff? Ha.

Dr. Stephens: Yes, I think that's a very common question about placebo or not. And there are very, very few clinical trials in CLL that would have you getting a placebo or a sugar pill. If there is a situation where you would be getting a sugar pill, that would be something that would be considered the standard of care, anyway. So, for example, if you're on a study for watch and wait and we were going to try to see, should we treat early or later, you might get a sugar pill because that would be what you would standardly be getting anyway, which is essentially no drug. And that would be upfront. people are not going to slip you a sugar pill unbeknownst to you. It's going to be told specifically, there are half of the people that are going to get a sugar pill and half of the people that'll get the active drug.

But again, that is really rare. And you don't have to, so you can listen to your doctor's explanation about these trials. And if it sounds scary to you to get a placebo, then it's not a good trial to enroll in.

And so, talking about safety it is actually very much your doctor's concern as well, that you all are safe. There are several steps that the drugs go through even to get to a clinical trial, they're

tested, first just in the lab in cancer cells. And then they go into animals for testing. And so, we can get an idea of the safety profile. And then even in a phase one study, and a phase one study means the first time we've used drugs in humans, what we actually do is we actually start at a really low level of the drug typically.

So we start at a level that was less than what would have caused toxicity or side effects in the animal models. And so just to make sure there's no difference between the side effects, maybe that we're seeing in the animals and people when we transition into clinical trials and people were very, very cautious. And so, a phase one trial is the only trial where it's possible you might be the first person to ever get the drug. But of course, on even a phase one trial, there's only one person, that's the first person to get the drug. And so, phase one trials now are actually quite big. And so, you may enroll in a phase one trial, which is the first time it's been received in people, but you may be the hundredth person that's received this drug. So we have safety information about the first 100 patients.

Clinical trials get shut down very quickly if there is any concern that there may be a safety issue, because we certainly... The purpose of these drugs is to help patients and if we feel like there's any reason why we have concerns that they're harming patients, they're going to get shut down and make modifications to make sure that it's safe for people.

And then, there's this whole other lot of the clinical trials, would be phase two, which means we've already tested the safety of the drug. And right now, in phase two, we're trying to see how well it works. So how likely is it to put you into remission? How much of your side effects does it take away? Those are the kinds of questions we're answering in a phase two trial and a phase three study is even further along.

And that essentially means that drug... Usually people are randomized to one of two things, either the new drug, which already has been through phase one and phase two. So, we know it's safe, we know it works and we think it might work better than what we have now. And so those phase three trials randomized you to the new drug, which has already been pretty heavily tested versus something that you could actually get a prescription for something that would be considered standard of care. So, there's-

Andrew Schorr: No sugar pill.

Dr. Stephens: No sugar pill. So, there's just lots of different varieties of clinical trials. And so, I don't want the words clinical trial to be scary because that means so many different things. And your doctor should be explaining these in great detail. You should receive something called an informed consent, which is usually actually frankly, a little bit overwhelming book of information about all the possible side effects and all the things that you're signing up for. You should have a trial coordinator that you're able to call at any time for questions. And so, really, I think, you never should be wondering about questions, just ask your doctor or your trial coordinator if you have questions about the drug.

Andrew Schorr: I want to follow up with Dr. Ma. Dr. Ma, you saw that a big portion of our audience is interested in trials. So, if they were your patient, are you initiating it? Or if they say, "Hey, Dr. Ma, I heard that there's a trial about a new BTK." Or whatever, what's the next step? How does it go?

Dr. Ma: So typically when the patient is at a stage where they require treatment, that's when we talk about [treatment options](#), and I'll often include the clinical trial as one of the treatment options. And so that all depends on what clinical trial we have to offer. And usually, we try to select carefully because there are so many clinical trials out there, right? So, each investigator in each institution will have a profile of clinical trials collections. And we typically choose carefully in the ones that we probably believe... That will have probably the best to our patients' interest. And we'll talk about those options. And then we'll talk about the pros and cons of each standard of care versus clinical trial. And I'll help the patient to make that decision. Sometimes the patient may bring to me, there are clinical trials they heard about that we may not have here to offer, and it could be exploring other institutions as well. Because there are so many trials out there. So, there are always some, especially for patients who are becoming refractory to some of the standard treatments, they might be exploring more other options as well.

Andrew Schorr: Okay. I do have a question for you in Chicago, major city, big medical centers. So, if you believe there's a trial across town with one of your peers that you don't have at your place, would you still recommend it? And sometimes we wonder, are the doctors going to tell us everything that's out there?

Dr. Ma: If I believed there's a [clinical trial](#), that's absolutely the best for the patient, which I don't have, I will have no hesitation in recommending that.

Dr. Stephens: And I agree with that. I'm in an island of no cancer centers anywhere near me. And still, if I feel like something is best for the patient, I will send them – I've sent patients to Seattle, I've sent patients to LA, I've sent patients to Chicago and, in the background, I'm trying to figure out how do I get that trial open at Utah?

Michele Nadeem-Baker: So, speaking of that, Dr. Stephens, when the trial opens, so that means that, okay, I'm in Boston, but you have a trial in Utah. You're the lead investigator. Can that be done where I live?

Dr. Stephens: Yeah. well kind of, so typically if the trial is open at my center, people will have to get any medication that's dispensed at my center. Although during COVID, there was some exception to that because we were able to mail out a lot more than we would have been before COVID. So typically, there are certain assigned days that you need to be there for the clinical trial. And so, you could come in, get the medication, the treatment, or evaluation, whatever you need to get and then go home. And that's an important discussion to have with your doctor. Whenever you enroll on a clinical trial, is what is paid for by the clinical trial. Because for me, since I live in an area where patients travel from many miles just to come to a cancer center, when I'm doing certain clinical trials, I'm able to provide money, reimbursement for travel.

So for example, reimbursement for mileage. And, if somebody lives in Boston comes to Utah, that's a lot of mileage. So, you could get probably enough money to pay for a plane ticket, to come out, to get on the trial. And so that's an important thing. And Andrew mentioned the cost of medications. That's one thing that's often a very big benefit of participating in a clinical trial, is very often the drugs are provided for free. Now that's not always the case. So that's something you need to have a discussion with your doctor about exactly what is provided on the trial. But that's one really big benefit to participating in the trial as well.

Andrew Schorr: I wanted to jump in and just mention a couple of things. We'll be publicizing on Patient Power of a very topical trial now, that the Leukemia & Lymphoma Society is doing, which I've enrolled in, assessing post COVID vaccination, your level of immunity. So, we'll stay tuned about that. But I have another whole area to ask you about first, Dr. Stephens, and that is [CAR T](#), chimeric antigen receptor T-cell therapy. My friend, Larry Saltzman, who happens to be at Leukemia Society, kept not doing so well and some of the drugs, they didn't last for him. So, he ended up a year ago having CAR T and here he is, he was not doing well, and now he's doing pretty well. So, what about that? Is it promising for CLL, Dr. Stephens?

Dr. Stephens: Yes, this is the really exciting new treatment. And just so everybody understands what it is, essentially it's a treatment that uses your own immune system, kind of modifies your own immune system to help your own body attack your CLL cells. So essentially you go in, you get blood collected, we take your T-cells, which is a really important part of your immune system in the lab. We – essentially, it's like training an army. We put in a vector that makes your, those T-cells really want to go after CLL cells. And then we essentially give you some additional chemotherapy to knock the immune system down a little bit so that it won't reject those cells when we put them in, then we put them back in and the cells go to work. So, we've essentially trained an army of your own immune system to help fight off the cancer.

So I think this is really exciting. It's still only available on clinical trials. Although I see really clearly that the companies who manufacture these cells are pushing to make this more of a standard of care, meaning hoping to get it approved by the FDA, sometime in the next year or two, but what's exciting about it, it's really kind of a completely different approach. We talk about, using these pills or chemotherapies to target something, or just essentially helping your body to fight itself. And so, it's a really, it's a different method. And so often when people have had multiple different types of therapy, maybe they've had chemotherapy with FCR, then they had [ibrutinib](#) and then they had venetoclax and they've relapsed after all of these therapies. I think this is a really exciting approach.

And another thing that's really exciting about it is, previously we would do more of something called a bone marrow transplant or a stem cell transplant. And that's a really involved procedure that not typically a lot of people that have CLL are not candidates for that aggressive of a procedure, just because most people, maybe they're older than age 65, or they have other medical problems that they just can't tolerate it. And something like a bone marrow transplant might be so toxic, it could potentially kill someone. And so, we have to be really cautious in who we recommend to, but in order to do a bone marrow transplant, your CLL actually has to be in remission. And so, if we can't get you into remission, then we can't do a stem cell transplant or bone marrow transplant.

What's different about a CAR T is you don't have to be in remission. In fact, majority of people are not in remission when they go into CAR T and, I think, it's a little bit too early to understand, what are really the long-term side effects. And it's not yet for people who are newly diagnosed with CLL, just because there are a lot of side effects when you stimulate the immune system, you can get a lot of side effects that can be dangerous. And so, it's not something we're widely

recommending to everyone by any means right now, but it's a very exciting, and it's really interesting, especially for patients who have relapsed or don't have any of our standard treatment options available.

Andrew Schorr: Right. That was my friend, Larry. From the CLL Society, Brian Koffman, many people know him. Brian went through the gamut, but here he is. Brian is helping lead the CLL Society, post CAR T. So, yay to that. People [living with it](#). So, Dr. Ma, just as we end this section, what do you want to say to our audience? We'll talk more in the Q&A, but about considering being in a trial with all the stuff you're talking about.

Dr. Ma: Right. So, I think from the overall CLL future point of view, we cannot move the field without testing new drugs. All of the wonderful new drugs we have benefited today are coming from prior clinical trials. So, participating in clinical trials is absolutely important for us to move the field forward. But from individual point of view, will this be of benefit? I think we should say that the clinical trial really provides the highest standard clinical care besides having the opportunity to get potentially new drugs. And the only reason why we typically run that clinical trials, is because we believe based on preliminary data. There's a lot of potential for those new drugs and new combinations. And there's a potential that it may potentially move the standard care, or maybe even better than standard care. However, we can say that without actually doing a clinical trial, to compare them side by side, for example, the phase three clinical trials.

So, it really, not only does it help to move the field forward, but is also beneficial for the individual as a high standard of care.

Dr. Stephens: And Andrew, I would make a comment. You said earlier, the doctors want to hug you guys that have been on clinical trials. Well, you know what, anybody who's ever received FCR should be hugging you because you're the one that allowed that. You're part of that, you're kind of passing it forward to patients that need that treatment in the future, because that's how drugs become approved. We do clinical trials and then they become available.

Andrew Schorr: Michele, as you, as we wrap up this section, as you hear it, because you and I are not cured. Are you excited for where these folks and their peers around the world are taking research?

Michele Nadeem-Baker: I want to thank both of you doctors and your peers, because without all of you doing your research and patients who are in clinical trials, we wouldn't be where we

are. And there's so much on the horizon for when we do relapse or for those who haven't been treated yet. And it just gets better and better. And then there is as, I think it was Carol said, the C word, the cure that we're all hoping for. And we keep hearing that probably during our lifetime. So, keep on going, thank you.

Andrew Schorr: That's kind of, your research puts you out of business for CLL. You can do something else -

Dr. Ma: I do want to add that to the biggest motivation for us to do clinical trials is really, we want to help our patients because we can see what a big difference it has made for our patient's lives. And there are still a lot of unmet medical need that we need more new treatments for our patients. So that's really the biggest motivation for us.

Andrew Schorr: Okay. Thank you so much. We can answer more questions about clinical trials during the Q&A, which is coming up shortly. Remember hit the Q&A button, our producers, Lizzie, Carey, Nate, they look at that. If you're on Facebook, put it in the comments and we'll discuss it. And somebody asked about CRISPR, we'll bring that up. There are all kinds of, we have some very smart CLL patients who read all the journals. They're like scientists. So, we'll go over that.

Okay. Well, lots more to talk about. I've been living with CLL 25 years, but Carol now is back introducing us with somebody even longer, right Carol? And Dr. Ma, thank you. We'll let you go. We'll be back with you shortly. So, Carol, who do you have?

Carol Preston: Well, I have someone who has my favorite first name. I have Ed Spuzello and Ed, if you would like to unmute and put your video back on, we can talk a little bit about what you have been going through. Yeah. I thought that Andrew was the champion at 25. Ed Spuzello, has lived with CLL more than 30 years. There he is. You've been very patient, and you've waited quite a long time and we appreciate it. So, love your name and love the picture that I saw of you with a bicycle, because that's something that I have taken up recently again. So, I really enjoy cycling. First and foremost, because your latest bout was just a few years ago. How are you doing today?

Edward Spuzello: Well, I'm doing great. I am off all drugs now, since last June, I completed my two years venclexta plan. And I went through [MRD](#) testing and I tested negative. So, I'm done for now.

Carol Preston: You are living life. And if I may be so bold, may I ask how many years young you are?

Edward Spuzello: 79.

Carol Preston: Fantastic. Fantastic. What a story. And there are many patients, patients fall into different groups. Some are, they go along with their community and colleges. They might see a specialist, but you have been a very, very active participant in your treatment and your care. First of all, can you recall off the top of your head, how many bouts of CLL you have endured? It's been a lot in the last 32 years.

Edward Spuzello: Eight or nine.

Carol Preston: Eight or nine.

Edward Spuzello: Including stem cell transplant and the clinical trial.

Carol Preston: And here you are today to share some information and your story with us. How did your diagnosis of CLL impact the way you approached treatment? Were you just trying to become an MD in a few weeks to learn as much as you could? How did it evolve?

Edward Spuzello: You mean back when I was first diagnosed?

Carol Preston: Yeah, exactly when you were first diagnosed and as you went through and you were relapsing and looking for new treatments, I mean, were you just, "I'll do what the doctor tells me." Or? It sounds to me like you were very active.

Edward Spuzello: Well, in 1988, when I was first diagnosed, no, I was not active in my own treatment. My doctor told me that I would take 10 months treatments of chemotherapy and hopefully then I would be in remission. And that's all I knew about it. I had started a business. I had a wife, I had a family, I had to work, so I didn't do anymore about it. I took the treatment, and I was in remission for 17 years after that. But then after that, starting in 2006, I was getting more into the thick of it because I was taken for toxin and these remissions weren't for long. And then I was headed to a clinical trial, and it was around this time that I started to get a lot more active in advocating for myself, reading about CLL, finding out something about CLL.

Part 4: Advice for Advocating for Your Own Care

Edward Spuzello: So when the time came in 2018, that I had had a big relapse, if you face still on that, what could I take, what could I do now? And Venclexta was on the scene. I hadn't known quite a bit about it and my doctors at Mayo Clinic are recommending that. And so, I was confident in that. And I took that pro to your treatment, like I said.

Carol Preston: And here you are today, looking fit, looking tan. And of course, Mayo has some of the finest CLL specialists in the country. So how blessed you were to be there, but you did become more active in your care, and it's not just in your care, but also in your lifestyle.

Edward Spuzello: Yes. Yeah.

Carol Preston: You are the picture of hope. Not just hope, but hope. So, tell us some of the things at 79 years young that you are doing today, and was there ever a time where you thought, "I'll just never be able to do these things again?"

Edward Spuzello: Oh yeah. Well, today what I'm doing, I do some form of exercise every day, at least for 30 minutes or so, sometimes longer. So, I'm doing aerobics exercising. I may be walking, some running and jogging. I may be doing strength training with exercise bands or machines. I may be doing swimming. I'm at my winter residence right now in Florida. We have a big pool here that I can swim in. We have a bike track; I could ride my bike. So, I'm doing all these things and I'm actually doing more now than I have previously. I don't know, I'm more encouraged now. I feel like I'm going to live longer. So, I'm doing good.

Carol Preston: Doing really well so far. I think we're all sending-

Andrew Schorr: Michele and I've been typing notes to each other. We love you, Ed.

Carol Preston: Yeah. I mean, you are my CLL superhero, which I was telling the group the other day. I said he is my CLL superhero because what you have been through, I'm sure we all have our ups and our downs, especially when we are in treatment, but you are an example of perseverance. And I know how you feel about the exercise because even during COVID, I've been participating in an outdoor parking lot fitness class, two bases apart, and it, just makes a huge difference. We're going to talk about mental health in our next segment, but-

Andrew Schorr: I was just going to mention something, point out, and I'll tell you again, later at the end of the show. So, Tuesday, folks, we have a program with two other CLL experts, Dr. Susan O'Brien, who was a disciple of Michael Keating, our doctor, and she's at UC Irvine and Matt Davids, who's one of Michele's doctors in Boston. And they're going to be talking about the long game of CLL, which Ed has definitely lived. And how you work with your doctors long-term to live a long life, which may be different therapies at different times. And have a plan. And probably you thought about that, Ed, if I do this, will it shoot me in the foot? So I can't have that. We're talking about trials; will I qualify for that trial? So, it's kind of a chess game a little bit, but fortunately it seems like for you, and as we're hearing today, there are ongoing options to live a long life and go swimming and go biking and go running and do strength training.

Carol Preston: So Ed, it also sounds, interestingly with the treatments that you've been on, it sounds to me like there are because of the research, the fast, the lightening pace of research, that you are going to have options. If in fact you should need options. In fact, you can return to venetoclax, but is that something that you have discussed with your docs? Like I know what I've been through and I'm a realist.

Edward Spuzello: Yeah. Well, when I was on Venclexta and my two years was coming up, sure, there was a discussion as to, well, if I stopped taking the treatment then especially, I probably was MRD negative, which I was at the end of that treatment, what's going to happen a few years down the road if I relapsed, can I take that treatment again or what? Well, they were confident that I could, yes, get right back on Venclexta but three or four years from now, we may be talking about entirely new drugs. So, I don't feel like there's any chance of me dying from CLL at this point, there will always be something there. For 32 years, there's always been something when I needed it.

Carol Preston: I think Andrew and I; we've had that conversation many times that our therapies can provide a bridge therapy. And one of the success stories, I think in the cancer story in terms of therapies developed lightning fast in the last five years. And in fact, it's getting to the point where it's tough to even keep up with the treatments. That's not the case with all blood cancers.

Andrew Schorr: By the beginning of the program Dr. Ma talked about, she explained to [newly diagnosed](#) patients, all of us today, it's a chronic condition. Now look, have some people passed away from CLL? Yes, let's be realistic. And I've known some along the way, but increasingly now we have many options. And so, if you can't cure it, can you live well with it? And Carol,

you're going to exercise class and Ed is zipping around from north to south and exercising and I am too. So, I'm very, very grateful.

Carol Preston: So Ed, I think, Michael Keating, Andrew and I at one time in our lives shared this CLL expert who at the time was just one of a handful now, with people like Dr. Stephens and Dr. Ma, we have dozens upon dozens of across the country, used to say, live with it and pass away from something else. That's where the therapies are going, that there's such success in the treatment. So, Ed, let me ask you about your message to others. What do you say to other patients, especially since we have a fair number of relatively new newly diagnosed or people on watchful waiting in our audience today, what is your message to them?

Edward Spuzello: Well, my message to them would be to not get overly excited about it, again, it's a chronic disease and that they will probably not die from this disease in this day and age anyway, but to be their own advocate and to learn all they can about, we've got internet resources like Google and so on and Patient Power. When I started watching Patient Power, I learned more in a few months that I learned in all the years before that about CLL, so it's the best source. And it leads you to research on your own to CLL.

Carol Preston: Ed, it's a wonderful story. We want to thank you for sharing it. And CLL, as you've said, can affect your mental health in a positive way and your daily living and Ed, in your case, a positive way, your relationships and as Andrew mentioned, and Dr. Stephens mentioned earlier in your pocketbook, so who can come to the rescue with that? Well, there are these wonderful professionals called oncology social workers, which I don't believe were available when I was originally diagnosed. And so, I want to bring back Michele and Jane Dabney to help us understand how patients can turn to oncology social workers like Jane and her peers, for advice and assistance.

Michele Nadeem-Baker: Thank you so much, Ed, for being with us, it was really delightful. And you put me to shame, really. You're like an Ironman at 79 with all of your different ways, you're exercising. And unlike Carol, COVID, because I was basically like a gym rat, because my gym closed, I let myself to get lazy and it's so hard to get back into it. And Ed, now you are my role model. So, I started a couple of weeks ago getting back into it. I'm on my own. And heck I don't know if I'll ever be able to be like an Ironman like you, but I'm going to try. And I challenge you to challenge me along the way, both of you and Carol. This has been great. And Carol, thank you for bringing up the whole oncology social worker issue. Jane, welcome back.

Jane Dabney: Thank you for having me. And Ed, I think you're my hero too.

Edward Spuzello: Thank you.

Michele Nadeem-Baker: Jane, there's so much to begin with as CLL patients on uncertainty and then add in COVID on top of it these days and us not knowing what's going to happen for us, with the vaccine, how effective it is. It isn't, do we or don't we do various things, see friends, family. So, there's all this initial fear. When you get diagnosed with CLL, then add in COVID, then add in everything else. And there's this term, social worker. Now, when I was first diagnosed, I have to admit, I had just gone through my mother having a very serious stroke. Social workers that came in to see her did something far different, I didn't even know there was such a thing as an oncology social worker. So, is this new, is this a new type of thing? And what do you do as a social worker in oncology for patients?

Jane Dabney: Thank you for asking and very interesting. I think our roles do vary across different settings and across the country and oncology social work is, is not necessarily new as a specialty. It may be that different centers value that role differently. So, I've been an oncology social worker for 20 years. So, it's not a new role, but I'll tell you a little bit about what we do. We, the way I see my role is really partnering with the patient and caregiver or family in their journey, their treatment journey. And we are part of the multidisciplinary team.

So, we're part of your treatment team with your physician, your nurse coordinator, your nurse practitioner, we're part of that team. And again, our roles can look differently at different centers, but we partner with you. We generally start out with an assessment to determine what your needs are and also to provide education coping with your diagnosis, coping with the chronicity of your diagnosis, and perhaps long-term treatment looking at where you are in this stage of your life. Are you a young person with young children trying to balance a job and home life and taking care of your children? Are you nearing retirement and having to make decisions about applying for disability versus just retiring or continuing to work? And how do you adjust to your work setting?

Michele Nadeem-Baker: Let's ask our audience through a poll. If they've met with an oncology social worker like you. Yes, no, but I'd love to see one. No, I've never heard of one. No. You know about, I'd say four years into my treatment, now this would mean I'd been on my journey

for about seven or eight years. At that point with CLL, I actually did learn about oncology social workers and started meeting with one. And it really helped.

Jane Dabney: Oh, glad to hear that.

Michele Nadeem-Baker: Yeah, it did. It helped me realize that I wasn't alone with some of the things I was going through, but they were specializing in blood cancer patients. Okay, here we go with our... Oh, look at this Carol, only 10%. Wow.

Carol Preston: Well, I'll tell you that, that really saddens me. So, we actually have a whole organization association of oncology social work that I belong to and is a great professional organization for us to get specialized training in working with oncology patients and also to share our knowledge with our colleagues across the country. So, I would encourage patients to ask their treatment team sometimes funding an issue at different cancer centers for hiring oncology social workers, because typically we're not a revenue generating profession in the hospital setting. So, I would ask your team about connecting with an oncology social worker, but there's also other ways you could connect with an oncology social worker and Leukemia & Lymphoma Society has social workers and staff who are there to answer questions.

There's also cancer wellness centers. The one that most people might be familiar with would be the Cancer Support Community. Also, some locations are also known as Gilda's club named after Gilda Radner. And then in my location in Cleveland, we have a place called the Gathering Place and what those are wellness centers for people with cancer and their family members, and usually provide support programs, educational programs at no cost.

Michele Nadeem-Baker: Oh, so what is the difference between what you would do for a patient and a psychologist? So, let's say patient doesn't even know there's such thing as an oncology social worker, they were brave and took the next step and started seeing a psychologist. Is there a benefit to seeing an oncology social worker in addition to seeing a psychologist or what would the differences be for someone?

Jane Dabney: What I can say is for social work, we were all masters prepared. We're trained to look at the person in the environment. So, we look at you in the setting that you're in. So as part of a family, as part of, if you're in school, part of a school, part of a workplace, in addition to having to deal with your diagnosis and we can help with a variety of things. So, sometimes we

are doing supportive counseling. In addition to referring to resources, resources that may be helpful to you.

Michele Nadeem-Baker: One thing I did learn, which I didn't realize is in addition to what you were just saying, and I know you briefly touched upon this, but on helping with financial resources, I've been learning that a lot of times the oncology social workers can help, then refer you to someone who can help lead you to the right places. Like you were mentioning different places that those could help. Some of them like LLS could also, they also help, financially or -

Jane Dabney: So Leukemia & Lymphoma Society is really a great organization focused on blood cancers. And they are one of the few organizations that offers financial assistance directly to patients in the form of copay assistance. Sometimes they have a travel grant that is available. They had a COVID grant, so they are a great organization to start with.

Michele Nadeem-Baker: And from what I they hear is just increased the amount that they're helping patients with. Because I know that it was limited, and it was probably in the hundreds versus thousands. And now, from what I understand, depending on someone's circumstances and situation, that they do go up to a much higher amount.

Jane Dabney: I can say all patients, I think it's up to \$8,000 for treatment. And that also will cover the cost of COBRA payments if you're on COBRA or your insurance premium and then certain copays. And during the clinical trial segment, I was thinking about, there can be a lot of extra expenses related to clinical trials that may not be covered by the clinical trial itself. There's another organization called Lazarex, that offers a lot of funding for travel and lodging for patients.

Michele Nadeem-Baker: Could you say that again? That organization?

Jane Dabney: Lazarex, it's L-A-Z-A-R-E-X.

Michele Nadeem-Baker: Okay, thank you.

Carol Preston: Jane, I think I mentioned at the top of the program that I have a friend in Eastern, North Carolina in Nags Head, who is an oncology social worker. And she's told me some very interesting things, increasingly people are trusting you and-

Jane Dabney: People talk so?

Carol Preston: Yeah. Trained, but then a lot of people might be leery at first because they think it's the department of social services, coming to do whatever DSS does, do good or, box them in. So, I'm just wondering, I want to keep everything positive, but what are some of the things that you hear from patients as you break through to gain their trust?

Jane Dabney: Well, I'll start out with we, over the years have done quite a bit of education with our clinical teams. So, they understand our role and understand how to introduce our services and talk about our services and normalize meeting with an oncology social worker. And the first thing I do when I'm starting out, working with a patient and family, is I ask them what their experience has been in working with a social worker, if they've ever met a social worker, or what do they know about social work. And then I explain that our roles, we have a lot of training in identifying mental health issues and helping with coping. And I explain what my role is in doing an assessment and that, that we can have different roles across different work spectrums. So, I explain what my role is and that usually helps them relax and realize that I am truly there to help. And that I'm not going to take anything away from them. So, I hope that helps to explain that we're really there to help.

Carol Preston: And again, as a quick follow-up, again, we're all about positivity and hope, but my friend also says that she helps with advanced directives, and talking about end of life. We hope for our CLL patients, as Ed says, just keep on going down that road of life. But that's, that's an important function too. And sometimes we're so caught up in the moment. We actually don't think what may lie ahead.

Jane Dabney: Right. Yeah. I address advanced directives with every patient that I meet. And what advanced directives are for those who may not be familiar, that's a healthcare power of attorney and a living will. And to me, these documents are a source of hope in that it gives you the control to [make decisions](#) about your own healthcare and to make them while you're healthy versus in a crisis situation. And the healthcare power of attorney is where you get to name someone to make medical decisions for you. If you're unable to make them yourself. So, a close family member or friend, and I would recommend talking with your team about completing those documents and you can find them online.

Carol Preston: I love how you've talked about it as actually an approach of hope. Because, Michele, I know you're experienced, certainly when you were diagnosed with cancer, when I was diagnosed, you feel as if you've lost all control and the name of the game is how do you regain control? How do you, in our cases return to some semblance of normalcy and living your life, working and so on. I never thought of an advanced directive quite that way. And so, Jane, I find that incredibly enlightening and heartening.

Michele Nadeem-Baker: You're right, Carol. When I go back to that, I really, even more so, wish that I had known there was such a type of discipline like yourself, an oncology social worker. Because at the beginning, it seems when you're diagnosed, I know when I was treated, I didn't even have anyone tell me, or until I was in treatment versus when I was diagnosed. And that I had such a critical time for CLL patients or any patient for that matter when they're diagnosed. But because we don't generally jump right into treatment, there are these years where you're living, you're going through what Carol had said. You start with, for some people that remains for many years for others, kind of, ebbs and flows. Now, do you usually see people or what would you suggest to people who are listening today about seeing someone, if they're not in treatment yet, or if they've just been diagnosed, how do you suggest that they would get help?

Jane Dabney: Again, I would recommend talking to your treatment team. You could also look at information at your cancer center and find out what the services that they do offer are and call directly for an oncology social worker. And some smaller centers may not have a social worker who is dedicated to oncology. So, reaching out to the professional organizations, Cancer Care is another one, they're based out of New York, but they service the whole country, and they have very well-trained oncology social workers.

Michele Nadeem-Baker: That's very helpful. I know where I go, they will only meet with patients if you're in treatment and within a year after treatment. And it's because of what you said, there aren't all that many that are at the centers. So, for people you need to advocate for yourself. Here's another case of that, Carol, where we have to advocate for ourselves. And if they don't have anyone at your cancer center, ask them where you are locally, if they can help you find one. And that's something else that an oncology social worker I guess could help with? Absolutely.

Carol Preston: Yeah. And You know what? For those of you in our audience today, we know that many of you are very active participants in your treatment and care. It is exhausting. We know how tight, and we know how exhausting it is when you hear the cancer word. We know how exhausting it is to seek treatment, to perhaps bounce from community oncologists to specialist. And it's worth it, but we know how exhausting it is. We've been through it. We'll go through it again. It is what it is. But what gives me hope, is the fact that there are people like the Jane Dabney's out there. And my friend, Janet Crieff, who are really looking at the patient holistically, we rely on our docs for the treatments. And we know that they love us, and they want to give us hugs. But this holistic approach is just critically important. So, Jane, I just want to thank you for the work that you do.

Michele Nadeem-Baker: Jane, it's been fabulous to hear this side and for patients again, if I had known about this originally, and Carol, you were saying, for you too, it could have really helped early on, versus thinking it's the end of the world or, for people who are just so motivated and stuff, and fast forward, and all of a sudden I was like, "Whoa, what am I supposed to do now?" It's fabulous.

Jane Dabney: Well, I certainly appreciate both of you for saying that. And I appreciate this opportunity to be on this program. Just a little plug, the month of March is National Social Work month. So, give an air hug to any social workers you know.

Michele Nadeem-Baker: I'll give one to you.

Jane Dabney: Thank you.

Michele Nadeem-Baker: And let's transition now. It's our final section. It's our final Q&A, right? Now we're going to go look at them. All the panelists will be joining us again, as we answer the questions we received in advance during the show. So, if you sent in questions and they have not been answered during the program, either in our Q&A function or by one of us, during the program, please stay tuned because we're going to be addressing those for the next 30 minutes. Wow. Carol and Andrew, I cannot believe it.

Andrew Schorr: Right, right. Again, just to remind people, get the Q&A button at the bottom of your Zoom screen. If you're with us on Facebook, go to the comments under where the video's playing, ideally, give us your first name and where you're from. We have lots of questions, but we have lots of experts. And I just want to say to Jane also, my mother-in-law is a social worker.

So, I am big fans of social workers and actually Jane, one of the questions I want to raise for you. And I'm on Medicare, like a lot of CLL patients. And so, while legislation may ultimately change it, we have some big co-pays for oral cancer drugs, but I know there are assistance programs. So, Jane am I right that a social worker... And sometimes there are oncology financial navigators, and some of the biggest funders too, to help us get some assistance, because I know I was put on one drug \$980 co-pay a month. So, am I right, Jane? You can help or maybe there's also a financial navigator at your center that can help.

Jane Dabney: Right. So again, there's some copay assistance programs, but also many of the pharmaceutical companies may have pharmaceutical assistance programs that you can apply for to get that drug at a lower cost or at no cost. One of the websites that I often use is needymeds.org. And that is really a clearing house of all of the programs that are out there.

Andrew Schorr: Right. We had a question from Denver on just about that. This particular patient is on Imbruvica. And so, depending upon where you are, whether you're on government insurance or commercial insurance or no insurance, whatever the laws vary, but both the company or various foundations may have assistance and someone like Jane and financial navigators can help you figure that out. You got to ask. And you may be somebody who's never asked for assistance before. Do not be ashamed. If there's assistance out there, you deserve it. Okay. So, who's got another question?

Carol Preston: I have a question. And Jane, we're sticking with you. Diagnosed 10 years ago, 35, still very young. And the question is whether there's a support group or a way to get in touch with other younger CLL survivors, there are lots of support groups, but people really like sharing similar experiences.

Jane Dabney: Absolutely. So, there are lots of different options and different ways to find them. Certainly, now during the pandemic, most things have gone virtual, which I think has actually helped quite a few patients access services. So, asking at your treatment center, if, if you don't have an oncology social worker at your treatment center, I would call the Leukemia & Lymphoma Society or Cancer Care to find out what is available to you. Also looking to see if your area has a cancer support community or something similar to that.

Carol Preston: So LLS or Cancer Care, two very good resources to get you started. And oftentimes you call one and you get leads to call other people and the CLL Society too.

Andrew Schorr: They do, they have support groups. And also, some of us have seen on our website, Carol, Heidi Yates, because she had COVID, Under 50 CLL patient. Her husband had it too, Heidi has a wonderful group on Facebook. So, look for the Under 50 CLL group on Facebook, Heidi leads it. She's a really cool lady. And Michele, you have a women's group too, right?

Michele Nadeem-Baker: Yes, I do. CLL Women Strong. And that's something for women who are diagnosed, dynamic and trying to still learn more about what they have, and sharing with each other what they've gone through. So that's all, this is so helpful for them. So, question that we just had that came in, has to do with night sweats. Now, Jenny, could you answer that about what causes night sweats and is this a sign that that you need to get treatment? Or is it something that people can have for a long time? I know I had horrible ones that felt like I was just one big night sweat all day long, like 24, seven.

Jane Dabney: I think we want to look more at the severity, as you mentioned, once in a while or rare a night sweat, we can get that reported. But if they kind of start to pick up and they're very drenching where you have to change your sheets and nightclothes and things like that, that gets to be much more severe and affecting your life. So definitely let your care team know if that's happening.

Michele Nadeem-Baker: And what does cause that? Night sweats. I'm going to ask that. I've never heard of what causes it. If people know I'd love to find this out myself too.

Jane Dabney: Yeah. It defers to the MDs in terms of the physiological reasoning behind it, but it can be indicative of the increase.

PART 5: Q&A with CLL Experts

Jennifer Boyer: Yeah, but it can be indicative of progression or increasing symptoms. So definitely be aware.

Andrew Schorr: Dr. Ma, so what is it? What causes night sweats?

Dr. Ma: I think it's the B symptoms related to CLL lymphoma are probably caused by cytokines. So those are inflammatory protein or factors that are released by the lymphoma leukemia cells that can cause symptoms.

Dr. Stephens: I think one thing that most people know is that the immune system helps your body to fight off infections. But what most people don't know is that it also tries to help your body fight off cancer. And so, the presence of these cells are what sets off that, what Dr. Ma was saying the cytokines. So, it's kind of like your body's way of trying to get rid of the cancer, but in CLL that process just doesn't work. And so that's why it's important distinction. If you're having night sweats and you have COVID most likely it's because you have a COVID infection, but if you're having night sweats and you have no other evidence of infection, there's a good chance that might be related to your CLL.

Andrew Schorr: Dr. Stephens. Here's a question that came in. We talked earlier about MRD, let's say minimal residual disease. So, the question came in, what is the median duration for being in an MRD negative state? So, talk a little bit.

Dr. Stephens: Yeah, that's a great question. And I think that's still emerging because it's pretty variable from one treatment to another. So, if we're talking about venetoclax, we're still having there on a lot of the studies people actually haven't reached yet the median duration of having an MRD undetectable remission, and so more to come on that, and again, it's variable depending on the type of treatment you receive. And again, it's a little bit rare to have that if you're receiving ibrutinib or acalabrutinib.

Carol Preston: So here's a question that came in and it's maybe under the heading of which camp comes first, the chicken or the egg. Let me put my readers on if that's okay, folks. Is a hematologist oncologist, a hem-onc as we like to say, is that okay? Is that okay to say as a CLL specialist or should I look for a CLL specialist? Or must I seek out a CLL specialist in my early stages? Or can the hem-onc or the hematologist oncologist monitor me for now? It's a mouthful. Dr. Ma what is your thinking?

Dr. Ma: So all of your CLL experts are a hematologist oncologist by training, but what's different between us and the community oncologist is that a community oncologist see all cancers. So, they're treating really the bread and butter of all of the cancers, but because they're treating all cancers, they do not focus on one area where we're in the academic centers where we're focusing on certain disease areas. So, for us, CLL is our expertise.

Carol Preston: Do you find as a CLL specialist that you may be several months or even a year ahead of the community oncologist in terms of what you may recommend for treatment? I don't ask it as a loaded question, but when you're laser-focused on one disease, is that a possibility?

Dr. Ma: Yeah. Yeah. I think it's perceivable, right? Our community oncologists are great. They're wonderful oncologists, but because you have to take care of so many cancers, so it's not possible for them to be up to date on all everything. Whereas we are the ones that are actually doing more clinical research, so we can be more looking to the future. So definitely I think there's also more clinical trial opportunities when you're coming to an epidemic center. In addition to the expertise and the knowledge.

Carol Preston: We've had a few people ask a few questions regarding how they know if on a clinical trial, is it better to be on more drugs in combination, a few have asked about three drug combinations, which are happening in clinical trials versus two, so that you hit the CLL from many sides, or does it add anything to it to have the three different options? Like someone was on a trial, they were talking about, I believe it was a monoclonal antibody, CD20 monoclonal antibody.

Dr. Stephens: If we knew the answer already, we wouldn't be doing the clinical trials. And so that's exactly the purpose of the clinical trials, is to figure out, would it be better to say first you get ibrutinib, then you get Venetoclax then you get idelalisib. Or is it better to just get them all at once and cause a deep remission? And so that's exactly what the clinical trials are trying to figure out. And another important thing is, all these drugs work really well, so it's possible maybe both work really well, but maybe there's a difference in side effects. And so that's also important too. And so that's why we're doing the clinical trials right now.

Andrew Schorr: Here's a question. I'll start with Jenny. So, Jenny, so let's face it. There are people out there who are CLL patients who've had COVID, like I've mentioned in my friend Heidi Yates, she's had COVID, her husband too. So, what's the story for people who've already had COVID and have CLL, or they have CLL, and they get COVID. So, any special case their communication with you as a nurse practitioner, I've got these symptoms earlier treatment. What do you want to tell us?

Jennifer Boyer: I would definitely say both threshold, if you have any suspicion of exposure or any questionable symptoms that you're not sure about, let your care team know so that you can

be tested early definitely. And, yeah, I think there's, as Dr. Ma mentioned in the earlier segment, unfortunately, a lot of question marks still, but if you've had COVID, still continue to be careful and take as many precautions as possible, we're just still not sure about re-infection and things like that. So just still be careful.

Andrew Schorr: Well, so Dr. Stephens, so we're wondering about immunity, and I know Dr. Mato one of your peers from Memorial Sloan Kettering, he had come out months ago with that study that showed the high mortality of hospitalized CLL patients with COVID, that scared all of us. I know there's more recent data, but what about the range of treatments you have for CLL patients, should we develop COVID?

Dr. Stephens: So that's an important point that the data that Dr. Mato published was really very early on in the pandemic and the data he's referring to, showed a high rate of death of CLL patients who contracted COVID. And I still think it should be taken very seriously. However, we have developed a lot of new therapies to treat CLL or to treat COVID and they might be available to you if you develop COVID. Those are things like antibodies that try to clear the COVID virus out of the body system. Those are things like convalescent plasma, so using someone else's plasma that has already had COVID or has been exposed to try to boost your immune system. And so, there's a lot of treatments. The thing I will say specifically about the antibody treatment, they're pretty new and they're not widely available yet.

And so for example, my state, and I'm sure most states also have this, there's a set list of criteria you have to fit within in order to get these antibodies. And so, the sooner you know that you have COVID, the sooner is good to reach out to your doctor because some of those treatments are only available if you've had symptoms for less than seven days. And so, some people don't even know that they have COVID for over a week. And so, some of those treatments might not be an option at that time point. So just be aware of your symptoms and make sure you're reporting to your doctor to see what's available to you.

Carol Preston: We're getting a lot of questions about testing and which tests are most beneficial and which ones should we have to determine whether we have CLL and type the CLL. But one test that doesn't seem to be used anymore is the ZAP-70. And I'm wondering Dr. Ma, is it no longer [inaudible] I need some water... as a prognostic indicator. You're not using it anymore.

Dr. Ma: We're still using it, but ZAP-70 is very technically challenging. So, a lot of the centers, especially local labs really do not have the capacity testing it, because it's a marker that's in the cells rather than the other markers that are actually on the surface of the cells. So, because of the technical challenge, the results might not be as reliable, it all depends on the labs expertise. So nowadays the one that is more reliable is the IGHV mutation and it's a genetic study and the results there's much less variability. And that really is kind of replacing ZAP-70. Because ZAP-70 is really kind of a surrogate marker for IGHV mutation status. So if you're able to gather mutation analysis, then that's probably a more reliable test.

Carol Preston: Dr. Stephens, we have a question from Churchill, Tennessee. How do you know when it's time, in [watch and wait](#), when it's right to go on to treatment?

Dr. Stephens: Good question. And this is something I try to remind my patients about every time I see them, if they're on watch and wait, because this is part of where the art of medicine comes into play because we have some criteria, but just because you meet the criteria, maybe there are some special circumstances that would say we need to do treatment a little earlier, a little bit later, but standard criteria would be these things we're talking about the B symptoms. So fevers or drenching night sweats that are not in the setting of an infection that are happening frequently, multiple times a week, weight loss. And this is unplanned weight loss of 10% of your body weight or more in a six month period of time. There's also indicators on your blood work that might indicate that you need treatment. And that might be that you're becoming more anemic.

And so that means that there's a measurement called hemoglobin or hematocrit that we follow. And if that starts to fall, it might indicate you're getting closer to treatment. And we look at hemoglobin less than 11 as something that you're in the range where we would consider treatment. Assuming that is related to your CLL. We also look at cells called platelets, which are the cells that help your blood clot. Whenever those platelets get down below a hundred, it might be time to consider treatment. Now with both of those that hemoglobin and platelet, there's also other things that could cause that. And there's something where your immune system kind of gets out of regulation and starts attacking those cells. Like your immune system thinks that your platelets and your red blood cells are like bacteria and starts getting rid of them. And that is treated in a slightly different way than treating fully the CLL.

And so your doctor's going to do some extra tests to sort out which one of those is the case. And then there's the big void of fatigue, which I think is the hardest thing about CLL. And that's because that affects so many patients. And some people say I'm just so tired. And I think it's my CLL. Could it be time to treat my CLL? And it could be, but the reason why I say it's a really hard thing is because there's a lot of other things that can cause fatigue. And we just want to be absolutely sure as doctors that we're making sure that you don't have one of those other things. For example, could you have low thyroid levels in males, could you have low testosterone levels that could be contributing or is there some other medication that you're on that's causing fatigue?

Because I think that the least satisfying thing for my patients and for me, I would say is if we think that the fatigue is related to CLL and then we start the treatment and maybe that fatigue wasn't related to CLL and this, so you still have fatigue. And then you have side effects of treatment on top of that. And so that's a little bit frustrating. And that's why I think fatigue is probably one of the most frustrating things for patients and for doctors, because it's really hard to sort out is that really related to CLL? And does it indicate that it's time for somebody to be treated.

Andrew Schorr: Good point. Here's a question we got in from Paul in Austin, Texas, and it's about liver enzymes. And Dr. Ma, I'll pose this to you. So Paul says, if there are no other causes and I have elevated liver enzymes, could it be the CLL? And would CLL treatment, if successful take care of it? And if you simply have elevated liver enzymes, is that a reason to start CLL treatment?

Dr. Ma: I have to say that even though CLL can involve the liver, but extremely uncommon to see liver enzyme epidemiology from CLL, so that if you have liver enzyme abnormality, the first step is to figure out why, because there are so many other potential causes of liver enzyme abnormalities, and also you can do imaging to see either some unusual involvement in the liver. Like sometimes people can have big focal involvement from CLL, although you cannot assume that it's CLL, you have to biopsy that to confirm. So, I'll say it's extremely rare that my patient would protrude them because of liver enzyme issues. Most of the time the liver enzymes are caused by other other issues. Allergies.

Carol Preston: Jenny, I'll pose this one to you about diet and I have a little bit of a tag question to go with it because the question has to do with what is the best nutrition and supplements

advice that we can be given, but part and parcel with that is there's been a lot of discussion and writing about sugar. Should we cut out sugar from our diets? Does it feed the cancer cells? So, I'm wondering if you would take that one.

Jennifer Boyer: Sure. Yeah. We tend to recommend just an overall healthy diet, most supplements you can get from your diet and that's how we would suggest going about it at least in the beginning, unless it's determined that you are especially deficient and you know one thing, and then perhaps supplementation with the advice of your care team could be necessary. But yeah, I think it's like a moderation, lots of good produce and vegetables and protein has really what's recommended just kind of an overall healthy diet.

Carol Preston: And Dr. Ma what about the sugar issue? Is that an issue or is that misinformation?

Dr. Ma: I think we can say cutting down the sugar is good for your general health. There are a lot of the laboratory research showing that cancer cells in general, are more relying on sugar for energy, compared to other molecules. So theoretically cutting down the sugar may help, but just remember that whatever you eat, your body will convert it to sugar. So even if you've been eating sugar, your body has an underlying mechanism to convert those to sugar for processing for a nutritional absorption. So, it's not just simply sugar itself in your diet. And I think cutting down the sugar is definitely help for your general health in general. Yeah.

Dr. Stephens: I feel like I get this question a lot from my patients and some of it's based on, there were some data looking at mice with leukemia and they found that if they did not give any sugar to the mice, that the leukemia in the mice would die, but guess what else died? The mouse. So, sugar is important for cancer cells, but it's important for your brain too. And so, I often say anything that sounds like a really strict and very regimented elimination, diet is probably going to be affecting other parts. You know, maybe it helps your cancer, but it's probably going to cause some adverse effects on the rest of your body too.

Dr. Ma: So we paired some questions for Ed, but ed had to leave. He's probably out running a marathon or out swimming 20 miles on the beach or something or doing pushups. But in the meantime, we do have a pretty detailed question. So, I'm going to read it. So I don't miss anything here. Dr. Stephens, we have someone who wrote in, their husband has CLL. His

brother has Waldenstrom's and the first cousin that died from CLL. Should their children be concerned? And if should they be tested?

Dr. Stephens: I think this is also a great question that I get a lot. And we have a really nice database in the state of Utah that allows us to study multiple different family members and patients that have cancer. And I've worked with one of the more basic science, genetic researchers and looked at families that have kind of that pattern of different kinds of blood cancers in it. And the hard thing is that there's no one specific genetic mutation that leads to these family linkages of cancers. So, I think Dr. Ma mentioned, in breast cancer, a lot of people have heard of like the BRCA gene, which is very common, and we can just do testing for it. And it's not the same for CLL patients because there's different genes in different families that might lead to this risk factor. We do know that there is a risk of about if you have a first-degree family member, parent, sister, brother, or children that you're about seven to eight times more likely to get CLL.

And so there's clearly some evidence of family linkage, but it's just not quite as clear as other cancers. And then the screening question I think is really important because the cancers that we screen for, so think about breast cancer, colon cancer. Those are cancers that if you catch it early, it makes a big difference in survival. Sometimes I feel like CLL is the cancer that is caught too early because a lot of times people get really anxious once they know they have CLL, even though their health is the same before or after they get diagnosed with CLL. And so, it may be that their family members might be at a higher risk, but if they're having no symptoms and their blood tests are completely normal, then I wouldn't pursue a screening specifically for CLL or other blood cancers, because the fact is if they're not having symptoms or other problems, we're not going to recommend treatment right now anyway.

Andrew Schorr: Okay. I just have a question for Jane before we have to go. So Jane, patient wrote in and she was saying, she's from, let me see. She didn't say, but she said she has fatigue. Doctor says, it's not your CLL. We already talked with Dr. Stephens about, could be many different causes. But it also could be depression, which during the pandemic could even be worse. So how do you sort out with people, whether it is depression that could be making them just not feel like they can get out of bed, for example,

Jane Dabney: Right. That's a really good question. And it can be difficult to tease that out. I would say if you don't have access to an oncology social worker, well, first of all, ask your doctor

for a referral to an oncology social worker. If you don't have access to one, I would call one of the organizations like Leukemia & Lymphoma Society, or Cancer Care, and talk to an oncology social worker over the phone to help you tease that out. Also, the Leukemia & Lymphoma Society has great handouts on fatigue that would be available to you as well. If you're truly having difficulty getting out of bed and your physician says that it's not related to your diagnosis, it could be more serious, and it could be depression. And so seeking support either from a social worker. Also in your own community, there could be therapists that you could talk with to help tease that out as well. It doesn't necessarily have to be someone from your treatment center.

Andrew Schorr: Right. The advocacy though, there are some doctors, and you know it well, who poopoo you bring up some symptom, whether it's particular say, "Oh, don't worry about it." So what would you say to our audience as we close, about being an advocate for yourself, to make sure you get an answer.

Jane Dabney: Oh, absolutely. Well, I would say to all of you who are on this call, you are your own best advocate and taking the step to engage in programs like this is very important. So just keep at it. And if you're, if you're not getting the response that you're looking for from your team, seek it out in your community, or again, through one of the national organizations. Also, my professional organization, Association of Oncology Social Work. On our website we have a section for patients and family members where you can locate an oncology social worker as well. So, you can check that out too.

Carol Preston: I know we have very limited time left, but Martin from London, we're delighted to have somebody from across the pond, who is in watch and wait, was diagnosed 15 months ago. He says he's had no prognostic information. And so, his question is, should he be asking his doctors to do some tests beyond determining that he's on watch and wait, anybody want to feel that one? Okay.

Dr. Stephens: Yeah. I do these prognostic factors, when people are diagnosed, just because I think it helps the patient to understand maybe some idea of what to expect in the future. Like could you be one of those people that maybe is never going to need a treatment and you need to put CLL the furthest back in your mind that you can and just go on living your life, or are you a somebody who's at higher risk? And so, you need to be followed a little bit more closely by your doctor. Maybe you need to make plans that say you're retiring soon, and your insurance might

change. And you want to make sure that you have an insurance that covers good medications because you're expecting likely to need to have treatment. And so I think it's important, but you is it going to change anything right at that time point? No. And so, some doctors choose not to choose, choose not to do those until a time point where somebody needs to be treated.

Andrew Schorr: Okay. We've covered so much ground. I want to thank everyone and get a closing comment from everyone. So I wanted to just go round robin for a second first with our medical experts. If you have just one sentence, you want to leave our CLL audience with, whether it's a pop or advice, what do you want to say? Jane, I'm going to pick on you first in Cleveland.

Jane Dabney: Oh, no.

Andrew Schorr: Yeah, yeah, yeah. But I mean, what do you want, an overriding message you want to say from your perspective as a social worker, what do you want our audience to hear?

Jane Dabney: That it's important to take care of yourself. And that doesn't mean just your physical body, but your emotional well-being as well. And please, don't be afraid to seek out help and to ask for help and ask for a referral to those who can help with your emotional wellbeing and you're coping with your diagnosis.

Andrew Schorr: Right? Right. You're not alone. Thank you so much, Jane, for being with us from the Cleveland clinic, you have a great center there. Thank you so much.

Jane Dabney: Thank you for having me.

Andrew Schorr: And then Jenny, from the Lurie Comprehensive Cancer Center at Northwestern, our partner today, what about you a final comment for your patients and those worldwide who are with us?

Jennifer Boyer: Well, I want to say that your whole team is here to support you and help you in your journey. And there's so many exciting things with CLL that we love to collaborate and discuss with you, so exciting time.

Andrew Schorr: It is an exciting time, Dr. Ma, also from the Lurie Cancer Center, a final comment you want to say to our audience today?

Dr. Ma: Sure. I'll say that it is important to learn to live well, despite your CLL. So, and understand there are a lot of treatment options available. You may need treatment, you may not need treatment. That it's important to continue on with your life.

Andrew Schorr: Right. There you go. And Debbie Stephens from Utah, final comment from you?

Dr. Stephens: I would say, just because you're diagnosed with CLL, you don't get to go to Vegas and gamble away your life savings because you're going to need them. We're doing a lot of good research. So you're going to be around with us for a long time.

Andrew Schorr: All right. Yeah. There we go. And Carol, a final comment from you. We've been around a long time, Carol.

Carol Preston: We have been around and I'm going to go out and buy a box of cookies. Because now I can eat all that sugar. I'm just kidding. Although it is lunchtime in the East. No, I'm just so hopeful from what I heard. And I'm so grateful for the information that allows me as a patient to continue having control, not only over the disease, but of my life as well. And I thank all of you for the work that you do.

Andrew Schorr: Yeah. Thank you. And Michele, a final comment from you?

Michele Nadeem-Baker: Well, Dr. Stephens, you spoke to me whether you realize it or not, about sometimes CLL is diagnosed a little too early and that I wish I had thought about that and just thought about continuing to live on with life and to enjoy each day as it comes, because guess what? We're all going to have many, many more, because there's so much research in the pipeline for us, which to me it's hope and I have less fear.

Andrew Schorr: Okay. Thank you so much to our guests in my cohort. We'll let you go. I have just a couple of notes for our audience. So first of all, I want to thank the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. They've been a great partner in this. And I also want to thank the CLL Society for letting people know we're going to link to their wonderful glossary that they have evolved the alphabet soup of terms and tests and everything. So, you'll see that on the Patient Power website as well.

Also know that Tuesday again, and it's listed on our events page on Patient Power. We have Dr. Matt Davids, Michele's doctor, and also Susan O'Brien, an old friend from UC Irvine talking about the long-term journey with CLL. So, take a look at that. I want to thank our sponsors, AbbVie, Genentech, and Adaptive, for supporting this program. Thank you so much for helping make this possible. And don't disconnect just yet, because as soon as Jordan pulls the plug on the Zoom feed, a survey pops up and that survey helps us so much in knowing how we did today and how we can do better in what programs, what topics you want covered in the future. All right, I'm going to say goodbye to everybody. I think I covered everything. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all. And the survey is next, please do it. Thanks.