Newly Diagnosed With CLL: What Do You Need to Know?

Susan Leclair, PhD, CLS (NCA)
Chancellor, Professor Emerita
University of Massachusetts, Dartmouth

Philip Thompson, MB, BS
Professor of Medicine, Department of Leukemia, Division of Cancer Medicine
The University of Texas MD Anderson Cancer Center

Andrew Schorr:
Hello and welcome to Patient Power. I'm Andrew Schorr. Stay tuned for just a wonderful discussion now for people who are newly diagnosed with CLL, What do I need to know? And I would say what does your care partner, caregiver need to know. I'm joined by a wonderful panel of experts. That includes my good friend Carol Preston, who was diagnosed with CLL. When was that, Carol? Back in 2006?

Carol Preston:
Correct.

Andrew Schorr:
Okay. And again treated again after that in 2010 after you relapsed. And then also Dr. Susan Leclair, laboratory science professor emeritus who joins us from Dartmouth, Massachusetts. Susan, welcome back to Patient Power.

Dr. Leclair:
Lovely to be here.

Andrew Schorr:
Thank you. And Dr. Philip Thompson, who is a wonderful CLL specialist at the University of Texas MD Anderson Cancer Center in Houston. Dr. Thompson, welcome back to Patient Power.

Dr. Thompson:
Thank you for having me. Delighted to be here.

Andrew Schorr:
Okay. Let's get started. I want to start with you, Carol, and then just go round robin, very quickly, what's a headline you have for our viewers, patients and family members, when they are newly diagnosed that you want to impart to them?

Carol Preston:
Get a second opinion with a specialist. Get a second opinion with a specialist.

Andrew Schorr:
Okay.

Carol Preston:
And the reason I say that, before you go on, is because I did not do that the first time, and as we get into the conversation I'm convinced there were ramifications from that.

Andrew Schorr:
Okay. We're going hear more from you about that. Susan Leclair, a headline for people newly diagnosed. You've corresponded over the years with so many patients, people ask you what's the headline you want to give them.

Dr. Leclair:
Take a deep breath and slowly exhale. This is something that you can take your time with. In a way, you have all the time in the world. This is not a panic. Carol's right. Go investigate the best person that you can have as a physician, but for your family and for yourself, take a deep breath and try and slow down.

Andrew Schorr:
Right. Susan remembers a woman who was a leader, a patient opinion leader on the Internet in CLL, Granny Barr Black Ritz, who was a big mentor to so many of us, and Esther and I spoke to her on the phone when I was first diagnosed in 1996 after we connected on the Internet, and she had two words for me. Chill out.

Dr. Leclair:
Yes, that would be what she would say. And that's I think the most important thing because, as Dr. Thompson will say later and I'm sure everybody else will, you can't be panicked in these conversations. You have to show down, take your time, and you'll be okay.

Andrew Schorr:
Dr. Phil Thompson, people come from around the world to see you and other MD Anderson physicians sometimes initially or the second opinion that Carol was talking about. You walk into the room, how do you start with people? What's the headline you would start with our audience now?

Dr. Thompson:
Well, I'd like to kind of echo some of the things that have already been said, and I would say it's very likely not as bad as you think it is. I think every patient that comes to see me, they've been told they have the L word, and they're terrified. They're starting to have images in their mind of when their funeral is going to be. And for the vast majority of patients that's not something that they're going to have to consider for decades, if at all, because of the dramatic advances that we've had in treatment and also because many patients don't even need treatment.

So I think that's the biggest thing in most first consultations I have, is just kind of going through the information and just being able to generally give people a lot of better news than they thought. And the other thing that I usually tell people is you're not going to have a bone marrow biopsy today.

Andrew Schorr:
Yay.

Carol Preston:
Yay.

Dr. Thompson:
I was saying to a patient the other day, they came in, and I sort of had gone through all of their prognostic information and talked about we don't need to treat you and all that sort of stuff, and then right at the end I said, oh, you don't need to have a bone marrow biopsy, and they kind the visibly relaxed. And I said to them I probably should open with that.

Carol Preston:
That's great.

Andrew Schorr:
There you go. Well, things have advanced, and I do want to just mention, you mentioned some people, there's a percentage of patients, the minority maybe, you don't need treatment or never need treatment, and that's my friend Pat Ford, who we've had on Patient Power.

He was also diagnosed in 1996. Does he have a somewhat elevated white count? Yes. Has it stayed more or less where it always is? Yes. So whether you call that smoldering CLL, whatever, he's just never had treatment. We're talking about 22 years.

Dr. Thompson:
Yep.

Andrew Schorr:
Okay. Let's go on. So CLL, I never heard of it when I was diagnosed. Carol had you ever heard of it? Had you ever?

Carol Preston:
Never.

Andrew Schorr:
Never. So it's like ah. And then hear "leukemia," and you think about a young child, four or five years old with leukemia, no hair, very aggressive treatment, and then if you've met people, older people maybe with acute leukemia, and fortunately the landscape is changing there, but usually a pretty fatal condition, you say, well, that's me. Susan, what is CLL?

Help us understand. What is it? You've looked at a million blood tests and your students, what do you see? What is it?

Dr. Leclair:
Well, I will tell you that the worst thing you're ever going to hear is somebody looking at you and saying if you had to get a leukemia this is a good one to have because I think that—yeah, I that's someplace where you want to murder people. But when we look at your cells they don't look that bad. You would expect with leukemia, with the word "leukemia," that you would have this, I don't know, unexplained explosion of cells that you've never seen before in your life.

This is a chronic condition. These cells look reasonably at times, normal. They may not work well, but they can look normal. You typically have a high white count. Well, what is high? High could be not high at all.

It could be hugely high. The high white count we talk about is of a specific type of cell called a lymphocyte in particular a subtype of lymphocyte most common, which is called B lymphocytes. But you will get an increase in that one cell line. Your red cells will probably be fine in the beginning. Your platelets will probably be fine in the beginning. No one knows. There are so many different variations and routes you can take, it's hard for me to say that those will be fine forever, but in the beginning there's usually just an increased number of these typically B, typically looking pretty okay cells. The problem is their function doesn't work.

Why doesn't their function work? Oh, if I had that, I would be on my way to Oslo to get a Nobel Prize.

Somehow, somewhere in the course of your life a mistake is made in a cell, in your genes, and from that stumbles a clone of cells that look kind of okay but don't work okay. That's what we see. That's how it happens. What genetic mutations? What are we up to now? Fifty of them that might be involved in this, so, in fact, no one will know that answer for a while.

Andrew Schorr:
Okay. Let me see if I've got this right. Too many B lymphocytes among the white cells, and you mentioned about bone marrow biopsy, but we're not going to have that right off the bat, you know, but, Phil, but the idea was when you can get too many it can at some point clog up the blood factory, right, and start affecting your ability to fight infection but the number of platelets you have to stop bleeding, things like that, it starts getting in the way of things. Is that right?

Dr. Thompson:
Yeah, absolutely. So the problems that you can have from these abnormal B cells, firstly, I think they can actually affect the function of your normal immune cells. So by having these B cells there, even if there aren't huge numbers of them, they can actually cause dysfunction of the T lymphocytes and the way in which they conduct your immune system's function.

So even—some patients, even with early-stage CLL where it's otherwise causing no problems, their other blood counts are normal, they can have an increased risk of infection. They can also have an increased risk of things like skin cancer where immune system is surveillance is.

And the second thing that can happen is they can accumulate in lymph nodes, they can accumulate in the liver and the spleen, so you can have enlargement of lymph nodes in your neck or your arm pits. The spleen can become enlarged.

And then the third thing that can happen is the CLL cells can also live in the bone marrow, and they can crowd out the normal bone marrow. And essentially I sometimes describe it to patients as you've got a factory for making cars, which is your blood cells, but it's piled high with junk, and there's just no room to make the normal blood cells. And so you can end up with anemia, which is not enough red blood cell and therefore not have enough oxygen-carrying capacity in your blood. People can feel tired, short of breath when they exert themselves.

And then you also mentioned the platelets. So the platelets are the things that clot the blood. If you don't have enough of them you may notice some easy bruising and bleeding. And so I mentioned earlier that many patients at diagnosis don't need to have a bone marrow biopsy because we can diagnose CLL without a bone marrow biopsy.

But if with we get to the point where patients are anemic or patients have a low platelet count, that can be a reason that we need to treat a patient. And we would always do a bone marrow biopsy before treatment, and we would do it if we needed to investigate why a patient was anemic or had the low platelet count.

Andrew Schorr:
Okay. We'll come back to that. So let's look from the patient and family perspective. So, Carol, you were told you had this leukemia you never heard of. I was too. How do you cope, or are you like on the floor in tears?

Carol Preston:
Yes. Let me just mention that I had a young cousin decades and decades ago who around age 4 or 5 died of childhood leukemia, so leukemia was not an unknown word in my lexicon or vocabulary, and as soon as I heard that word attached to a diagnosis for me, pretty much, yes, you had to scoop me off the floor compounded by the fact, and I think many patients have gone through this, it never seems to be a really good, convenient time to get sick.

Andrew Schorr:
No.

Carol Preston:
Right? So when I was first diagnosed, when I was first diagnosed it was around the Fourth of July week, and there were many people, many specialists and physicians who go on vacation that week, so I didn't have a lot of options. When I relapsed, it was right before Christmas in 2009, and, Andrew, you and I both share a third cancer—a second cancer. I know that's not the discussion, but again right after Christmas when nobody's around.

So compounding the fear of this word "leukemia" and the disease about which I had never heard was the fact that people were hard to reach to move forward. So that in itself becomes very frightening, from my perspective.

Andrew Schorr:
Right. So I'm going to add one other element, which is so true. Susan, you commented on it when you said you look at the cells and in some a cases they're not doing much. It's not an aggressive cancer. Many of us are familiar, unfortunately, and our families and friends with people who maybe had more aggressive cancers, or where it was treated more aggressively. Woman has breast cancer, I want it out. Somebody has lung cancer, maybe you're going to start treatment right away, whatever it is. You have skin cancer, we're going to cut it out.

But something happens right away, but there's this approach in CLL for many, for me it was four-and-a-half years, watch and wait. So what are we watching, Susan? What are we watching? Because for us it's unnerving.

Dr. Leclair:
Yeah, and I think I'm going to change that. Physicians will tell you, other healthcare providers will tell you watch and wait. I think the correct term is watch and worry.

Andrew Schorr:
Right.

Dr. Leclair:
Because no matter how strongly you believe in your physician walking out that first day with someone saying to you, yes, you have leukemia, and I'll see you in about six months. Maybe four, I don't know. It's not really exciting yet. You are clanned psychologically to the get it out. Well, you can't get out a leukemia. There's no place to get it because it's in your blood, and it's in the lymphatics, and it's in other places, so it's very hard to deal with that.

And having said that, because I wanted to say something about watch and worry I've forgotten your question, so could you just…

Andrew Schorr:
…what are we watching for?

Dr. Leclair:
Okay.

Andrew Schorr:
So in other words Dr. Thompson or another doctor may say, okay, you don't have to see me for a while, but I want you to go get a blood test. I'll get the results, whatever, but we're not doing anything now. Okay?

Dr. Leclair:
Okay. That's kind of, that one at least is a relatively easy—unless you ask why—item to explain. These cells live on their own. They have decided that they're not going to answer any control mechanisms that the normal cell responds to. As long as they sit here and do nothing, like a 16-year-old in the summertime, I guess, we're not going to be overwhelmingly afraid of them because they're not moving, they're not acting out.

But at some point they will start to increase in number, or they will change in morphology, and either one of those suggests that there's some movement, there's some activity going on. May not be anything overwhelming. Could be you have a cold.

Maybe something even, I don't know, you got a bruise because you fell, or it could be that B cells are continuing to become destabilized and are becoming more assertive. It takes them a while to become aggressive, so I'll…

Andrew Schorr:
One other question. You talked earlier about the white blood count may be fueled by the B lymphocytes in CLL, so is the number, is the number, just the number necessarily worrisome, or does that vary by person? So somebody could have a much higher number, feel like they're living well, and somebody could have a little bit over the edge high number, and they're pretty sick.

Dr. Leclair:
I'm going to steal Phil's thunder. No good physician treats a number. They treat a patient. Sorry I stole it, I know. He's laughing at me now. But it's true.

If you feel good at 20,000 cells, that's wonderful. If you feel good at 200,000 cells and everything has been stable for a while, then that's wonderful too. The number itself is not as important as the change from the last time or the time before. This is a long-term consideration, so want to see a year's worth of data maybe, minimally, six-months' worth of data in order to be able to make the sentence these cells are really just sitting there doing nothing, or they're becoming more assertive or something's wrong. You need a time limit here.

Andrew Schorr:
Okay. Let's get to our Dr. Phil, Dr. Phil Thompson. So in my case, no treatment for four and a half years under the care of one of your mentors, Dr. Keating at MD Anderson, and my white count finally got to 253,000.

And I did have some swollen lymph nodes and I was--he said, are you tired? I didn't know it, but I was, so I was having fatigue as well. Okay. First of all, take us through what tests are you going to do? If not a bone marrow biopsy early on, beyond just a normal CBC are there other tests you will do to understand what is that patient's status, and then what changes will you look for where you begin to say watch and wait or watch and worry, maybe we're coming to the end of that.

Dr. Thompson:
Well, I guess the first time you meet a patient or when a patient is first diagnosed you've got kind of a snapshot in time, and you don't necessarily have longitudinal data about what's been happening for the last five years or so. So when you first see that person you don't really know what the pace of change of the disease is going to be.

Some patients will come to see you and their white count will be just above the normal range, and they'll have absolutely no symptoms, and it will have been picked up on a routine physical assessment. And in that case it's likely that you could observe that patient for many years though they won't develop symptoms, they won't develop low blood counts, and their white count may remain stable.

And then there's the complete opposite end of the spectrum. For example, I met a patient once who had a white cell count of over a million, and he had a spleen that was almost into his pelvis, and he had very advanced CLL. And in that case—he was anemic and a low platelet count. In that patient I didn't need to observe for any period of time to know that watch and wait is not going to be appropriate. But then there's everything in between.

But for a patient who is newly diagnosed and maybe isn't going to need treatment straight away, you don't necessarily have to do a lot of tests to look at the genomics of CLL, because I guess there are two ways that you can work out what is going to happen to this patient's CLL over time. The first is you can watch it over time, but that's not going to allow you to give any information to the person right now.

The second is you can have a look at what are the genetics of this CLL, because that can give you a good idea about what might happen in the future. It's not perfect, but it gives you a much better idea about what will happen to an individual patient, because there's a huge spectrum of changes that you can have in CLL where the cells look the same but genetically they're completely different, and they behave differently, and they respond to different treatments differently.

But we can get a lot of that at diagnosis just with some simple blood tests, and it allows us to give a patient a lot more information. So when they come to see me it's usually because they want the most information, and so we often do all of these tests at diagnosis, and that allows me, I guess, to counsel people as best—to the best of my knowledge, this is what is likely to happen in the future.

Those tests, we look at the chromosomes of the CLL. So everyone has 46 chromosomes. You get 23 from your mother, 23 from your father. And in the CLL cells you can have missing pieces of chromosomes or a whole extra chromosome, and the knowledge of that can help you determine is this going to be an aggressive CLL or a stable CLL.

We also try and divide CLL into two groups. One is called unmutated CLL, and the other is mutated CLL.

And that mutated or unmutated refers to what we call the immunoglobulin heavy chain gene. "Immunoglobulin" is another term for antibodies, and antibodies is something that your normal immune system uses. In the normal immune response, your B cells try and make the best possible antibody to fight an infection, and by doing so they actually mutate their immunoglobulin gene.

So a CLL cell can arise from a B cell that's previously fought infections and has a mutated immunoglobulin gene, or it can come from a B cell that's kind of newly born or naive, has never fought an infection before, and that's what we call an unmutated immunoglobulin gene, CLL.

Now, counter-intuitively it's usually better to have a mutated CLL. People think, oh, mutated, that must be bad. In this situation, an unmutated CLL has the potential to grow much quicker than a mutated CLL.

And also they have a slightly different response to treatment, which we might talk about later.

And the last thing we can do is there's a huge array of knowledge that's come about from gene sequencing tests that have been done over the last seven or eight years, and we now know a number of gene mutations that can happen in the CLL cells that can drive their behavior. And we have a standardized test where we look for 29 of these mutations at MD Anderson, I mean, most of our newly diagnosed patients and anyone who is about to have treatment, and that can kind of give us additional information about how the disease is likely to behave.

So we can get, I guess, in a snapshot of time a lot of information about the CLL cells and how they're likely—how that patient's disease is likely to behave over time.

It can vary from patient to patient even with similar genetics. Because maybe those don't give us every bit of information, but they can be very useful.

Andrew Schorr:
Carol, wouldn't you agree, though, for me, for you, I want to know. I want to know because it's not do I have CLL but what version of CLL do I have mutated, unmutated. This chromosome missing a piece, that chromosome missing a piece, I want to know, don't you?

Carol Preston:
Well, not only do I want to know, there's a lot to unpack from what Dr. Thompson said, and he's familiar with both of us, and he and I have met several times. Let me start with my headline that you asked for about seeking a second opinion. Starting toward the end of what Dr. Thompson said about mutated versus unmutated and understanding that.

Here's the difference. We love our local oncologists, and we hope that—and I say this to anybody out there who has CLL or any other cancer with which they're dealing, we definitely would like synergy, we like the coordination between our local oncologist or hematologist and a specialist. But a couple of things happened to me, and probably heard by some of your audience on Patient Power, but I'm going to say it again.

The first was that the local oncologist wanted to treat immediately, and from my perspective, what did I know. I had cancer. He said he offered, you know, had a treatment. Let's get to it. He was recommended, and so that's what we did a couple of weeks after initial diagnosis. The terms out that the regimen that he recommended, and I won't go into all of the history, was an older regimen.

He was concerned—Dr. Thompson mentioned the different stages—I did have stage IV, which meant enlarged spleen and lower platelets, I think anything, according to Dr. Leclair, anything that could go awry was going awry, so it probably was necessary to treat, but it was with an older regimen which lasted a very, very short time. Because his concern was the enlarged spleen.

When I went for my second opinion at MD Anderson admittedly four cycles in, it was with Dr. Thompson's mentor, Dr. Michael Keating, it was suggested to me that perhaps that wasn't the best regimen to be on, although it knocked back the CLL pretty quickly. And so he said we don't change it if it's working. So that's fine.

We mentioned at the beginning that I relapsed three-and-a-half or nearly four years later, and when the genetic testing came back I got that very frightening diagnosis, 17p unmutated, poor prognosis. Poor prognosis. And then I really did think it's curtains, and I best get my affairs in order. Wisely, this time, since I was already a patient of Dr. Keating, I ran as fast as I could to MD Anderson. I sent him the slides, and he said, there's unmutated and there's unmutated. And he said, let me tell you that you have very few unmutated cells.

You're not going to get this from your local oncologist, which brings me full cycle about getting that second opinion. As Susan said, take a breath, exhale. You have time.

And I don't know what would have been had I just stuck with that original genetic report and gone—I don't know what the local hematologist, who's a very fine doctor and I do see him several times a year for blood workup, but I don't know what would have been, what would have been suggested had not Michael Keating talked me off the ledge before Christmas. He said, enjoy the holidays, and he said, come see me in January, and he said you fall within the normal range of treatment, in this case, Andrew, with what you were originally treated with, the FCR. You know, the fludarabine (Fludara), cyclophosphamide (Cytoxan) plus rituximab (Rituxan), and so I actually was able to do as Susan suggested, I was able to exhale.

But that's why—you know, I'm going to sound like a broken record—with so many superb CLL experts now around the country, and, Andrew, when you were diagnosed and even when I was diagnosed originally that wasn't the case. By the time I was diagnosed, there were maybe six prominent names, and today we have so many more. So there should be some major medical center where somebody can go, if you go for nothing else but that consult. Get that second opinion. These specialists are more than happy to work with your community oncologists.

In fact—and I think so I don't speak out of turn to say that you don't necessarily want every CLL patient from around the country knocking on your door. I don't think you can accommodate all of them at MD Anderson.

Dr. Thompson:
I'd have some trouble at home.

Andrew Schorr:
You'd never, ever get home. Susan, so we—thank you for those comments, Carol.

So, Susan, we were talking sort of about prognostic factors because now we're talking about unmutated, mutated, and Dr. Phil Thompson talked about parts of chromosomes missing, so those are all things we can test for now, as he said, right? So that's where we start talking about what version of CLL you may have, and that's going to start to inform treatment either now or down the road, right?

Dr. Leclair:
Absolutely. And a word of—again, taking that deep breath. Nobody learns all of this stuff in a day. You learn it in months and maybe years because you will learn things as you need to know them. It's—in a sense it is very much like the student who comes to you and says, do I have to know this? Is it going to be on the exam? No, I just told it to you to fill up time, but that's in class.

In real life the answer is no, you don't need to know all this stuff. You need to know what you need to know that makes you feel comfortable in your current surroundings. So if you need to know whether you're unmutated or mutated and that gives you a sense of the world as you now see it, then maybe at this point some of those other complete genome sequencing or some of the expensive now esoteric possibly not in the future tests will come, and you will understand those when they are needed to be understood. So don't panic about the language.

And, yes, it is true. When science became acceptable again in the renaissance you got burnt at the stake if you were doing that, so you invented a language no one understood. And then when people starting understanding that language you went to abbreviations, so now we talk about FCR, because we're not going to explain to you that that's really these three different names of tests, because we still think we're going to get burnt at the stake.

Andrew Schorr:
Three different medicines, all kind of medicines. It's bewildering.

So I think, to underscore something Carol said, is where you want to end up with is a CLL healthcare team that you have confidence in and where you can have dialogue where you each have an understanding of what you're dealing with now or on your journey. And then that will ultimately lead to a question of do you need treatment and then how do you decide what. So let's go on to that, Phil.

So I had this four-and-a-half year, 1996 into 2000, watch and worry, and at some point Dr. Keating said, hmm, we're observing this and that, not just the white count but the lymph nodes and the spleen and the fatigue, some sweating,

people can get night sweats, other symptoms, I think it's time to treat, and I think I have something for you that I'd recommend.

So let's go through is, am I right? Those are the kind of triggers for treatment, some of these things? Carol had spleen. You said everything had gone awry. So what does it say? When is it time to treat? And then help us understand the discussion about goals of treatment.

Dr. Thompson:
So the decision about when to treat, I think of it as when the symptoms of the disease and what the disease is doing to you is worse than potential risks of treatment.

Historically, we didn't have very good treatments, and so the kind of paradigm of watch and wait came from an era when we may not have had treatments that could dramatically affect the disease course, and so there were some big studies done that showed if you treated someone at diagnosis or soon after diagnosis, it made no difference to how long they lived compared to if you waited until they developed significant symptoms, and so that's really where that paradigm comes from, is this idea it's not going to make you live longer if I treat you earlier. And so that's why in terms of the approach to decide when to treat someone it's really based on symptoms.

So symptoms can be things like exhaustion and severe fatigue. It can be drenching night sweats. It can be lymph nodes that are growing and becoming uncomfortable.

It can be hemoglobin dropping in the blood or the platelet count dropping in the blood to the point where that puts you at risk of, in the case of platelets at the risk of bleeding and in the case of hemoglobin of being severely fatigued. We look for those things. The white count is not a useful marker in terms of do we need to treat you or not because if the lymphocytes are circulating around in the blood they're usually not doing much. It's when they're packing out the bone marrow and preventing you from making normal blood that may cause some problems—or if they're growing in the lymph nodes and the lymph nodes are getting very big, and they're causing problems.

But some patients may have a white count of 200,000 but completely normal hemoglobin, completely normal platelet count, no lymph nodes and feel absolutely fine. Now, that patient doesn't need to be treated. Whereas another patient may might have a white count of 20,000 but actually have an enormous spleen that's pressing on his symptom, and he can't eat properly, and he's losing weight, so that patient needs to be treated even though their white count is much lower.

Where the white count is useful I guess is if it's changing very rapidly over time. So we look for how quickly it doubles. We think of a lymphocyte count that doubles in less than 12 months as being fast, and particularly it's less than six months. Anything more than 12 months to double is relatively, relatively slow. So I guess those are the things that we base a decision to treat a patient on is like what are the symptoms, and do those symptoms warrant treatment that will hopefully actually make you feel better.

People often think, oh, I'm going to go into treatment, the treatment is going to make me sick. But usually when you've made the decision to treat actually once you get onto treatment you feel a lot better. And sometimes the symptoms sneak up on you. So people don't quite realize how many symptoms they have from the disease.

I remember a relatively young woman that I treated who had a white count of 350,000, hemoglobin of 8.5, and she said she felt absolutely fine. And so we actually watched her for some months, and eventually she decided, oh, look, I think I'll have treatment. And after we treated her and the white count was back to normal and the hemoglobin came back to normal she said, oh, my God, I can't believe how much better I feel.

Andrew Schorr:
Yeah, that was me. That was me. I didn't realize how fatigued I was. Let me ask you about this: So now we talked about these different prognostic factors.

Dr. Thompson:
Yeah.

Andrew Schorr:
Mutated, unmutated. Carol found out she had the 17p deletion. Some other people have other deletions, you know, when you do these tests, workups that Susan's—all her lab students all over the country now do.

So, okay. So how do you know what—and this get to the goals of treatment. Like, for instance, the FCR acronym, fludarabine, cyclophosphamide and rituximab that I had years ago, some people have and Carol had. So that was six months of infused therapy. Now you have oral therapies. Now you have oral therapies combined with infused therapies. You have some traditional chemotherapy drugs, like the cyclophosphamide and all that that sort of blasts a lot of stuff, and you have other targeted therapies. So what discussion do you have with people about what's right for you?

Dr. Thompson:
Right. So I think actually this is where these prognostic factors that you're talking about are really important because they're not only prognostic in the sense of—we think of a prognostic factor that tells you what is your outcome likely to be.

But actually some of these tests will tell us you'll respond to therapy A but you won't respond to therapy B, so we're heading into a world of kind of individualized therapy based on what a patient's CLL genetics are like and also I guess based on what the patient themselves is like.

But the two things that enable me to decide what's the best option for a patient is what are the genetics of this patient's CLL and what are the—I guess how old is a patient, how fit is a patient, what are their other medical problems because those things will enable me to determine will they tolerate the treatment well.

So the traditional—I guess, prior to 2010 we treated most patients with two regimens.

The younger, fitter patients would get FCR or something similar to FCR, which is a relatively intense multiagent chemotherapy or chemoimmunotherapy treatment, and that is very good at getting the CLL down, but perhaps an older patient or a patient who's got other medical problems might not be able to tolerate the FCR well.

And then the other thing we used was chlorambucil, which is an oral chemotherapy medication which we tended to give to older patients we didn't think would be able to cope with FCR. Now we have this whole array, as you said, of oral targeted therapies, and the advantage of these oral targeted therapies—well, there are two major advantages. One is they tend to be easier to take for patients than FCR.

The second is they work better than FCR in certain situations, in particular patients who have a 17p deletion or a mutation in this TP53 gene because those patients don't tend to respond well to therapy.

So I guess it then brings us to a discussion with patients about what is the goal of care. So in a young person, maybe someone in their 60s or younger, the ideal treatment I think you want to have is something you can take for a short time and then hopefully get a very long remission from the treatment, and in that sense we're hoping for 10 years or more and potentially even for some patients a cure of the disease.

Whereas for a patient maybe who is 80 and has a lot of other medical problems, the main goal may be you want to control the disease,

have minimal symptoms from the disease, minimal symptoms from the treatment and have a good quality of life without necessarily needing to have a 10- or 15-year remission. So that's where the kind of patient and the genetics comes in.

Now, in terms of the genetics, we've worked out a profile for the group of patients who are likely to have a very long-term remission from FCR. Again, it's not perfect, it's not a crystal ball, but we've identified a group of patients where about 60 percent of them we think are potentially cured with FCR.

So the conversation I tend to have with patients once I have all of these prognostic factors back is, this is the prognostic group you're in, this is what I would expect if I gave you FCR, and this is what I can expect from some of the newer therapies.

Now, the new therapy that's approved for untreated patients by the FDA is a drug called ibrutinib (Imbruvica), a pill that you take every day, and it blocks a protein called BTK in the CLL cells that they need to grow. It's very effective at reducing lymph nodes, at reducing the white count, at improving other blood counts and improving symptoms, but most patients end up with a small amount of CLL left over. And what that means is you pretty much have to take the drug indefinitely.

And so it then gets to a conversation about, well, do you want to take a pill every day for the rest of your life. And so some patients who have the good-risk CLL that do well with FCR may prefer to say, okay, I'm going to take six months of treatment and then I'm done for a long time rather than taking pills for the rest of their life.

So I guess there are those two different treatment paradigms that we can offer.

But the really important thing about the prognostic factors is that if you have, say, a 17p deletion on your CLL the average remission after FCR for a patient like that is only about a year, and generally when the disease comes back it comes back worse than what it was before. And so for patients like that they tend to do much better with some of these new drugs like ibrutinib than they do with FCR, and that's a conversation that you can have after you...

Andrew Schorr:
...one thing I think we should assure people about is that you have lines of treatment now. So you have ibrutinib (Imbruvica) that's approved, and then you have other lines of treatment like, well, Gazyva, or obinutuzumab, as opposed to rituximab.

You have venetoclax, or Venclexta, and you have others coming.

Dr. Thompson:
Yes.

Andrew Schorr:
So if you find that despite your best efforts something isn't working, you've got somebody in the batter's box, right?

Dr. Thompson:
Yeah, absolutely. So that's a very important thing to keep in mind. And I guess that also speaks to treatment goals. So for some patients the idea of getting cured is extremely important, but for other patients, they may say, well, you know, if I take ibrutinib every day and it works for 10 years I've still got venetoclax down the line. I've still got other treatments. There are all sorts of things coming down the line that almost seem like science fiction, like CAR-T cells, which people may have heard of. So definitely there are lots of options for patients whose disease has relapsed after initial therapies.

So that's important to keep in mind when you're talking about what the first treatment is going to be. But we do like to, you know, with the first treatment, some of the clinical trials that we've been doing, we've been trying to target the treatment paradigm to specific patient populations, like I was saying, but overall what we've been trying to do is design a treatment that has the least amount of toxicity to get the deepest response that we possibly can and the longest remission, hopefully without needing indefinite therapy. And so that's where we're moving with the clinical trials.

But for a lot of patients that are not on a clinical trial, indefinite treatment with an oral medication is still going to be a really good option because you can get a prolong disease control that way.

Andrew Schorr:
Okay. Susan, you're probably familiar with this now. There are some pretty sophisticated tests coming out for what they call minimal residual disease, MRD testing, to see is a treatment working, or is it knocking back the disease to undetectable levels. And now with a test that you're well aware of you can look for, I don't know, one in a million CLL cells, I mean really supper sophisticated. So that's coming now to see, are the treatments that Dr. Thompson and his colleagues are doing, how well are they working, right? Not just did they shrink the lymph nodes or do you have less fatigue, but what's happened with the number of cells, right?

Dr. Leclair:
Right. Originally the concept of remission, which is the word that we used, was we didn't see anything noticeable in you, but that was a clinical remission. That meant that your white count would drop down to an acceptable level of CLL.

But that's kind of a gross testing. Yes, you feel better, but I don't know how much leukemic cells you've got in your lymphatics or in some other part of your body. So there became a—sadly gradual, but it became a process of getting to be more and more sensitive in your testing. For example, if you take a half gallon of any liquid, dump out the liquid actually, put one black marble in there, fill all the rest of that half gallon with white marbles, that's what we want to test for. We want to be able to see—a half-gallon is about the size of your normal bone marrow, so we want to be able to see if there's one bad cell amongst that. We can't do that.

It's just too, too precise, too sensitive a level. We can though say that you only have a million cells—I know that sounds like a huge number, but when you have in scientific lingo we use numbers, 10 to the 6th, 10 to 10th, 10 to the 12th, you were diagnosed with 10 to the 15th-ish cells in that bone marrow. We can get down to 10 to the 5th now, 10 to the 6th cells. That's a huge drop from 10 to the 15th. That's 10 with 15 zeros after it versus 10 versus 9 versus 9 zeros after it. That's a large number of cells. So, yes, we have gotten more and more sensitive.

The problem with sensitive testing, which is always the issue, is you tend to get false positives in them so sometimes a number that is barely possible or barely not positive could be somewhat iffy because the tests aren't that wonderful.

The problem with that also is I can't tell you if you have zero cells or 999,999 cells that are malignant. There's no way I can tell that really consistently at this point in time. So you have to think of things like, I'm kind of like a diabetic. It's always there, but as long as I control it I can live a healthy, high-quality life. Maybe in a few years we'll get more sensitive than that, but right now that's the best we can give you.

Andrew Schorr:
And I'll say that Dr. Wierda, one of Dr. Thomson's colleagues at MD Anderson, some years ago, and I was originally treated in 2000, so maybe around 2010 or 2011, I had what was available then, an MRD test.

They've gotten much more sophisticated, and he said, well, you're not MRD negative, and I kind of freaked out. And he said, some day you may need treatment again. Well, I went many years. It was 17 years between when I had the initial treatment of FCR and when later, I happened to have Gazyva, or obinutuzumab, and some steroids is what I had, but anyway, that was last year, but it was a long, long time. So while I was not MRD negative I lived my life.

And so, Carol, I wanted to talk to you about that, living your life. Whether it's watch and wait or watch and worry, or in between remissions or never knowing how long a remission is going to be but it's still there in even barely detectable levels going on with your life. What would you say to people about living with CLL rather than that being really depression on your life?

Carol Preston:
Go on with your life. I mean, that is--when I was originally diagnosed, after I picked myself up off the floor, when I was treatment, and this was before I went to MD Anderson, but when I was in treatment—I'm a communications consultant and I do workshops. I was still flying, oops, I was still flying. I was working, commuting. Perhaps I didn't clean my airline tray as best I could, but I just kept on going on because feeling normal is what keeps you going. If suddenly you recede or you pull back from everything then you can't go on.

Then suddenly cancer wins. Cancer takes over. And cancer patients who have survived—and I know there are a lot of cancer patients there are so many different kinds, that they do get sidelined. They have to stop. They have to take precautions.

But not only feeling normal but talking to the company with which I work on consulting, and my boss said to me, if you tell me you can do it, then I'm going to let you do it. You will be assigned. He said, if you tell me you can't, then we won't. And he said that was our deal, that I would be honest and he would be honest, and it didn't prevent me from doing anything.

Now, I was fortunate enough, it's never fortunate to get a serious diagnosis, but that both of our sons were already grown and basically gone in graduate school, working. I'd have to think back about where they were, so I didn't have the additional challenge of taking care of young children.

And I do have a spouse. I would call him more of a partner than a caregiver, and he will be the first to acknowledge. He said I didn't do—I didn't do much caregiving, but he was always there. He went with me when I needed him to for appointments and so on and so forth.

But I also developed a ring of people of support, support on whom I could draw when I needed it. For example, under my original treatment I was given diphenhydramine (Benadryl), which makes you very sleepy and you're not supposed to drive if you've been on Benadryl.

So my husband was working at the time, and I made arrangements for support people to pick me up. And, by the way, there's a wonderful tool now—there are probably many, but the one that is very prevalent, and I'll just pass this along to patients who are looking to line up their team of support, it's called SignUpGenius, all one word, SignUpGenius, where you can create a template. I need to be driven to the doctor this day, I need to be picked up this day, and people can sign up. They can check it off rather than making phone calls, which is exhausting.

Because the hardest thing to do is really to pick up the phone and make these calls and ask. But this is a way that you can solicit and elicit support, and everybody wants—then people say ah, now I know what I can do. Make a meal. Now I know how I can help.

So there are lots of cool tools. And I know that this is a wide-ranging discussion on newly diagnosed patients, we all have so up much information, but I get very excited about the ways that we can reach out and have many people touch our lives and help without feeling like they're interfering or without turning away. So many times people don't know what to say, and as Susan, you said earlier, so they say, well, you know, if you had to have—and I had many, many people by the way who said that to me well, if you had to get a cancer, this is a good one.

Andrew Schorr:
No cancer's good.

Dr. Leclair:
That's right.

Andrew Schorr:
No cancer is good. Let me just—as we begin to wrap up I want to mention a couple of things just quickly for me. First of all, you, Mr. or Ms. with CLL, are not alone. Not only do you all the people on our screen here but you have thousands of other people who have gone before you.

And then the other thing I would say is, and Carol and I are big believers and I know Susan is, and Dr. Thompson is very accepting, walk in to that doctor you trust and ask questions. Have your list of questions. We got this test result back, you know, and here's what it says. What does that mean? Or you use these acronyms, whether it was FCR or ven plus this or I plus this or some other thing or a clinical trial, I don't get it. Wave your hands, I don't get it. Please say that in English, right, Susan? You're a big believer in that.

Dr. Leclair:
Absolutely. And I want to add to what Carol was saying. Find—the single best thing you can have is your pen. When you have a question write it down on a piece of paper. Bring that piece of paper in to your physician. If you don't want to read it, hand it to him or her and say, answer these questions.

And if you do have someone who comes with you, have them take notes. Again, I'm going to steal Phil's thunder and say that a lot of physicians will say that the immediate first sign of a serious diagnosis is deafness because the physician looks at a patient and says, I'm terribly sorry but you have, fill in the blank. And then that physician begins to talk about whatever it is that he or she feels like talking about. You, however, have become deaf because the last word you heard was "leukemia" or "cancer." Bring someone with you to take notes because you're not going to.

Have them put a tape recorder on the desk because you're not going to believe your husband's or wife's notes. I know we've been through this in my family. I know this. So you need to have someone there to fill in the gaps until you can catch up, until you can take over.

And that is a critical thing to have, a pen and a person to help you discuss things with your physician. Sorry, Phil.

Dr. Thompson:
No, I couldn't agree more. There are two things that prevent people from remembering. The first is the shock of the diagnosis and the fact that—there are either some people seem to go blank and some people I think start ruminating about all of the negative ramifications of what this might mean and therefore can't understand the next series of things that you say.

But the second thing is you then start talking about concepts that this person has no background in, background knowledge in. And it's very, very difficult to—it's like you imagine trying to remember a random series of letters or a random series of numbers. It's impossible.

And that's what this is like. You know, when people start talking about an immunoglobulin-heavy chain gene, you don't know what an immunoglobulin heavy chain gene is. Or a SF3B1 mutation. Some people don't even know what a chromosome is. You know, it's very difficult to remember these types of things. So if you write, I think if people write them down on have their support person with them who writes them down it gives them the option to then go away later and say, okay, he mentioned all of this, and then they can look it up. And at your leisure you can go and read all of these things. And then I often find people will come back to me at the next appointment or even shoot me questions afterwards and say, you said this, and I was doing some research and I just wanted to clarify these things.

And I always find that to be a really important part of the process, is those kind of subsequent clarifications of what at the time was just information that the person had no handle on.

Andrew Schorr:
Phil, I want to get one final comment from you, and it's what I've asked you before. It's about hope. So here we are, our audience of newly diagnosed people and family members, and we can talk about chromosomes and we can talk about ranges of treatment, but tell, me as a CLL specialist, should I be freaked out or in this particular disease do you feel you have or are developing the tools that can help me or my loved one probably live pretty well for a long time, probably.

Dr. Thompson:
I would say exactly that. Are I say to most of my newly diagnosed patients, and there are always exceptions, but for most people they're going to live a long life and a life with good quality.

And those two things are both very important, and in some cancers they may not necessarily marry up. Some cancers have treatment that's so toxic that it may make you live longer but your quality of life suffers. I think in CLL we're very fortunate that we can select therapies that are both extremely effective but also are well tolerated and lead to good quality of life. So I would say for the vast majority of newly diagnosed patients with CLL there's a huge amount of hope.

I can't say to a patient don't worry about the fact that you have cancer because that's a ridiculous thing to say, but I think I can say to most people you're going to live a long life, and you're going to life a life with good quality.

Andrew Schorr:
All right. Amen. What a wonderful note to end on.

I hope this gives hope, confidence and knowledge, kind of the trademark of what we try to do at Patient Power for people who are watching and people who care about them. What a great group. Carol Preston, thank you so much for being with us, and long life to you, Carol and your commitment to other patients. Dr. Phil Thompson, thank you so much for being with us from MD Anderson once again. And go cure CLL, okay? Go do it.

Dr. Thompson:
We're working on it as fast as we can.

Andrew Schorr:
Okay.

Dr. Thompson:
I think we're getting there.

Andrew Schorr:
Yes. You are making a lot of progress. And, Susan Leclair, your devotion to patients and understanding all this for decades thank you so much.

Dr. Leclair:
I started when I was very young.

Carol Preston:
Very young.

Andrew Schorr:
Thank you so much for being with us. This is what we do at Patient Power. I hope it's been helpful. Thank you for financial support from AbbVie Incorporated for making this program possible.

And be sure to check out everything we have on Patient Power and look for all these resources we mentioned. You are not alone, and hopefully in your CLL case you'll do very well for a very, very long time. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.