Understanding the Ins and Outs of Watch and Wait

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

Jackie Broadway-Duren, DNP, RN, FNP-BC
Family Nurse Practitioner
The University of Texas MD Anderson Cancer Center

Cathy Hamilton
CLL Patient

Andrew Schorr:
Hello and greetings. So there you are, diagnosed with CLL and you're told no treatment begins for a while, maybe months or years. How do you cope with this watch-and-wait period? I had to do it for four years. You're going to meet somebody who's right in the middle of it, right now. We'll discuss all that in the next 60 minutes. Greetings from Carlsbad, California, north of San Diego. I'm Andrew Schorr.

You may have a question for yourself or a loved one about this watch-and-wait or watch-and-worry period. Send your questions in to cll@patientpower.info, again, cll@patientpower.info. Now, we're specifically in this program discussing this watch-and-wait period so you may be looking ahead to treatment, but it's less about treatment now and more about why watch and wait, what are you watching and how do you wait? How long and what are the indications for treatment? That's what we'll really be discussing today. And remember not to make your questions so specific about you because we don't want to practice medicine over the Internet. That wouldn't be fair to our panelists or you. Always discuss what you learn on our programs with your own healthcare team so you get what's right for you. Okay.

Are you ready to go? For the next 60 minutes, let's meet our panelists. First, let's go down to Houston, Texas, for our two experts joining us from MD Anderson Cancer Center. First, Dr. Phil Thompson. Dr. Thompson is a CLL specialist. He's been on our programs before. Phil, welcome back.

Dr. Thompson:
Thanks, Andrew. Nice to be here.

Andrew Schorr:
Okay. And working hand and hand another doctor, who is a nurse practitioner, and that is Jackie Broadway, who's worked with CLL patients for decades now. Am I right, Jackie?

Dr. Broadway-Duren:
That's correct.

Andrew Schorr:
And I've seen you many times. A great team, and Dr. Thompson and Dr. Broadway work very closely to support CLL patients who come to MD Anderson. We're going to talk to them about watch and wait a lot during this program.

But let's meet somebody who's living with it, and that's my new best friend, Cathy Hamilton, who joins us from Lawrence, Kansas. Cathy, you've been in this watch-and-wait period now for 10 months, right?

Cathy Hamilton:
Just—yes. 10 months plus.

Andrew Schorr:
Okay. How did this start for you?

Cathy Hamilton:
It started with a routine annual physical that I got last January. I went in early to do my blood work, and when I showed up for the exam a couple weeks later my internist told me that my lymphocytes were slightly elevated, and I emphasize slightly, and my neutrophils when a little low and that she would like me to come back in three weeks and test again because it was right after the holiday and I'd been with my grandbaby at the time and she was thinking that maybe I picked up some kind of virus.

So I went back and, sure enough, got a call phone call on a Friday night from the doctor herself, and as our doctor friends know that's usually not good news, that phone call. So she said the numbers hadn't changed and that now they were seeing some smudge cells on the slide, which was indicative of CLL. So two weeks later I find myself at an oncologist's office. I was getting a flow cytometry test, and that confirmed the diagnosis.

Andrew Schorr:
Okay. Now, you had never heard of this.

Cathy Hamilton:
Never heard of CLL. But leukemia put the fear of God into me, I'll tell you that. That word was frightening. I just didn't realize at the time that there were acute kinds and chronic kinds and was relieved to find out that I had a very slow-progressing indolent case so far.

Andrew Schorr:
Right. And that's true, and I have to tell you there's some people, me included, back in 1996, I wasn't really clear that leukemia was a cancer, right? And then you talk about acute, chronic, is it this type, is it that type, is it indolent. Okay. So we're going to continue. But first, Phil, you have had to give that bad news to people who have no frame of reference, maybe were referred to you from their general practitioner. And I know when I walked into MD Anderson I had never been into any oncology clinic, floor, office. It was like a terrifying stranger in a strange land. So, first of all, how do you explain this to people, first, what they have?

Dr. Thompson:
Yeah, so I think what you're saying is true. I think people come in with an image in their head when they hear the word leukemia or of people with no hair, horribly nauseated, vomiting, you know, IV lines, terrible quality of life. And I think one of the things I try and do is dispel as much as of that as quickly I can. Also, people tend to come in terrified that they're about to have a bone marrow biopsy and all sorts of other tests. So I try and kind of put people at ease, tell them that we're not going to be doing all these things before we start so that people can hear the rest of the conversation.

Andrew Schorr:
Yeah, and I know I didn't hear much. I was on the—not on the floor, but Esther, my wife of 33 years, we were in tears. And, Cathy, what about you? Did you hear everything the doctor said?

Cathy Hamilton:
No, I didn't. My internist had warned me that she thought this was what it was because I always ask. As a former reporter, I suppose that's where this comes from, like, okay, what's the worst-case scenario. Tell me now so I can Google it, which isn't necessarily the most calming thing to do, but that's how I operate.

So I didn't hear everything. I did hear that there would be no treatment, and that was confusing to me. It's sort of a good news/bad news situation because any time you hear the word cancer you think, well, let's just get it. Let's just attack it. Let's throw everything we can at it. But in this case it was no, we're just going to sit back and so see what happens. So from my personality type that was a little bit hard to take.

Andrew Schorr:
Yeah, me—well, actually I wanted to forget about it. So if I could forget about it for an extended time, because I felt good. So, Jackie, how do you explain to patients whether you or one of the physicians based on the test results and everything tell somebody sitting across from you they have CLL, but we're not going to do anything right now? You've heard the same confusion that either I have had or Cathy's had. How do you explain that to people?

Dr. Broadway-Duren:
Basically, as Phil stated, when people hear the word leukemia they immediately look at worst-case scenario, which is generally acute leukemia. So the first thing is to help them understand the nature of the disease, the nature of their diagnosis. And secondly, to sit down and review what those prognostic indicators mean, both the purpose of doing those and how those will determine at what point we think treatment may be indicated.

So I—we generally spend a lot of time going over lab work and particularly the FISH test, the gene panel, and so it's important for the patient to understand there are certain prognostic factors that have a positive connotation while others suggest more aggressive disease. So I think when you can show them something visually as you're explaining the watch and wait, I that help to calm the patient and kind of allays their fears, and they are more willing to consider watch and wait at that point.

The other thing I think is they have to—it's very difficult for patients to differentiate CLL versus lung cancer, whatever, because, as you stated, they want to get some treatment. They want to do something right now, and they want to know that it's there. So it is sometimes difficult to get them to understand. Yes, you have leukemia. No, we don't need to do anything, and it may be some time before you will need anything if you need any treatment at some point in time.

Andrew Schorr:
Right. So, Phil, let's understand. What is the rationale among you CLL specialists why not to treat on day one? How come?

Dr. Thompson:
Yeah, so I think that the idea that you need to get cancer early, treated early comes mainly from solid tumors. And so, if for example you have bowel cancer and you discover it when it's small and it's localized to the intestine, then you can surgically removal it and you're done. Never have to have any treatment other than that initial operation because it's only located in the one place.

Now, CLL is a very different beast, because at the earliest stages of the disease it's everywhere in your body. It's circulating around in the blood. It's within lymph nodes. It's within lymphatic tissue that's present in organs in your body. It's in the bone marrow. So there's no quick fix that you can do at that early stage so that it's gone forever and you don't have to worry about it.

So with a few exceptions what you're doing is managing a chronic disease. And so when you're managing a chronic disease you have to weigh off I guess the risks of treating the disease and toxicities that are associated with treatment versus the risks of doing nothing. And sometimes for patients, well, very often for patients with very early-stage CLL you can watch them for many years. They don't have any symptoms related to the disease. The disease is not causing them any harm. And if I were to give a treatment to that patient that would have a—that they could potentially have a significant side effect, I may be doing more harm than good by doing that.

Andrew Schorr:
Or costs, as we look at some of the new therapies.

Dr. Thompson:
Well, there's that as well.

Andrew Schorr:
Okay. So I have one other follow-up question for you, Phil. And that is is there a price to pay, though. So for instance have I had a tougher CLL journey by waiting four and a half years, and it proliferated to a certain point. My white count got to 253,000 and I had the swollen lymph nodes and my spleen got enlarged. Is there—while letting more cells circulate, if you will, do we ever recoup from that, or was it just this balancing act you were talking about?

Dr. Thompson:
Yes, so that's a—I mean, that's a really good question, and there's probably not super robust data to actually answer that. You know, in the past the studies that were done to try and determine is it better to treat a patient earlier were done with pretty ineffective drugs like chlorambucil (Leukeran), for example, which is really completely outdated therapy now, and it never got rid of all of the CLL. So exposing a patient earlier to the drug just meant that you had to maybe potentially use it more times.

Now, if we look at sub-groups of patients who may be potentially even cured by treatments like FCR, then you can make an argument that if, well, if we know we're going to need to treat you then maybe we should do it a little bit earlier before you get really sick, and perhaps if there's less of a disease when we treat you we could do better. We don't actually have data that tells us that that's the right approach. So really there are a number of clinical trials that are being done looking at earlier therapy with a number of drugs that are, I guess, less toxic than FCR. So it will be interesting to see how those play out, I think. But it is a very good question.

One thing I do with patients is that not all watch and wait patients are the same. So some watch and wait patients might have a white count that's just above normal, they don't have any lymph nodes. When we do the genetic profile of their CLL it looks like what we call favorable genetic profile.

And then on the other hand, you may have some patients who are in watch and wait where every six months or every 12 months their white count doubles, they have lymph nodes that are growing, and so even though they may not meet formal treatment criteria you can clearly see they are progressing and they may be progressing relatively quickly. And in that setting sometimes we don't wait quite until they meet those formal treatment criteria. We may say, well, that's where the art comes in. We say, we know you're going to need treatment in six or 12 months, why don't we just get started now. But you don't want to do that in a patient who could go 10 years without needing therapy, if that makes sense.

Andrew Schorr:
So, Jackie, so that goes back to you. So you take a look at these test results with your patients and you help them understand, and then for follow-up visits you're discussing with them the change or not and the rate of change and what that's telling you, right?

Dr. Broadway-Duren:
Correct. And as an afterthought from the first question, another thing I think that helps people to understand the watch and wait is that I first try to help them understand this is a chronic disease, and the CLL was there likely years before they were ever even diagnosed. So my point to them is there's no urgency today, because this is a chronic disease, so you're just getting the diagnosis now.

But on subsequent visits when the patients come in, we do a very thorough physical exam on them to check lymph nodes to see if there's been any advance in the size of the nodes or the liver or spleen, and we again review the labs very closely when the change is in the absolute lymphocyte count or hemoglobin and platelets. Those are indicators that would indicate to us whether the patient is progressing.

Andrew Schorr:
Cathy, let's see if you're willing to share a little bit for you, and we're going to discuss how it's different for everybody. So when they did your blood test, do you recall what the white count was initially, the white counts?

Cathy Hamilton:
Yes, so I would just say I'm the first patient that Dr. Phil—sorry, Dr. Phil—mentioned. I had a very low white blood, I mean, relatively speaking my white count at the start was just 12.8, and at my last follow-up it was down to (inaudible). So, again, I have a just a smidge of CLL I call it. I'm not symptomatic. They were just—they were high enough for someone to sound the alarm, but really it's not that I've been told I have the good kind of cancer, but I have been told I'll probably die with it, not from it. I don't know what consolation that is, but, you know, my numbers are not that scary.

Andrew Schorr:
And how often do you have a blood test?

Cathy Hamilton:
Well, I'm not going back until May now because I'm going to have my blood checked at my annual physical. So it was three months, then four months, and now it's not until May at the oncologist's office.

Andrew Schorr:
Okay. And have you had this, Jackie referred to, this FISH testing or any of these other more sophisticated tests?

Cathy Hamilton:
Not yet. That's in the plan for next year. I had a very positive I think it's called CD38 marker from the flow cytometry test that he said was really good prognostically, but that's really all I know. I'm just kind of—I'm just spreading out the expense part of it.

Andrew Schorr:
Right. And you've had a bone marrow biopsy or not.

Cathy Hamilton:
Not.

Andrew Schorr:
Okay. All right. So we're going to go on. Oh, swollen lymph nodes or night sweats?

Cathy Hamilton:
No, and that's what I was told my by oncologist. I want to hear from you immediately if you have drenching night sweats, debilitating fatigue, swollen lymph nodes. He checks my spleen and all my lymph nodes every time, and so far so good on that count. I will say I do intend to find a CLL specialist. There doesn't happen to be one in my area.

Andrew Schorr:
You have two on camera with you right there.

Cathy Hamilton:
I know, so I'm pretty much halfway between MD Anderson and the Mayo Clinic, and then my son just moved to Denver and I know there are a couple of experts out there. So my big thing right now is trying to figure out where I'm going to live in retirement and then finding a CLL specialist close, so that's going to take about a year to figure out.

Andrew Schorr:
Yeah. And I'll just mention for me. So I'm living with two blood-related cancers, CLL, which I've been treated for twice, and so I chose to be in San Diego to be near Dr. Tom Kipps of UC San Diego. I have another condition, myelofibrosis, and at that same center they have a specialist in that. So that's kind of where I chose to be living my Internet life here with Esther.

So one other question for you, Cathy, and then I want to probe our medical experts further. And again send in your questions to cll@patientpower.info.

And that is so you've been told there's like a scent of smoke in your kitchen somewhere but there's no fire and you don't have to worry about it. How have you coped with that?

Cathy Hamilton:
Well, I wasn't ever going to be happy with sitting around doing nothing, so I really did take—I read up a lot. Patient Power, I have to say, brought me up the learning curve—which is very steep, by the way—it brought me up that curve very quickly. And I am grateful to you and Esther and your whole team for that because I think it would have taken months without the internet to think about what I was looking at.

And I just decided to make some lifestyle changes that I thought would just make me healthier in general and perhaps fend off those secondary cancers that we worry about when we have CLL. So I had all my necessary screenings done and I switched my diet and I started to exercise more faithfully. I'm taking a couple of supplements, not crazy stuff, but I just got healthier.

Andrew Schorr:
Sunscreen, although more for me in California than you in Kansas.

Cathy Hamilton:
Oh, I've had precancers frozen off my face. I went in immediately and had a full body skin check. I had a mammogram that I was about nine months late on, and I'm getting a colonoscopy on schedule next year. So those are just the kinds of things that—I don't think watch and wait means doing nothing. I think you can do things to make yourself healthier in general and just be more proactive, and I think that gives you a sense of control and empowerment versus just wait to see what the universe is going to deal you, you know.

Andrew Schorr:
By the way, Cathy has done a little program for Patient Power where she takes us through her routine including her exercise TV, bouncing at the TV on your little exercise ball and all that stuff.

Cathy Hamilton:
I don't know why I sent you guys that video, but I bounce on the stability ball to keep my lymph system going.

Andrew Schorr:
Okay. So, whatever. So, Phil.

Dr. Thompson:
Yes.

Andrew Schorr:
What are we watching? So first of all you mentioned, I think it's clear for our audience, we have a pretty smart audience, not all CLL is alike. So if somebody goes to MD Anderson or wherever she goes for further testing—and she mentioned one kind of protein on cells, CD38—what are you looking at to say, Mr. Jones, Mrs. Smith, here's your CLL situation, and here's what we're going to watch. What are you looking it?

Dr. Thompson:
Okay. Well, so generally at diagnosis we look for a couple of things. One thing is a test called FISH, and FISH is a way of looking at the chromosomes in the CLL cells. You have 46 chromosomes, 23 from mom, 23 from dad, and in CLL there are four common abnormalities in the CLL cell's chromosomes. Now, those are not present in the other cells in your body. They're not inherited. They're acquired abnormalities in the CLL cells only that are part of the reason that the CLL has developed.

And the importance of looking for those is twofold. Firstly, it gives us an idea of how quickly is the disease likely to grow, because some of the chromosomal abnormalities that we find on FISH, for example a deletion on chromosome 13q, are generally associated with a slower growing disease, whereas some of them like a deletion on chromosome 11q or 17p are

generally associated with a more rapidly growing disease. Now, not always but in general. And then those things can also give you an idea of what the best treatment might be later on.

The second thing we look at is what we call the immunoglobulin heavy chain variable mutation status, and we usually just shorten that to mutation status. It gets a bit confusing for patients, because this is a situation where it's good to be mutated, which is counterintuitive. Basically what it means is that the CLL comes from a B lymphocyte, which is part of your immune system. And a B lymphocyte's job is to go around in lymph nodes and circulate around in the blood until it finds an infection.

When it finds infection it has a probe on the surface called immunoglobulin, which is the same thing as an antibody, and that recognizes a microbe like a bacteria. And then when it does that it tries to make the best possible antibody, and in order to do that it actually mutates the antibody gene or the immunoglobulin gene. And when you have a CLL that arises from a B lymphocyte that has a mutated immunoglobulin gene it's a more mature B lymphocyte. It's been around for a while, and it has less growth potential than an unmutated CLL. So we look at that, and actually that's a very good indicator for us as to how likely a patient's disease is going to grow more or less quickly over time.

Now, do you have to do that when the patient's first diagnosed? I would say no, you don't, because we're always going to follow patients anyway by seeing them generally after diagnosis I would see a patient approximately every three months, and we're going to keep checking their blood tests. And we're going to keep examining their lymph nodes and their liver and spleen, so we'll be able to tell if they're growing quickly or not, and that's actually best test. But a lot of the time patients when they come to see you initially they want to know the most information that they possibly can, and that's the reason we like to do those tests.

The other thing I would say is that the mutation status of the cells doesn't change over time. So if you do it once, you don't have to keep repeating it down the line. It will be the same for the whole course of a patient's disease. So those are the two biggest ones we do.

You can look for mutations in individual genes within the CLL cells. That has more relevance, to be honest, in terms of deciding treatment rather than deciding how quickly it's going to grow at the start, and in many cases it's not done outside of a few research centers.

Andrew Schorr:
Jackie, I have a question for you just related to the white count number.

Dr. Broadway-Duren:
Yes.

Andrew Schorr:
You said at diagnosis your white count was 12 point-something.

Cathy Hamilton:
Me?

Andrew Schorr:
Yes.

Cathy Hamilton:
Oh, yes. 12.8.

Andrew Schorr:
Okay. And mine at time of diagnosis turned out to be 18 or 18,000. And I think normal, Jackie, is between 5 and 10; is that right?

Dr. Broadway-Duren:
Yes, thereabouts depending on the lab, but yes.

Andrew Schorr:
Okay, so now people come to see you for these follow-up visits, and their white count may be changing. Should they measure how they're doing simple by the white count? In other words, it's like a score card, I got an F on a test or whatever. Should this be unnerving? Should they—is their body letting them down simply if there are changes in their white count?

Dr. Broadway-Duren:
Is that question for me?

Andrew Schorr:
Yes, ma'am

Dr. Broadway-Duren:
Okay. No, that's not the only thing. That's definitely not the only indicator. We do have patients who may begin with a lower white count, 15- or 20,000 and we see them back in three months it may have progressed to 25- 30,000, but they still have no palpable lymph nodes, or there's no organ involved, or the hemoglobin and the platelets remain stable, so there's no need for concern. And again, that's the time we try and allay patients' fears, because in some patients if there is a 5,000 increase in the white count, they think, okay, it's growing so now I need treatment. So you constantly try and allay those fears and encourage them.

So to answer your question, no, it's not just the white blood cell count. It's how fast it's progressing, the white blood cell count, not the fact that it went up in increments.

Andrew Schorr:
Dr. Keating, who's one of the senior folks at MD Anderson was my doctor 22 years ago when I was diagnosed, he said we don't treat the numbers.

Dr. Broadway-Duren:
That's right.

Andrew Schorr:
And so I think you'd agree with him, Jackie. All right. We're starting to get some questions. I want to pose them, and we'll continue our conversation with all three. So Susan wrote in, and I'll pose this to you, Jackie, she said, the doctor of a friend of mine who has CLL told her to watch for petechiae, little red dots I guess on your skin, on her arms and legs. The doctor hasn't mentioned it to this woman who has CLL also. So is that an indication of treatment if you're getting either bruising or little red dots, or can that just be part of aging, Jackie?

Dr. Broadway-Duren:
That could be an indication to treatment, but at that point you'll need to draw a complete CBC with a differential. You'll need to look and see what the platelet count is doing at that time. The other thing you also have to consider is what is the patient's history. Do they have any kind of bleeding disorders or any platelet dysfunction in their history? So there's certainly no reason for concern. It just needs to be investigated more.

Andrew Schorr:
Okay. Phil, we got this question in from David, and I think we discussed it with one of your colleagues, Dr. Wierda, recently on another program. People are confused. They hear this diagnosis of SLL, small cell lymphoma, I think, but they know it's basically very related to CLL, and they say, well, are there other tests that relate to that or is it all really, SLL, CLL, kind of all the same?

Dr. Thompson:
It's a biologically identical disease. So it really—it's monitored and treated exactly the same way. It's just that—you remember I was saying that CLL is a disease that's present everywhere in the body, but it's just to varying extents in varying places in different patients. So some patients may have a white count that is very high, 2- or 300,000, but actually their bone marrow is functioning completely normally, which is what it needs to do. So their hemoglobin is normal and

their platelets are normal. They have no symptoms, and their lymph nodes are not big and uncomfortable and their spleen is not swollen.

Whereas another patient may have a normal white count but huge lymph nodes that are causing significant discomfort, and that's when we call it SLL, when the lymphocyte count is below a certain threshold. So they're not different diseases, they're just different manifestations within a different patient of essentially the same disease.

Andrew Schorr:
Phil, I want to go back to one thing you were talking about, 11q and 13 and this can and that and 17p. And so there's Jackie, and she's going over the test results with the patients. And if 17p pops us and we've read that that can mean more aggressive CLL, they say oh, my God, I'm going to have to be treated aggressively and soon. But my friend Carol Preston had some 17p and that was not the story. So even with the 17p, people vary, right?

Dr. Thompson:
Absolutely. And they can vary enormously. The thing about the test results is that they only give you a proportion of the picture. And part of that is because we don't I guess fully understand all of the biology of an individual CLL patient. But it's more important what's going on with the patient than what the test results show. So it's important. Are they anemic? Do they have a low platelet count? Do they have debilitating fatigue? Are they having drenching sweats? Do they have big lymph nodes? All of those things are more important than do you have 17p deletion, or do you have 11q deletion or whatever.

We actually don't make the decision about whether to treat someone or not on the basis of those genetic prognostic factors that we look for in the CLL cells. The decision to treat is a clinical decision, and it's based on those other things that I mentioned, you know, the anemia and low platelet count and lymph node size. So I've had patients that have been in watch and wait with 17p deletion as long as 10 years. So there is a sub-group of patient who could have a 17p deletion or a TP53 mutation and not need treatment for a long time.

Andrew Schorr:
Okay. One other one we did and that is trisomy 12?

Dr. Thompson:
Twelve, yes.

Andrew Schorr:
What about that one?

Dr. Thompson:
Well, likewise. So that is generally, that's a kind of a biologically unique subtype of CLL, and it tends to grow quicker than a patient with 13q deletion, for example, but not always. And it depends sometimes on some other mutations that occur uniquely in trisomy 12 patients. But it—again, it's not an indication to treat a patient differently.

Now, when you come to make a treatment decision later, so if a patient needs to be treated, then these prognostic tests are critical in determining the optimal type of treatment, but they're not critical in determining when do I need to treat.

Andrew Schorr:
Okay. And, Jackie, James wrote in this question. He said, well, during the watch-and-wait period is there anything available to moderate or reduce night sweats? So first of all, I know night sweats could be one of the things you look at whether other stuff is going awry too, but simple for the night sweats, what do you do?

Dr. Broadway-Duren:
Well, first of all, it depends on the intensity of the night sweats. That is, of course, a question that's asked every time a patient comes in, and sometimes the patient—if they are females and males at times, you have to consider whether it's maybe hormonally related or something. But there's really no cure for night sweats. I tell them, you know, you just have to make some alterations in your bedding and things like that. I'm not aware of any miracle things that you can do to prevent the night sweats.

If they are related to the disease, if they're drenched in sweats and coupled with other symptoms, it may be an indication for therapy.

Andrew Schorr:
Right. So we have some other questions about it. So, first of all, Cathy, Dr. Thompson mentioned about this mutational status. Do you know whether you're mutated or not?

Cathy Hamilton:
No, I don't. I haven't had those tests yet. And, in fact, I'm encouraged by what the doctor says because that was sort of my oncologist's take on the whole thing. Like why don't you just get used to this news, and we've done the flow cytometry test, and if and when you need treatment, yes, we'll have to take those tests to determine how to treat you, but in the meantime it's strictly up to me. And I'm curious, but I'm really in no big hurry. I'm more in a hurry to find a specialist that I can sort of work with as the years go by versus the testing itself, so it will be interesting. I will probably get that done next year, but I don't feel the urgency to know.

Andrew Schorr:
Okay. Let me just mention for our friends that—related to specialists. First of all, many of them have been featured on Patient Power programs. You'll also see them on the website of the CLL Global Research Foundation, cllglobal.org. Obviously, there are folks like Jackie and Phil who are on with us today. We'll be doing more broadcasting, I'll mention, from the American Society of Hematology meeting with some other CLL specialists. I'll talk about that in a little bit.

And also The Leukemia & Lymphoma Society has a learning resource center. You can give them a call. It's on their website, LLS.org, and it's leukemia.org as well, and then call them, and they can tell you about doctors who specialize in leukemia in your area. And then you can have a discussion, and you can play off of them some of the things you hear on our programs and say, well, do I need this test now or what do you think. And then you can always get a second opinion as well.

I will mention I was seeing an HMO doctor in Seattle, Washington, who has to take all comers. He mostly saw people who were 68 or 75 years old with CLL, not somebody who was 45 at the time I was diagnosed. And he really had to treat breast cancer, colon cancer, lung cancer, in his normal day of work.

So no disrespect to him, but then I identified a CLL specialist. In my case, in Seattle then there was not one, and then I went to MD Anderson, a long plane ride, but that made sense. It may be now simply another exit on the freeway or across town if you're in New York City, or it could be the next state. But seeing a CLL specialist maybe will be comforting to you, so there's a clear picture. But it can be unnerving in this watch-and-wait period.

And there's Cathy sitting in Lawrence, Kansas, where I guess you know there's not a CLL specialist, and so you're wondering well, should you go to Denver, a bigger city, where there are some and would that give you more confidence as well? So that's a decision you can make, and we'll all try to help you. Again, if you have a question, folks, send it in to cll@patientpower.info. A lot of people have.

So, Dr. Thompson, Nancy heard Cathy mentioned the worry about second cancers. I developed one about 11 years later. Whether it was related to me having the kind of immune system, but CLL developed, or did it come from the chemo drugs that I had or what? Nobody knows for sure. But tell us about CLL and the risk of second cancers and whether new treatments may be changing that picture.

Dr. Thompson:
Yeah. That's a super important question. There are two things I talk about with all of the patients who are in the watch-and-wait group or the watch-and-wait stage of their disease. So CLL, even in the early stages of the disease is associated with some immune dysfunction, and it probably relates to the way the CLL cells actually directly interact with some cells in your immune system. And your immune system is important for two things. One is fighting infection, obviously. And the second thing is preventing the development of cancer.

So there are some cancers that are much more common in patients with CLL, even early-stage CLL, than people without, and skin is the biggest of those. So the most common kind of second cancer or other cancer that patients with CLL get is skin cancer. Mostly nonmelanoma skin cancers, but also melanomas are increased in risk in patients with CLL. So I tell everybody you should have a dermatologist. You should go and see them at least once a year. Some patients have to see their dermatologist every month or two, particularly people who've lived in the South and have complexions like mine and spend a lot of time out in the sun. So that's one thing.

I tell them to get their regular, you know, their age-appropriate cancer screening for prostate cancer, bowel cancer, breast cancer, and cervical cancer. Those are not actually specifically increased in patients with CLL, but it's a good opportunity to kind of talk to people about their general health maintenance.

And then I talk to people about infection prevention, so I really encourage people to get immunized against influenza every year. It's safe to do so because it's not a live vaccine. And I also—the most common type of infection that patients with CLL get that that's serious is pneumonia. So there's a vaccine against a specific pipe of pneumonia, called pneumococcal pneumonia, and you've probably seen it advertised on TV and generally targeted at patient over 65. But because patients with CLL have a suppressed immune system we generally recommend that they get that vaccination done.

Andrew Schorr:
Okay. So, now, what about changes I referred to about newer treatments? (Inaudible) treatments, like I had FCR. Some doctors say does it set you up or slightly for a higher risk of a second cancer. I developed one. Or these newer medicines, ibrutinib (Imbruvica), venetoclax (Venclexta) and then the list is growing now, is there a lower risk there?

Dr. Thompson:
Yes. So the biggest second cancer that's associated with chemotherapy is actually a secondary leukemia or a myelodysplasia, which is like a preleukemic condition and those probably arise from mutations that are induced by chemotherapy in developing bone marrow stem cells. Whether or not the disease, CLL, is in any way related to the development of these diseases is a little harder to tell, but you can see these secondary leukemias develop in patients that get chemotherapy for other reasons like breast cancer as well, so it's probably mostly the chemotherapy that's associated with that type of cancer. Also, fludarabine (Fludara), which is part of the FCR regimen, is a pretty strong immunosuppressive medication and probably contributes to other immunosuppression-related second cancers.

So there are a number of new treatments that are available, oral medications that are more targeted to the CLL and have less collateral damage. In particular, they don't cause DNA damage in normal cells, which is how chemotherapy works. So you would expect that the risk of other cancers developing from using these drugs is going to be significantly less than with chemotherapy. Unfortunately, there's a big lag—well, fortunately there's a big lag time usually between getting the treatment and developing the other cancer.

So, because these new drugs have been around for a relatively short period of time, we don't really have the length of follow-up that's required to identify are they also associated with an increased risk of other cancers. But based on the mechanism of action you would think probably not, that they're probably associated with lower risk of other cancers developing.

Andrew Schorr:
Okay. And this will be a continuing discussion we'll have, but I know people are concerned about that. (Inaudible) discuss with their doctor when it's time for treatment.

Cathy, I want to talk, you and I for a minute, and then I want to bring Jackie into it, about coping. So here we are in this watch-and-wait period. For me, I kind of forgot about it for a while, because I didn't have the swollen lymph nodes, my white count was just creeping up a little bit, and so I wasn't troubled by CLL. I just knew I had it. Once I figured out it probably wasn't going to kill me or anytime soon and it wasn't the acute that Jackie brought up earlier.

How have you coped? I mean, you talked about—it sounds like what you've done is try to take control of everything you can.

Cathy Hamilton:
Well, yeah, I'm sort of a controlling kind of gal. So it's a very weird paradox, isn't it? You have this—it's always in the back of my mind. It's always there every morning when I make my smoothie and put all the healthy stuff into it, I know it's because I have this diagnosis now. So it always lives in the back of my brain somewhere. But when it comes rushing to the forefront is—and maybe this will go away eventually—but it's when I get this weird sort of twinge in my side or just something happens in my body and I think, okay, is that the CLL, you know. It's curtains. And I don't really have that dramatic of a reaction.

But there are times, and it happens weekly when something will happen in this 62-year-old body, and sometimes I swear I can feel my spleen, but it's probably those side stretches I did at the gym. So it's a psychological game that I play with myself.

But it really helps that I feel so good. I haven't felt this good I think in three or four years, just in terms of I haven't had a sinus infection all year, and I usually get one or two. So I kind of see the benefits of this healthier lifestyle I've taken on, and that gives me some peace of mind. But it does just spring to the forefront at the weirdest time, less and less, though.

Andrew Schorr:
I went to this—now I'm not in watch and wait anymore but I went to this organic restaurant we found last night and had arugula and quinoa and all this. I feel so good. So, Jackie, is that what you tell people, is there's certain things that they can do to feel in control? It's kind of in this period of how do you as the patient not feel like a victim but be in control and feel confident in your communication with your healthcare team but if something changes, there will be a plan. I mean, what do you tell people during this period, for their head, you know, and maybe for their spouse or children's head too?

Dr. Broadway-Duren:
Yes, oftentimes patients are accompanied by family members when they come into the clinic. So what I tell them is that you continue to live, lives doesn't stop now. As long as you're feeling well continue to do what you can do. We have a lot of patients who are runners. I tell them to go to the gym, continue to work and just do whatever you feel like doing. And then yoga and exercises, mental exercises. There are some patients I've even referred for alternative counselling to help them cope better. What I do not tell them to do is go to the health food store and buy every supplement that that's available, because many of them, we have no idea what they're doing anyway.

Andrew Schorr:
Right.

Dr. Broadway-Duren:
But you're absolutely right. There is not a weekday goes by that I don't get a phone call that someone is asking me, well, I had an ache in my left arm, do you think it's the CLL? So Cathy is right that every little thing, they start to be paranoid. But I try to get them to focus on positive things and family. If the family accompanies them, I try to get the family to assist in getting them to focus on things that are positive.

Andrew Schorr:
We all have these sort of memorable moments in our life, and, Jackie, I don't think you were in the room, but it was 22 years ago when I was visiting with Dr. Keating at MD Anderson. And Esther and I considered having a third child but we thought, well, if I'm going to be dead from CLL not a good idea, right? We had two kids, we're very grateful. And Dr. Keating looked at all the blood test results like you were referring, thought I'd be in watch and wait for a long time and that newer treatments were in development, and he gives me and Esther a big hug, as he's likely to do with people, and he says, go have your baby. So what happened? Four-and-a-half years, finally had treatment, was in a clinical trial. It worked with a really extended remission.

And that baby is 21 years old, Eton. We call him the miracle baby. But if we were like, you know, all bets are off. It's a five-alarm fire, don't consider having another child, don't go about our life, don't travel, don't do Patient Power, life would have stopped. So I can't do it. All right.

Let's go on with some other questions. But just one other word about anxiety, and Esther has shared this on programs. So we went to a counselor. It wasn't me who was going off the rails. Esther will tell you it was her because she has tended to

be an anxious person. So we went into family counselling. And, interestingly, the counselor, his wife had leukemia. He'd lived it, and that helped a lot. So eventually, and Esther will admit this too, she eventually went on an antianxiety medicine, which has helped her a lot, and yoga and exercise. And I do daily exercise that helps me.

So, it's all, Cathy, about whatever we need to do. Could be our spouse as well, to take back control, right?

Cathy Hamilton:
Yeah. I think too that—and while I will say that Patient Power in particular and the Internet in general—if you know where to look, because there is some bad info out there—has been both a help and then sometimes it's anxiety inducing. I had to learn to step back, especially in the beginning when I was trying to get up to speed about my diagnosis. There were days when I had to pull back, because like there are so many different kinds of cases and stages and tempos of this disease that if you focus on what could happen you start feeling—a lot of what-if scenarios come up.

So I really do have to step back sometimes from all the research and just live my life, because I tend to overthink, just in general.

Andrew Schorr:
Do you think that some women process this differently from men? Because you may have a friend with breast cancer and needed treatment right away or somebody else with another female cancer, treatment right away, and yet you're working with this? I know for me, and I think with a lot of men, let's forget about it if we can for a while.

Cathy Hamilton:
Yeah, I think if we're going to generalize that's probably true. I think we women, we—you know, I was so focused on what my loved ones were going to—how they were going to react when I tried to tell them—and that went very badly, by the way at first. I was so worried about them and their reaction that I got—that alone was anxiety inducing. I read a lot about this. I belong to a wonderful Facebook group for women with CLL, and I read those comments all the time about worrying about family. What's my family going to think when I tell them this news, and I think that's probably a woman thing.

Andrew Schorr:
So first I have to tell ourselves, and this is what a very famous woman years ago on the Internet in CLL said to me, Granny Barb Lackritz, she said to Andrew and Esther, chill out. Chill out. And so I have to remind myself. But then you're telling your child, you have kids in their 30s. You have a grandchild and a husband, you know, you want them not to worry either and get over this concept that all cancer needs to be treated like that.

Cathy Hamilton:
Right. So that learning curve I talked about that took me a good three months to climb, it's almost like you have to convey that in one conversation when you're telling someone your diagnosis. My mother sort of got it right away although it took me three attempts, three lunches, to spit it out and tell her, but likened it to prostate cancer, which a lot of her old male friends have at her retirement facility. Oh, so it's like that slow prostate cancer. And I said, yes, that's what it's like. And the next time we had lunch, she'd completely forgotten I told her.

Andrew Schorr:
Well, Jackie had great advice, and I think, Jackie, you say a lot of your patients bring family members with them.

Dr. Broadway-Duren:
Yes.

Andrew Schorr:
And I think if people can hear the same thing at the same time. And, Phil, I don't know if you've done this, but now we have things like face time like if you have an iPhone or there's other kinds of live broadcasting. Facebook, even use YouTube is providing live broadcasting now where I think I'll just make a suggestion and the technology world, hey, Dr. Thompson, my daughter lives across the country, is on the phone. Can I press the button where as you talk about my situation she can watch?

Dr. Thompson:
I've definitely had that before, and I think it's useful. The more people you have that are there the more likely information is to be retained. It's such difficult information to retain for two reasons. One is that patients are often so anxious, and you know when you're anxious you get tunnel vision and people can be talking and your brain is focused on one thought and so everything else just goes past, and it's helpful to have someone else there to write things down that you might have a missed.

The second thing is most people have no frame of reference for the concepts that we're discussing. It's a pretty complicated disease that we have 10 years plus of training to be able to understand. So I think repetition helps. But some of my patients will write things down in the consultation, and some will even record it. And, you know, I know some of my colleagues probably worry about people recording conversations because they think, oh, my god it's going to get used against me later in a lawsuit. But it's actually enormously helpful for patients because they can go back and say, well, I can't remember what the doctor said about X, and they've got it there on the recording. Oh, he said that. So I think as long as you're kind of transparent about it, you know, I think that can be a useful tool.

Andrew Schorr:
I want to mention just—and we've been at this a long time, folks, 22 years. Cathy's now learning now, 10 months, and Jackie's been doing it decades. Phil has been around it for a decade or so now. Here's a thing: Get the right healthcare team, okay? And then there will be these follow-up visits or blood tests. Even when I was in Seattle during that watch-and-wait period I had the cooperation between my general oncologist and the folks at MD Anderson, and they were faxing—remember faxes?—they were faxing my blood test result. And then at some point bing, bing, bing, Dr. Keating says, hey, given what I'm seeing and how you're telling me you feel we should discuss treatment, right?

But the point is have that collaboration. Have a team that you feel good in, and then communicate with them if something's going on and go on with your life. Jackie says she gets calls, oh, my arm hurts, could it be the CLL. Well, she's there to answer the question for you. So get the right team. And then it may be an extended time.

And then, Jackie, how long can this watch-and-wait period go? I have one friend in Seattle, he's been in watch and wait for the same 22 years that I've undergone treatment. It's very variable, right?

Dr. Broadway-Duren:
It's very variable, so it can go on for years, as you stated. So it's individualized depending on the patient and all the different factors that we discussed and what those are.

Andrew Schorr:
Right. So wouldn't it be a shame if you're so overwrought with anxiety and you've got four years, five years, 10 years, two, whatever it is, and you've wasted today or tomorrow—I don't mean to be a psychologist, I'm not, but I'm just saying that's what—I've been around this a lot, is how to go on.

So one last question for Phil and then we're going to wrap up a little bit and we have a lot more CLL programs coming. Joe, we got a question in and he asked it, Deborah said in the watch and wait, is there anything I can do as a patient to slow progression?

Dr. Thompson:
Yeah, well, that's an interesting question, and I think people have probably done some research about some supplements and things that they have been able to take that have activity against CLL. There was a clinical trial at the Mayo Clinic about using green tea extract. There's been some data to suggest that turmeric has some anti-CLL properties, so there are a lot of people out there that try these things. I have to say, you know, I would say that the—in clinical trial that was done at Mayo there was some anti-tumor activity seen though it was relatively modest. So some of these things probably work.

I do think they're kind of better to be formally studied in a clinical trial, because a lot of chemotherapy drugs came from natural substances, and it wasn't until they were kind of systematically studied that you worked out, A, how effective they are, and B, were there any unexpected side effects. So we really don't know if we take a huge dose of green tea extract or

turmeric, is it going to potentially have some side effects. But I don't generally recommend for people take those things. If people are already taking them, I don't tell them that they have to stop unless they're having other treatment.

I always tell people to exercise. I think it's super important. Right across oncology people, do better from cancer—cancer-associated outcomes if they're fit. And I also think it's just good general advice. I tell people to keep a good relationship with their primary care provider and get all of their regular health screening done because some people get so focused on their leukemia that they forget about everything else. And I say, I've had to say to patients before I say, you know, you have all of these cardiac risk factors, you know. I'm going to be really mad at you if I've cured your CLL, and you die from a heart attack. So I tell people to focus on all of those things.

And then I—you know, a lot of people want to know is there a specific diet that I can eat that might be helpful, and it's a hard question to answer, because there's a bit of a lack of systematic evidence. But for example we have been trying to do a clinical trial for a number of years with an extract that you get from cruciferous vegetables like watercress. It's called PEITC. It has a very long name.

But there are probably many things in our diet that can help prevent cancer, and I think that's been shown with vegetarians versus non-vegetarians and things like that. But once you actually have a cancer it's likely, it's hard to eat enough broccoli or enough watercress to get pharmaceutical amount of this stuff to actually do something significant to the disease. But I do tell people I don't want you to eliminate food groups. I want to you eat a generally healthy, balanced diet and look after your weight, because overall the prognosis from CLL is so good that you have to kind of continue to look after the rest of your health. It's not a ticket to drinking a bottle of wine a night and a one-pound steak every night.

Andrew Schorr:
Right. Thank you for that. I want to just point out to our audience as we get close to wrapping up, and thank you for sticking with us, on the Patient Power site we have a number of programs with an oncology nutritionist, Julie Lanford, L-a-n-f-o-r-d, so look up those. I think she's also, has her own website, cancerdietician, I think, .com, might be .org, but take a look at that. She's certified in this area. She's down in North Carolina.

So, Jackie, final comment for people from you related to people watch and wait. What do you want to say to the audience if they find themselves in this watch and wait? What do you want to say to them?

Dr. Broadway-Duren:
I want to say make sure that you, as Phil stated, make sure that the other coordination of your health is taken care of. Continue to follow up with annual screenings. Make sure you have some type of support system, whether that be your family, whether that be a CLL support group or something in the faith-based community.

But you got to have something to focus your mind on other than, as Cathy said, just sitting there dwelling on this and that way continue to live. You can't just stay home. And we'll be monitoring you closely enough when we see you in our clinic or whatever clinic you're going to that if there are changes, we'll be the first to let you know. So until then, just live your life to the fullest that you can.

Andrew Schorr:
Right. Like Dr. Keating said to me and Esther, go have your baby. And we did. Dr. Phil Thompson, from MD Anderson I want to thank you for your devotion. And because you're a younger physician you still have to carry on what Dr. Keating promised us years ago. Will you please cure CLL?

Dr. Thompson:
We're working on it. I think we're making a lot of progress actually.

Andrew Schorr:
Okay. And Jackie, you've been so devoted to us for so many years helping thousands of patients. Thank you for all you do in your role at MD Anderson.

Dr. Broadway-Duren:
Thank you.

Andrew Schorr:
Okay. Cathy, just being a participant in this program was this helpful for you to hear this today?

Cathy Hamilton:
Oh, absolutely. Yeah, it was just reaffirming in many ways. I got some new information, and it was an opportunity for me to thank you guys at Patient Power because, I'm not kidding, I found you like the night after I was diagnosed and immediately felt just a little bit better about the whole deal. So thanks.

Andrew Schorr:
Okay. Thank you, Cathy. We wish you all the best. May your watch and wait go forever, but if it doesn't I think we'll be talking about how there's a lot going on. And I wanted to mention that just as we close.

So, first of all, I'm here in the San Diego County and just 30 miles south is the San Diego Convention Center. And this year, Dr. Thompson and a whole lot of people, maybe Jackie as well, but like 30,000 people from around the country, many of whom specialize in blood-related cancers are going to be there, and the latest research is presented. And we are covering. And so there will be live broadcasting on Saturday, Sunday and Monday, our wrap-up. And you can sign up for it, so make sure you're signed up from the daily wrap up from ASH for Patient Power, and we'll make sure you have the link to that if you haven't already signed up. Esther and I will be hosting that.

It won't always be about CLL, but I know we'll have Dr. Nicole Lamanna, who some of you have seen, and Dr. Jeff Sharman. Two CLL experts will be with us to break down the CLL news. That's on December 3rd specifically.

Also on December 5th after this American Society of Hematology meeting we're going to talk about the financial and insurance issues related to cancer and, of course, CLL as we talked about these expensive oral medicines and even where more than one may be used in combination. How do you afford that, whether you're on Medicare, commercial insurance, whatever it may be? So look for that.

And always go to patientpower.info/events, e-v-e-n-t-s and we'll give you all the information. I want to thank the CLL Global Research Foundation for sponsoring today's program, Dr. Keating and the team there. And I want to thank the financial supporters, Gilead and also AbbVie Incorporated and TG Therapeutics. Thank you all. And so we'll see you from ASH if we can, American Society of Hematology this weekend. And I hope if you are in watch and wait or your loved one that you take some confidence, a little calming from this and know that we've got your back.

I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.