

## Transcript | Answers Now: CLL and Fatigue

### **Brad Adams:**

Hello, everyone, and welcome to today's episode of *Answers Now*, the *Patient Power* series on CLL. Today we're going to be discussing something that I think is near and dear to all of us, and that is fatigue and what we can do about it.

For those of you that don't know me, my name is Brad Adams. I was diagnosed with CLL in 2010. I was treated with FCR (fludarabine + Cytosan + Rituxan) in 2014. I relapsed in 2019. In September of 2020, I joined a two-year clinical trial that combined obinutuzumab (Gazyva), acalabrutinib (Calquence), and venetoclax (Venclexta). And I finished that trial about three weeks ago and I am in remission. Yes. And really, I feel blessed on this 12-year journey that I've been on with CLL. And so I've made it my mission in life to help as many CLL patients as I can, and I hope that by hosting these webcasts, I'm doing that.

Our guest today is Dr. Carmelita Escalante. Dr. Escalante is a professor in the Department of General Medicine at MD Anderson Cancer Center, where I'm treated, and she's also a clinician in the cancer fatigue clinic at MD Anderson. Dr. Escalante, welcome, and thank you for volunteering your time and your expertise.

### **Dr. Escalante:**

Thank you very much. I'm happy to be here with you and the group.

### **Brad Adams:**

So, a little bit of housekeeping, everybody, before we get started. I want to thank our sponsors today, Janssen Oncology, and Pharmacyclics LLC. As with all *Patient Power* programs, they have no editorial control whatsoever over our content.

If you have a question for Dr. Escalante, please use the Q & A button at the bottom of your Zoom window. If you're watching us on Facebook, then enter your question as a comment. Our producer is monitoring the questions and will be feeding those to me, and Dr. Escalante will answer as many as we have time for. I have a feeling we're going to have a lot, so be patient with us. We'll get to as many as we can.

Dr. Escalante. I have to admit, I'm embarrassed. I've been at MD Anderson for 12 years and I did not know about the fatigue clinic. So how about starting us with a little bit about what the fatigue clinic is and what you do?

### **Dr. Escalante:**

So we started the clinic over 20 years ago because fatigue is the number one symptom in our patients in the cancer population. It surpassed pain. And at the time, there was a lot of discussion on how can we make this better. As our treatments became more extensive and aggressive in our conquest to cure cancer, there were long-term residuals from treatment effects, fatigue surpassing all the others.

So several of us got together and developed a multidisciplinary clinic to try to help patients with fatigue. I am the medical director of the clinic. There are a couple of physicians. It is a fairly small operation. But very few centers have a cancer-related fatigue clinic solely dedicated to that symptom.

**Brad Adams:**

So that-

**Dr. Escalante:**

We see patients all throughout MD Anderson, both solid tumors and hematologic patients, as well as patients with myelofibrosis, and sometimes, preceding cancer or diagnosis transition to leukemias.

**Brad Adams:**

So you actually answered my next question, and that was, are there many other fatigue clinics like ours in the U.S. or around the world? So this is-

**Dr. Escalante:**

Minimal. We often have guests that will come to see how we do things, but there are a lot of resources that go into it to dedicate an effort to treating fatigue. We're a large comprehensive cancer center, so we have the volumes of patients and the resources to be able to do it. But many times, especially in smaller cities or rural areas, or even non-academic hospitals, there just are not the resources to do this.

**Brad Adams:**

I know a lot of CLL patients are in rural areas and don't have access to cancer centers like MD Anderson, and a lot of CLL specialists offer consulting remotely. Does our clinic offer that service?

**Dr. Escalante:**

We do do consults via telehealth since COVID began.

**Brad Adams:**

Mm-hmm (affirmative).

**Dr. Escalante:**

And we have been doing telehealth, both follow-up visits as well as new consults. But they are MD Anderson patients that have been seen, in some aspect, through our oncology clinics at MD Anderson. So they are not patients being treated by outside oncologists that we're just seeing for fatigue. But COVID helped transfer a lot of our technology, and so we have been able to do this throughout the last two to three years via telehealth.

**Brad Adams:**

Okay. So let's say I'm a CLL patient, and I'm in fatigue and I come to the clinic. What typically do you do, and what are the options that you look at in terms of treating fatigue?

**Dr. Escalante:**

So the first visit is the most intensive. Fatigue is very nonspecific, and many times, there are numerous factors that may be contributing. So some of the first things we do is a comprehensive history and physical exam. Some of the aspects specifically having to do with fatigue that we look at is, what is the extent of the malignancy at the time. We know that patients with more advanced disease tend to have more fatigue. What are the treatments they have had in the past and are they currently undergoing treatment? We know that multimodality treatments, meaning different lines, like chemotherapy with radiation, with surgery, our SCT patients that are heavily treated tend to have more fatigue.

We look at other symptoms and we do a symptom survey, a validated tool prior to entering the room with the patient that encompasses fatigue, pain, depression, anxiety, stress, sleep, and apathy. And I tell my patients, I don't treat numbers. I treat patients. But it helps guide me because we know that the larger symptom burden can increase fatigue.

We also look at other comorbidities because uncontrolled diabetes, or hypertension, or heart disease can contribute to fatigue. And many times, it's multiple factors. I also ask specific questions about the fatigue like the frequency. Is it every day? Is there a pattern? Is it worse at a particular time of day? Did you recognize particular factors that make the fatigue better or worse? Those are some examples of the specific aspects of the history that I want to know regarding the fatigue. And of course, when did it start? Is it better? Is it getting better, worse, or the same?

**Brad Adams:**

So, once you've done that comprehensive checkup, what treatment options do you look at?

**Dr. Escalante:**

So the interventions, unfortunately, are limited, especially pharmaceutical. But the best data and the number one intervention that has been shown in cancer-related fatigue is exercise. And it sounds contradictory because patients are telling me they're fatigued. And one of the first things I'm going to have them do if they're not already doing it, is to start moving. Again, there's been a number of studies, most of them rather small, with different types of cancers, a lot of breast cancers. Different types of exercise. Different timeframes, some during certain aspects of treatment. The bottom line is fatigue got better and quality of life got better. And what I tell my patients is that exercise is not only good for fatigue. It's part of healthy living. It decreases cardiovascular risk. It helps with weight control. And it helps with mental health, both depression, and anxiety. So there are a lot of positives to exercise besides just managing fatigue.

The other intervention that has good data is what I call behavioral intervention. And those include things like prioritizing activities. Determining which things on your list of to-dos have the most impact. Trying to correlate those. If many of my patients can tell me the part of the day they have the best energy – doing your harder task when you have the most energy. Doing the easier things when you have lesser energy. And of course, trying to delegate some of those tasks, or trying to drop them off the list if they have no impact. Many times we have a list, and it doesn't really matter if you do it today, tomorrow, next week, or never. And so, trying to be realistic about it.

The other big pot of things is energy conservation. Trying to save the energy you have for the things you value most. For example, looking at how you do things. Some of my patients like to cook. So, trying to get a stool to sit on, to stir the pot, or chop the vegetables, or even, wash the dishes. Some of my patients like to garden. Instead of sitting down and bending down over the ground, sitting at a table and potting plants might be a solution that still allows you to participate but the energy use is not as much. So those are some examples.

Those two have the better data. Now we have used stimulants. Stimulants or drugs. The one most commonly used in trials has been methylphenidate or Ritalin, which is a long-time drug used and approved for attention deficit disorders. None of the stimulants or drugs, any drug, is approved for cancer-related fatigue, so we have to use them off-label.

In my experience, and in doing trials, you have to have a placebo arm because there can be a placebo effect. Most, we started in very low doses and escalate, but the data is not as good as exercise or as behavioral interventions. So, especially, when my patients have more than physical fatigue and may have some cognitive fatigue as well, it may be more effective because, of course, most of these drugs have been for attention deficit disorders. We have used two stimulants: armodafinil, which is Nuvigil, and Provigil, which is modafinil. Those are approved for sleep dysfunctions. But they're more expensive and they're harder for patients to buy, and many pharmacy coverage plans will not pay for them because they're not approved for cancer-related fatigue.

**Brad Adams:**

I was actually on Ritalin several years ago. I was dealing with fatigue, and my specialist at MD Anderson at the time said, "Let's try this." And unfortunately, I couldn't sleep because the Ritalin just kept me wired all the time. But it's interesting that there aren't really many pharmaceuticals that are of much help. What about caffeine stimulants during the day? What's your advice on that?

**Dr. Escalante:**

Caffeines are very mild stimulants. So they fit into that stimulant category, but they're very mild. The same with these energy drinks or tea. They have caffeine or caffeine-like products in them, but they're very weak stimulants. Some patients, if it gives them a boost, may use it. You have to be really careful how much caffeine you're drinking throughout the day. Of course, it can cause diuresis which means you go to the bathroom a lot. And you can go through withdrawal with coffee if you drink a lot of coffee and then you stop.

**Brad Adams:**

Yeah. Is there any evidence that any kind of supplement can help with fatigue?

**Dr. Escalante:**

There's no real evidence. There have been several that have been studied. But at this point in time, there's no hard data that really shows about supplements. Many of my patients ask about vitamins. And unless you're deficient in vitamins and you're replacing a low store of vitamins, it doesn't really help. Or a multivitamin, I would only prescribe if you don't have a healthy diet and you're not eating well, then maybe take a multivitamin. But the data hasn't shown that a multivitamin if you're eating well, is going to improve fatigue.

**Brad Adams:**

I know, for me, there were times when I was not in treatment, and I was really tired. And then when I was in treatment, especially in this two-year trial, either the venetoclax or acalabrutinib, I think, made me tired. So how do you distinguish between fatigue caused just by the disease itself and then fatigue caused by the treatment you're on, or does it really matter?

**Dr. Escalante:**

Well, sometimes, when I evaluate patients, I can identify factors that may be contributing to fatigue, and maybe multiple factors. Some things I can do things about. Some things are not under my control, for example, past treatment effects. I can't do anything. That's done. And going forward, sometimes in active treatment, unless fatigue is overwhelming and you can't function, most times, both the patient and oncologist really don't want to scale back the treatment unless it's absolutely necessary.

So we look at other factors. For example, if there's depression. If there's uncontrolled pain. The real challenge has been insomnia or sleep dysfunctions, and many of our cancer patients have those. And we do know that if you have poor sleep, with a lot of getting up and down during the night, you're going to have fatigue the next day. Now, what I can't tell you is how much each factor is contributing to the fatigue. And so, we have to go and try to work on the factors we can control and see if we can bring that fatigue level down. And what I tell patients is, I may not make it zero. But if we can go from a severe level to a moderate level, or moderate to mild, most patients will really see a difference in their ability to do things.

**Brad Adams:**

When would you tell a patient that it's – so, a patient's experiencing fatigue, and he or she is not really sure that – "I'm just tired," or whatever. When is the right time to go to your specialist and then maybe to you, for example, if you have the option, and say, "I'm really dealing with some fatigue." I guess a general definition of cancer fatigue maybe would be helpful.

**Dr. Escalante:**

So the National Comprehensive Cancer Network, NCCN, has a cancer-related fatigue guideline, as well as ASCO, the American Society of Clinical Oncology. I sit on both those groups. So there's a panel of experts and we come up with guidelines. They also have patient material. We encourage patients, even before they start treatment, they should be educated about fatigue. And then they should learn about early things, general education before it happens. But certainly, during their treatment, they shouldn't feel inhibited to talk to their oncologist and say, "I'm having fatigue."

I guess there's a fear that the treatment may be decreased, or there's nothing anyone can do that might discourage them, as well as the caregiver, the physician, or the clinician, that it's hard to deal with. It takes a lot of time. There are not a lot of options, and they may not be the most expert in that area. But I definitely think they should discuss it and bring it up to their provider. And for example, in our center, we have another area that they can be referred to, where we do an in-depth dive into cancer-related fatigue and try to see what we can do to help our patients.

**Brad Adams:**

Getting back to exercise. You said that was really the number one thing to do. Do you have any recommendations in terms of what kinds of exercises to do, how often you should do them, and so forth?

**Dr. Escalante:**

So it all depends on where you're starting from. And I tell patients, especially patients that have been in treatment and have not exercised in a while, you cannot pick up where you left off, unfortunately, with exercise. You have to start over and you have to pace yourself. So it also depends on whether they exercise and what's their functional status. Some patients may have been quite an exerciser before their diagnosis, whereas others may have never exercised. It may start off with just walking. Certainly, if they have significant cardiovascular diseases or angina, we may want a workup before starting an exercise program. Some of my patients start with rehab or physical therapy, especially if they've really had a decline in their functional status.

But the recommendation is a goal of a minimum of 150 minutes a week of exercise however you want to cut it up. It could be 10 minutes three times a day. It could be 10 minutes one day, 60 minutes another day. But I tell my patients, especially those starting from baseline, it may take

six to 12 months or longer to get there. And if they try to do too much too quickly, they'll hurt themselves. They'll pull a muscle or fall, and then you have to start over.

The type of exercise depends, again, on functional status. Data has shown that aerobic exercise may be more helpful in fatigue. But I'm a proponent of a balance with resistance and with aerobic so that you have muscle toning as well. It could be armchair exercises for some that are very debilitated to start with. Just doing arm exercises or using a rubber band. It could be with a trainer for those that have the means to hire a trainer. It could be yoga, rubber bands. Some of my patients, bike, play tennis. Again, it all depends on where we're starting from. But it means gradually building up the conditioning and stamina as you exercise. And the fatigue improvement takes a couple of months of consistent exercising to see any change in fatigue. It's not going to happen with a few weeks of exercise.

**Brad Adams:**

Okay. A question from the audience, Dr. Escalante. A little bit on a different subject. This particular patient got their second booster, and was sick for a few days, and then fatigued for two months. Things gradually got better. Is it what you would consider a normal reaction for people like us who are immunocompromised to have had that fatigue reaction?

**Dr. Escalante:**

I'm not an expert in COVID fatigue, but it is possible. Even patients without cancer can have side effects from the COVID vaccines, whether it's the initial vaccine or the booster, and it's variable. I mean some of my patients get it and have a minimal reaction. Others have more prolonged. I mean if the timing's with the vaccine, it's likely related to the vaccine, and it may be some of the component of reaction to the vaccine. But it's not really considered cancer-related fatigue, per se.

**Brad Adams:**

Okay. I'm going to keep going with questions from the audience. Does fatigue improve after you've finished something like venetoclax, which I just finished three weeks ago, or other drugs, and you're in remission? So this question really could have come from me.

**Dr. Escalante:**

It can. Yes, definitely. And what I tell patients is, when they finish radiation or treatment, it's not going to get better the week after. It will take a while, depending on the drug, depending on the half-life of the drug, or the radiation. Most patients, within six months, sometimes up to 12 months, they'll kind of plateau, if they get no other treatment once they finish. For most patients, it'll gradually get better. Now whether it goes back to zero is unknown. Again, some of that depends on all the other factors contributing to fatigue and how heavily treated. How long were you treated? Did you have previous treatments? Et cetera. But generally, by six months, the majority – sometimes, up to 12 months, then it'll plateau, and you get an idea of where you're going to level off.

**Brad Adams:**

I know for me; the fatigue level has decreased dramatically in the time since I stopped. Usually, at about 10 o'clock in the morning, I would hit a wall, and I had to sit down and have some caffeine to get me going again.

All right. Another question from the audience about anything you can recommend to improve the chances of getting a good night's sleep. Any ideas? A routine to get into or something?

**Dr. Escalante:**

Yeah. I mean, insomnia is a real challenge. Not only for cancer patients but for all patients. But cancer patients tend to have lots more problems with sleep disruption. And part of it is falling asleep and staying asleep. The longer contiguous hours you have – there are four cycles of sleep, and REM is where you get refreshed. Every time you wake up, get up – and some of my patients may wake up and go to the bathroom, or just wake up three to four times a night, you disrupt that sleep cycle.

So, sleep hygiene techniques are important. Some things for sleep hygiene – going to bed at the same time. Getting up at the same time. A bedroom with no TV. No watching TV in bed. The bed is only for sleep and intimacy. Cool, dark room, with nice linens, to make sleep conducive. Eating your evening meals several hours before bedtime and exercising earlier. Exercise is stimulating. You do not want to exercise before bedtime. Avoiding caffeinated products in the evening. Things like tea, coffee, chocolate, anything with caffeine products in it.

Then if you wake up, or if you can't fall asleep once you turn the lights out, wait about 15 or 20 minutes. And if you're still awake and you're not falling asleep, you go in another room. You don't pull out the screens. You need to turn off the TV, the phones, the computers – they're all stimulating – at least an hour before bedtime. Read a book. A *real* book, and not a suspense novel. We want you to fall asleep. Or listen to relaxing music or nature sounds. Once you get sleepy, you go back and lay down. And you keep doing that as many times a night as you have to, but you have to get up at the same time. You can't sleep in. Those are some basic things that might be helpful. We have a fatigue education book, that has all of these things in one resource, that we give to our patients when I see them at the initial visit.

But sleep can be exceptionally challenging. Hypnotics or sleeping pills are meant to be very short-term, and we don't typically use those. Melatonin may be helpful, and you can try melatonin, but sleep is behavioral. And so it's very difficult if you're dieting. Are you trying to get off tobacco products? It's a lifestyle change. So it's changing your behavior, and it's hard. It can be very difficult.

**Brad Adams:**

So, another question from the audience. Do we really understand the underlying cause of fatigue in CLL, especially when you're not in treatment?

**Dr. Escalante:**

No. Cancer-related fatigue, there's lots of interesting work going on. We don't know the pathophysiology, what causes this? There are lots of hypotheses, our thoughts of how it might happen, and people studying it to see if they could figure it out. Because if they can figure it out, then we may be able to target a treatment, but that hasn't happened yet. But some things that people are considering, is it cytokine release? These small substances that are inflammatory in nature. Is it a genetic component? Is it a muscle metabolism disorder? Is it related to the hypothalamic area of the brain? Those are all thoughts about what could be triggering it, but no one really knows.

**Brad Adams:**

Okay.

**Dr. Escalante:**

And also, we don't know, for example, how the stimulants work or exercise for that matter. Is it

the release of substances from the brain during exercise? No one knows yet how that interferes and improves fatigue.

**Brad Adams:**

Okay. Here's a question that's near and dear to my heart. How do you feel about naps?

**Dr. Escalante:**

Naps are fine as long as they don't interfere with the night's sleep, okay? When they start getting really long and a lot of them during the day, and then you can't fall asleep at night or you can't stay asleep at night, I tell patients, "Set an alarm." But shorter naps, that refresh you and do not interfere with your night's sleep, I'm fine with.

**Brad Adams:**

Okay. Another question from the audience. "Been in watch and wait for a long time. Used to exercise regularly, but now having a hard time recovering. What recommendations do you have to cut down the exercise and improve recovery?"

**Dr. Escalante:**

Well, generally, when we increase the exercise, recovery improves. But it has to be paced. Recovery can be a lot of things to a lot of people. It can be physical recovery. It can be emotional recovery. And so it's a fine balance. And some of my patients, before they start exercising, say, "I can't do it. It just wears me out. I can't do it." And so I'll say, "Well, let's start slow." Sometimes I'll write a physical therapy prescription, to just start with general conditioning. Sometimes we'll start with armchair exercises.

If you go to YouTube, there are lots of videos with armchair exercises or other – if some of my patients have a lot of joint problems, we start with water-based therapy. Water aerobics. Or, if they have a pool, walking in the water even. Sometimes it's counting steps, using your phone in the app, just to count your steps. Get a baseline. Maybe it's 2,000 a day, and we'll say, "Let's try to get to 3,000 and see how you do." Then "Let's try to get to 4,000."

So I think it's a fine balance. But at some point, recovery encompasses being able to move. Being able to do your basics. Being able to get out of the house. And unfortunately, you get more deconditioned if you don't move.

**Brad Adams:**

Yeah. Several people have asked about whether the guidelines for treating fatigue, that you've talked about, are available on the MD Anderson website. Is that all of that information available?

**Dr. Escalante:**

I'm not sure if they're on the MD Anderson website. But *NCCN.org* and ASCO have them posted under their pathways and algorithms.

**Brad Adams:**

Okay. So, *NCCN.org*.

**Dr. Escalante:**

So they could probably – and they do have patient education material. If you go to their website, they probably have a way that they can see them. I mean, I sign in, so I know I can get to them.



**Brad Adams:**

Mm-hmm (affirmative).

**Dr. Escalante:**

But I don't think MD Anderson has them directly on their website.

**Brad Adams:**

Okay. And what about the book that you mentioned earlier? Where can people get that book?

**Dr. Escalante:**

Oh, the education booklet? We have it through our patient learning library. It's there.

**Brad Adams:**

Yeah.

**Dr. Escalante:**

We also have a link. But I forgot; I'm trying to think of what – the patient education helped us develop it.

**Brad Adams:**

Mm-hmm (affirmative).

**Dr. Escalante:**

So through patient education. It may even be on their website. I'm not sure. Since we've been doing telehealth, we've been sending the link to our new patients. But when the patient comes to see me, they get a hard copy that we printed up with the help of our patient education group.

**Brad Adams:**

Okay. All right.

Back to some of the questions that I'd had in my mind. Do you see different fatigue levels depending on the category of treatment? For example, with CLL, there are the BTK inhibitors, ibrutinib (Imbruvica), acalabrutinib, et cetera. There's the Bcl-2, venetoclax. Is fatigue different depending on which of those drugs you're taking?

**Dr. Escalante:**

I mean fatigue can vary a lot. If we just look at the drug – and there are always new drugs coming out, even phase I. Early drugs that we don't even know some of the side effects yet. That when you're on a clinical trial, they track all your symptoms to determine how bad is this drug going to be for "X, Y, or Z," including fatigue, which is a commonly-tracked symptom when you're doing a clinical trial, especially with these oncology drugs. We do know that certain groups of drugs may be worse.

My patients, after they've experienced them, it can fluctuate depending as well on anemia. If there are dips up and down, we know when the hemoglobin goes down more that the fatigue is compounded. Surgery alone does not tend to cause a lot of fatigue, but radiation can. And of course, chemotherapy, immunotherapy, other types of therapies. And of course, more, I guess, lines of treatment, more heavily-treated patients, it may have a more synergistic effect.

But yes. There are groups of drugs that cause more profound fatigue. But it also depends on the baseline of the fatigue of the patient and these other factors we talked about. Do they have pain? Depression? Sleep issues? Because that's going to make it even worse with – you have the drug, plus all these other factors, versus another patient that may have just the drug, but not the other factors.

**Brad Adams:**

Okay. What would you say to patients in these rural areas, or areas where they don't have access to a cancer center, where there might be better resources when they're dealing with fatigue? Where should they go? Certainly, they should go to their specialist first. But what advice would you give them?

**Dr. Escalante:**

Well, we try to put education programs out, like this and others, for patients. We try to educate the clinicians out there in different venues as well, to try to provide more care out in the rural areas. I mean obviously, if they're one of our patients and they live in a rural area, we can even do telehealth as long as some of the states allow it. You know that since the pandemic, we were doing – for example, in Louisiana, we can no longer do telehealth in Louisiana. So some of my patients now have to physically come in to see me, which makes it harder, both on their fatigue as well as all the other factors, when you have to drive in from a distance and stay at a hotel, et cetera.

**Brad Adams:**

Right. One last question, and then we'd better wrap up. Any clinical trials that are specifically studying fatigue in patients?

**Dr. Escalante:**

Presently, no pharmaceutical trials, at least that I'm aware of. I mean, and that's a big gap. We really need more options. There have been more non-pharmaceutical types of trials in the past with yoga, which has been shown to help with exercise, and other sleep interventions, and other interventions. But there is a huge gap in pharmaceutical clinical trials for fatigue, and none that I'm aware of that's ongoing right now.

**Brad Adams:**

Okay. Dr. Escalante, thank you very much for your time today. You and others at MD Anderson have been so generous with your time. We greatly appreciate it.

**Dr. Escalante:**

Of course. My pleasure.

**Brad Adams:**

And I want to thank again our sponsors, Janssen Oncology, and Pharmacyclics LLC.

A couple of things to remind you of. After the webcast ends, you'll be asked to complete a survey. If you would, please fill that survey out because that drives our content. So it directly impacts the content that we provide to you, and hopefully, makes our content better.

Also, I would suggest that you subscribe to the *Patient Power* newsletter. It's a weekly newsletter, and it's full of good information; webcasts that are coming up, webcasts that have been done, and I strongly advise you to consider that. There also is a recent video that *Patient*

*Power* did on hypertension, and you might look at that. So, if you go to *patientpower.info*, you'll find it there: *CLL and Hypertension*.

Again, thank you all for joining us today. I hope this was useful to you. And remember, knowledge can be the best medicine of all.