



## What Causes CLL Fatigue and How Can It Be Treated?

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### **Jeff Folloder:**

Anybody here experience fatigue, raise your hand? Okay, even up here on the stage. I'm sure most of the people in our online audience also experience fatigue. If you read my most recent blog on Patient Power, you'll see that I started off my CLL journey by thinking that I was a typical, early-40s, guy who had a penchant for napping. Turns out, you're not supposed to nap that much in your 40s. When we talk about fatigue, Dr. Lamanna, what are we talking about? Are we talking about napping? Are we talking about just being a little tired? What is fatigue?

### **Dr. Lamanna:**

Yeah, so, obviously, this is a very difficult thing to, to quantify. Some of us raised our hands, whether we have CLL or not. So, fatigue is always a difficult issue to grapple with, because the question is, obviously, it certainly could be related to your disease, absolutely. And, it could be related on different levels. For some, it could be because their blood count's, particularly their red count, is low.

So, if their red cells are the ones, think of them as the ones that carry oxygen to all your organs, they're like having gas in the car of your tank. And so, you know, if you're anemic, or your red count is very low, you can be tired all the time. When you climb a flight of stairs, you're huffing and puffing, you know. Run-of-the-mill activities become difficult, because you get more short of breath. That could be because your blood counts are low. But, then, there can be this fatigue of—not because your blood counts are low. So there are other things that are probably playing into effect, on your immune system, that the disease is impacting, that can contribute to levels of fatigue that we're having a harder time to try to measure or quantify in the clinic, to say this is absolutely, we can measure this cytokine, or this, you know, and this is why you're so fatigued.

So, this becomes a much more challenge for us, for you, obviously, as patients, but for us as the doctors, trying to figure out, you know, for fatigue, is this based on your disease, how do we best treat this, if by other measures, it doesn't seem like you might need treatment for your disease by other markers, so then what do we deal with? How do we deal with this? And, obviously, Michael and some others have been looking at some ways to sorta look at maybe more gentle therapies, or ways to target to see who might benefit from even less intensive therapies, to see if we can manage folks, where we do think the

fatigue might be really related to your disease, but maybe you don't need full-blown therapy. And so, this is an ongoing question that we're looking at.

So, certainly, fatigue can be absolutely part of your disease, I think we grapple with how to measure that, and whether or not somebody needs treatment for your fatigue, based on other parameters about your disease. So, this becomes a little tricky. Michael, you wanna say more about that?

**Dr. Keating:**

Yeah, I think that it is certainly the commonest symptom of CLL. By a long shot, even at very early stages, people will just come in, say I just—and part of it's sort of like an apathy. You're not quite as interested in doing the things that you thought were the fun things that you would get on with in your life, and you just put them off. Now, serendipitously, we found out that a lot of people will respond to methylphenidate (Ritalin)-type drugs. And, at a very modest dose. Fatigue is more common in women, and women have the best response to these Ritalin-type therapies, and Jackie and Alice Lynn, who works with me, one of their major jobs is to make sure that we fill the prescriptions on these patients that are responding very well to that.

Now, we think that they're related to liberation of what are called chemical signals, or cytokines, that go from immune cells to other cells, etc. And, Dr. Estroff, took a drug that was used in a different part of the disease, called ruxolitinib, or Jakafi. And, found that, in a lot of patients given this medication, the fatigue index went down quite strikingly, and many people are continuing on that, and interestingly, it has a bit of an anti-leukemic effect. But, I saw a patient just this week, that her main problem was fatigue, and we tried some monoclonal antibodies, and we tried a little bit of this, and she said, I'm just getting more and more tired.

And, I couldn't find any disease, so I said, let's have a look at your marrow. And, her marrow had no leukemic cells. But the fatigue was terrible. And, one of the things that you mentioned was that when you get on the targeted therapies, a lot of people in a short period of time feel terrific. So, I got some ibrutinib, and just gave one a day, which is about a third of the regular dose, and within two weeks, this woman said that it transformed her life, even though it wasn't working against the malignant B cells, it was modifying them, probably to normal B cells. So, the good news that happened this week was that we announced that there's a new chair of symptom research at MD Anderson, because it's not just CLL patients that have fatigue. We have a fatigue clinic.

Because cancer is associated with fatigued, and therefore, to say that we're improving the quality of life, we've gotta get to the point where people feel energetic enough to actually enjoy it

**Dr. Keating:**

But, you know, one of the things is that, as Jackie mentioned, the first thing she asks is, how's your fatigue level? That's an indicator that something's out of balance. And so, the wonderful things that are happening now is, how well we can identify different immune cells, and different cytokines that may be associated. So, I think that there are gonna be drugs that will be very specifically developed for the fatigue situation, in all of the cancers, over the next little while.

**Dr. Lamanna:**

But, but fatigue can be multi-factorial, so there could be many reasons, so it's an important thing to bring up.

Obviously, depending upon their different degrees of fatigue, and how to manage them could be different for each individual. So, it's really, really important to talk to your physicians about them, because they could be related to something else, and some infections, and viral things. There could be a lot of other things that could be related to fatigue, so it's an important thing to bring up and talk about.

**Dr. Keating:**

And, if you can convince patients that are feeling fatigued to actually get up and exercise, exercise generates your own adrenaline, and so that you get a little more perky. But, and I can honestly say that I push that very hard, because I don't exercise, personally.

**Dr. Ferrajoli:**

I do instead, because fatigue tends to be a cycle, and if you can break the cycle by doing regular exercise, it's very likely that your fatigue level will decrease and so, I do tell my patient that these are the same recommendations as taking your medication. Do your exercise.

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