



Patient Power

What Does MRD Mean for CLL Patients?

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Jeff Folloder:

What is MRD? And why is being MRD-negative a good thing?

Dr. Cohen:

Is this for me as well?

Jeff Folloder:

Yes.

Dr. Cohen:

Okay. So...

Jeff Folloder:

And then we're gonna go down the line if any of you guys have anything to add.

Dr. Cohen:

...so, I guess just to even take a step back, what are we trying to do when we treat a patient with CLL, what is our goal? The first goal especially if somebody's having symptoms, is to have them feel better. That's our first measure of success is that if somebody's having symptoms from lymph nodes, or fatigue, or from anemia, or whatever it may be, we want them to feel better. That's what we're trying to do. But once we've accomplished that goal, then we start to really look at more objective measures of response to treatment, and that helps, at least helps me, get a sense for how long is this response going to last, and how well may this patient do over a long period of time?

And there are a number of ways that we can objectively assess response to treatment. And the easiest is to draw your blood and to check your blood counts; so, if you had a low hemoglobin or a low platelet count, we can see those start to recover. If you had an elevated white blood cell count we can see that start to go down. We can see lymph nodes shrink. So, those are all objective measures of response. And for a long time that was sort of the way that we would assess response to treatment. In recent years, we've started to develop newer ways to go beyond that.

So, yes, your blood counts may be normal, yes, your lymph nodes may be gone; but we know in most cases a patient's disease is going to come back, and we can't always tell at the time of finishing therapy how long that's going to be. And so, we have newer approaches to look into that. And what that group of approaches is collectively referred to is MRD, or minimal residual disease. This means disease, so in this case would be CLL that is still present in the body but that is not detectible by our most common means. And there are a number of different ways to test this. And, depending on the type

of therapy that you've receive, this may or may not be a critical piece of your case.

So often, for example with people that receive chemotherapy and that are stopping treatment, MRD is a little bit more of a common goal. Whereas patients that might be on oral therapy where the rate of achieving MRD negativity is not as high, if those patients are tolerating their therapy well and have had a good response, I may not care as much about whether or not they achieve MRD negativity because what we're going for with that treatment is a little bit different. The last thing I would say is that MRD testing, and I'll be interested to hear what the others have to say, in CLL is still a little more of—it's just on the cusp of being used in clinical trials and started to carry forward in clinical practice.

I would say that at least in my own practice if I were to test somebody for MRD and they were still positive and they had completed chemotherapy, I wouldn't necessarily immediately think that they needed to go back into treatment. So, if you are having an MRD assessment, or if you end up enrolling in a clinical trial and MRD is part of it I would make sure that you have a good discussion with your physician about what does this MRD mean for you and what to expect for you moving forward.

Dr. Rogers:

Can I go now?

Jeff Folloder:

Everybody wants to jump in the pool here, I can see.

Dr. Rogers:

So, there's a couple things that people commonly ask me about MRD that I just wanna say because I think it's really important towards understanding it. One was what Jonathan just said, and that it's not really important to assess in people that aren't in clinical trials in most cases. So, it's not something that is routine or needs to be done. So, if you're taking an oral agent like Ibrutinib (Imbruvica) that works extremely well even though it doesn't really cause a lot of MRD-negative responses, it's more of a research question than a regular clinical practice question. A couple things about it. So, it's Minimal Residual Disease and you wanna be MRD negative, meaning there's no detectible leukemia, but that doesn't actually mean that there's no leukemia left in the body, it just means we can't...

Jeff Folloder:

...that's a mean fact.

Dr. Rogers:

Yes, exactly. It just means that when we looked with whatever test we used, we couldn't find it in the blood; or couldn't find it in the bone marrow; or couldn't find it in the blood, or the bone marrow. But that doesn't mean that it's not in some of the tissues of the body. You know CLL is a blood cancer and can go anywhere the blood goes, which is everywhere. It also means that there could be leukemia still in the blood but our tests just aren't sensitive enough to detect it. I have people that come back that are in clinical trials and ask if they're cured, is the CLL gone forever? Because they're MRD-negative, and the answer to that is no, actually we don't think so it just means that it's below the detection limit of our testing. Does that make sense?

Jeff Folloder:

That makes great sense.

Dr. Rogers:

The other portion of it is the most commonly used test is the FLOW cytometry test where they take blood, it's really exciting, they paint antibodies on the white blood cells and fire it in front of a laser to see if there are CLL cells in there. It sounds fun, because there are lasers and in reality, it's like a big machine that...

Jeff Folloder:

And sharks too.

Dr. Rogers:

...yeah.

Jeff Folloder:

Sharks with lasers.

Dr. Rogers:

But you don't get to see the lasers, right? Anyway, that's the most common test. There are now, some research assays because like I said this test there could still be some leukemia that this test doesn't pick up, so there's some research assays looking at some sequencing tests to look at a particular genetic change to try to find leukemia cells in even smaller amounts than the regular FLOW test can pick up. Those are really exciting to researchers but aren't necessarily important for people that aren't really into research and that kind of thing. So, some people just don't wanna know about these things, it's kind of individual on the patient's side how invested they are.

After chemo, immune therapies which is like the IV chemotherapy regimens that we were talking about having no detectible leukemia generally improves how long you'll remain in remission, or how long before you need a treatment again. I think it's probably going to be true with these new oral targeted agents and these exciting clinical trial combinations of targeted agents. But those are very new and so we don't have the 10-year follow-up that we do with IV chemotherapy. So, as Dr. Cohen alluded to, there's a regimen called FCR which I'm not gonna talk about in detail but in people who are IGHV mutated who took FCR some of them still have no detectible leukemia in the blood at 10 years, which is really exciting.

But that's not something that is necessarily gonna happen with FCR regimen for everyone that undertakes it. So, you also have to be careful what your goals are, what you expect out of treatment before you think about is having no detectable leukemia something that matters to me.

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