Achieving CLL Treatment Goals: Why Is MRD-Negative Status Important?

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Esther Schorr:
Why is the goal of achieving MRD-negative status very important if it doesn't last more than a couple of years anyway? Maybe the goal should be a supportive therapy and reducing the side effects, particularly for older patients.

Dr. Sharman:
I love it. That's a great question, and it actually captures a lot of the debate we've had in the field over the last number of years.

Dr. Lamanna:
I'm glad you got that immediately. It's very sophisticated when you say it.

Dr. Sharman:
Yeah, no, that's great. There has been a general principle that the deeper the response, the longer it lasts. Of course, we're not always right, but generally, the more cancer you get rid of, the longer you stay free from symptomatic cancer. And MRD, the analogy I use, it's when my wife asks me to go to the refrigerator and find something, and I don't find it. It's not that it's not there. I just didn't look hard enough.

Esther Schorr:
That was good.

Dr. Sharman:
You like that? So, MRD we should just say is a very good way of looking for very small amounts of cancer. You should with MRD testing be able to find one out of 10,000 cells as a CLL cell. It's a marker that really got its start when we were talking about chemoimmunotherapy, because chemoimmunotherapy we used to compare studies. And it was, well, my MRD is better than your MRD. So, this study, this is better than that, and that's how we argued in the field. We're actually getting very close in the field to a place where the FDA was going to accept that as proof that one therapy was better than another. And then along came ibrutinib, and ibrutinib is that other therapy that you talked about—that sort of slower, more chronic therapy. And, in fact, I think I probably have the longest treated Ibrutinib patient in the world just on the very first study. And she's been on therapy now for over ten years, and actually, she's still got visible CLL in her blood. I can see it, and it's been there for a long time. And she's doing just fine. Thank you very much.

Dr. Lamanna:
Just hanging out.

Dr. Sharman:
Just hanging out. And MRD went away, and then along came Venclexta or venetoclax, which actually does get very impressive rates of MRD negativity and once again introduces this idea that a fixed duration therapy can leave people free of symptomatic disease for a length of time. Now, I understand the concern is, well, if it only lasts for a couple of years. Well, for a patient with symptomatic CLL who gets a fixed duration therapy and is able to maintain multi-year remission without taking chemotherapy, that's progress in the field compared to where we were. MRD is back in vogue after being gone for a while, and I think a very reasonable question is how we're gonna use it in clinical practice, because I'm not totally sure I know the answer.

Dr. Lamanna:
Agreed. Well, that example was perfect, because I think what we're trying to say is it is important, because we may be able to do utilize this for patients where we really had to fine-tune some patient care with regards to therapies. But Jeff just gave a prime example of somebody who still has detectable disease but doing very well. We always go back to the phrase I always use is does one size fit all? Is that still the case? It may not be because you can have somebody who may do very well on single-agent therapy for years and be fine and have no side effects, and so why muck with that because they're doing great? Versus other people will need other therapy and so I think MRD is back, but we still have to learn how to use it and how to apply it.

Andrew Schorr:
You're having MRD testing, and right now it's very low, right?

Lee Swanson:
Yes. I came out of the Murano trial MRD negative, and it's been now 20 months without any medication. It's back in the flow tests. It's back, but it's not to the point.

Andrew Schorr:
And you're living well?

Lee Swanson:
Yeah.

Andrew Schorr:
You're living well.

Lee Swanson:
Going on about my day.

Esther Schorr:
So, you're really talking about quality of life. If somebody's hanging around and there are some CLL cells in there, but they're doing their daily activities, they're feeling good, so how are we going to use it?

Dr. Lamanna:
I'll take it one step further. Again, in the era of chemoimmunotherapy, we would treat, but then they would be observed. So, after six cycles of FCR, regardless of your response, you were monitored, if you got a complete remission or a partial response. So, how do we use MRD here? Do we introduce the drug sooner, or do we wait until patients actually really, truly have progression and then reintroduce drug? These are things we still have to learn and get to.