Advances in Treating CLL at Any Age

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Andrew Schorr:
Hello. I'm Andrew Schorr. I'm sitting with two CLL experts from one of the leading leukemia centers, and that's MD Anderson Cancer Center in Houston, Dr. Nitin Jain, Dr. Alessandra…

Dr. Ferrajoli:
Ferrajoli.

Andrew Schorr:
…Ferrajoli. I have to get my Italian pronunciation right—and they've done a lot of groundbreaking work in CLL. And some of the areas that they've studied have also been helping for older patients get the best chance at a long, high quality of life. So let's start with you, Alessandra. Should an older patient feel that they get second best, that they can't get the best medicine today?

Dr. Ferrajoli:
No, definitely not because, first of all, when we look at the person, age is not so important as fitness and how your other organ functions are and whether you have any important other diseases. So when we evaluate the patient, we have to consider all those components.

So we may have an older person that is otherwise fit. They can receive what you may call a little more aggressive treatment. But we also may have at times a younger person for which we need to make adjustment. So I truly feel that an older person has the same options than a younger person has. They may need to be personalized. They may need—the therapy may need to be modified but not to the cost of being effective.

Andrew Schorr:
Okay. Dr. Jain, so it used to be with some of the more aggressive types of CLL like 17p…

Dr. Jain:
Right.

Andrew Schorr:
…that you would say oh, my goodness, well, maybe you're going to need a transplant, and that's a heavy approach. But now you're seeing with some of the medicines, which would be appropriate for older patients, that even with 17p you may have a pill they could take.

Dr. Jain:
Sure. I think this concept of older patients versus young patients or, you know, fitness status, I think was more relevant I think in the chemotherapy era. But I think in the new concept, newer targeted therapies patients, older patients are getting equal benefit as younger patients. These drugs are not generally toxic. They don't affect the kidney functions, liver functions, and the tolerability in older patients for drugs such as ibrutinib (Imbruvica®) or idelalisib (Zydelig®) is thought to be equal to younger patients. So I think that bar of younger versus old is kind of going away in the era of targeted therapy.

Now, specifically you mentioned about the 17p deletion, and I think that's correct that if you use chemotherapy-based approaches—which we were doing before the targeted therapies because that was the best available, that was not the most optimal therapy. After FCR treatment, median time that a patient stays in remission is just around a year with 17p deletion.

But now we are seeing with ibrutinib, idelalisib and other drugs in the pipeline that these patients are getting first remission of the order of three, four years, perhaps longer. So I think this says the new drugs are remarkable, and especially for patients with deletion 17p. And I think the issue of transplant, that's another kind of discussion about patients with 17p, but I think these drugs are making a big headway for all groups of patients, older patients, 17p deleted patients, And I think we're going to see gradually in younger patients also in the frontline setting.

Andrew Schorr:
Do we know how long these newer drugs will work for someone? Because many people living, you know, in their late 80s, maybe even 90s, living with CLL, so now you're going to have them take a pill. What do we know about what's come up in some other areas of cancer, resistance where the cancer kind of outsmarts it? Do we know yet? And if there is resistance, might you have something new that's going to come along that they could then switch to?

Dr. Ferrajoli:
So this is a very good question. We don't know a lot for the majority of patients. What we know is that the median duration of response for a patient with 17p pretreated, so we're talking about a very—a relatively advanced patient with ibrutinib is in the order of two years.

We don't know what the duration is for a patient that receives it as an initial therapy or as their first salvage therapy, and that doesn't have aggressive features. It's likely to be much longer than two years, just based on how long we have been running those trials. My educated guess is that it's going to be in the order of several years.

Now, the development of resistance is a problem, but it seems to be happening in a very, very, very small percentage of patients. So—and the mechanism that is one of two that have been kind of identified, but not for everyone. So that is, you know, a field…

Andrew Schorr:
That's good news.

Dr. Ferrajoli:
…where we are looking at it, but it's good news. It doesn't seem to be a problem, and there is definitely not a clock. We are not like seeing, oh, everyone at 18 months developed resistance—no. We are not seeing of this.

It's also true that thinking about what to do if resistance occurs or if, you know, for any reason tolerance, possible side effects—we don't know what the side effects of some of the treatment may be in year four, year five, year six. If for any reason we need to change therapy, what I tell my patients is similar to what they may tell you in a store or a restaurant. The menu is getting longer and longer.

Andrew Schorr:
Right.

Dr. Ferrajoli:
We are having more and more agents. For example, venetoclax, that is AB-T199, is extremely effective, so that is likely to be one of the most effective therapies to use in this setting.

The new CD20 antibodies are also effective, and also we have to think that maybe in the years to come people may use the targeted therapy more as first line. They may not even be exposed to the monoclonal antibodies. And then, you know, we have so many other. We have older development around the cellular therapy, the CAR T cells will likely be refined.

Andrew Schorr:
Lot to talk about.

Dr. Ferrajoli:
Lots to talk about.

Andrew Schorr:
Dr. Jain, just to sum up then, she's rattled off a long list, a growing list of treatments. So people use you, as a CLL specialist and researcher, as their barometer for hope. What do you want to say to the CLL community about how you feel about the change and how it may benefit them generally?

Dr. Jain:
Well, I think—when I think the therapies we know right now, the new therapies, the targeted therapies have all significantly advanced the field for CLL patients as compared to what was with chemotherapy. Though, I mean, there is a subgroup of patients which I think chemotherapy is still is valid option—but for a majority of patients I think we're moving to targeted therapies.

And I think in the years to come, in the next I think two, three years, four years, I think we're going to see more of immune-based therapies for patients with CLL. There is already interesting data generated with chimeric antigen receptor therapy, and I think in the next one or two years we're going to see clinical trials with immune checkpoint block inhibitors, PD-1, PDL-1, which are the drugs which are now approved in melanoma setting and some solid tumor setting.

I think we're going to see those trials coming up, and I think that will be a very interesting combination because those are again based on the fact that you're targeting the immune system of the CLL patients not targeting the CLL cells. So it's a new phenomenon which already works for patients with melanoma, solid tumors, in some group of patients. So I think those trials we will have to see. And those have the potential, potentially the potential of long-term disease-free survival, long-term remissions, possibility of a cure. But I think the next few years are going to be crucial in that aspect.

Andrew Schorr:
So you're feeling very positive.

Dr. Jain:
Right. I mean, yeah, I think those are the trials we are involved in at MD Anderson, the checkpoint inhibitor trials, so we'll have to see how—they should open in the next few months, but we'll have to see in the next one or two years how—what data we generate from that.

Andrew Schorr:
Tremendous change going on in CLL and tremendous hope for a broad group of patients no matter what your age is. So stay tuned and stay informed.

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