CLL Research Developments on CAR T-Cell Therapy

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Andrew Schorr:
There are some people who have been very sick and have had a lot of lines of therapy. And there have been some—are some trials in CAR T-cell therapy for CLL. And I know you have a colleague that's doing research in NK research. So, let's talk about CAR T first. So, this is expensive making a medicine of your cells, personalizing it.
It has some toxicity for sure. And we know people who passed away. And we know other people who have done well. So, where does CAR T fit in?

Dr. Jain:
So, I think CAR T, for acute lymphoblastic leukemia or non-Hodgkin's lymphoma where it's currently approved, I think, for relapsed refractory ALL, B-cell ALL, relapsed refractory non-Hodgkin's, diffuse B-cell lymphoma, I think, it's true. There are patients who are, as you can imagine, have achieved durable, long-term remissions. But, at the same time, especially in ALL, we are seeing relapses.

Patients achieve a response, but then, a few months down the line, their disease comes back. I think, in the context of CLL, actually just this morning, there were three abstracts presented updating about the CAR T experience from University of Pennsylvania, Fred Hutch, and a more junior study looking at multiple sites in the US, looking specifically at CLL. So, thinking in the CLL, for the last few years, had been that the early studies in CLL showed that the response rates were only like 15 percent to 20 percent, which is much lower than what were noted with All and with non-Hodgkin's lymphoma.

But the studies, which were updated this morning, do seem to suggest that you could achieve a high level of remission, a complete remission, and high level of MRD-negative remission, in relapsed refractory CLL populations, with the CAR-T constructs, which they are using right now. So, in the CAR T, I think the response is it's very dependent on the patient population but, at the same time, it's very dependent on the construct, the actual product, which is being used. So, I think the data, which was presented today, actually, looked quite exciting for patients with relapsed refractory CLL.

Certainly, there are patients who are achieving deep remissions and some of the patients have relapsed. But I think the data today, for me, it was quite kind of nice to see some really positive data.

Dr. O'Brien:
Well, just like talking about next generation care, PI3K, we have to keep in mind that the CAR T's are evolving all of the time.

They're early, really, in their development. And there's first generation, second generation. So, it's really evolving. The other interesting aspect, and I don't know if there's any trials in CLL, but you alluded to the fact that you've got to take the patient's own T cells. Well, right off the bat, that, potentially, is a problem in CLL because we know CLL T-cells are dysfunctional. So, that may be partly why, historically, the CAR T has not worked as well. But you have to take the patient's own T cells. The patient has to wait, while we send them to the companies or wherever they're doing the trial, so that they can set the construct in, manipulate them.

And then, they have to send them back. And then, we have to give them to the patient. There are now companies that are investigating what we would call off the shelf CAR T. So, they're formulating the product, so that they're, I'm saying, off the shelf where you're not using the patient's own T cells.

So, that might get around the problem of the CLL T cells not being so functional and would get around this aspect of waiting, the patient who might be sick, waiting for the T-cells to be harvested, sent out, manipulated, sent back. And so, I think that's a very promising technology, although that's very, very early.

Dr. Pinilla:
I just want to add that I think another very, in my opinion, fascinating story that is evolving with the CAR T and with the BCR inhibitor is that we still don't understand very well how these BCR inhibitor, in this case, BDK inhibitors who have off target effect can't really have an impact on the T cell's immune system. And it was presented this morning that it seems like a patient who had received ibrutinib (Imbruvica) before the CAR versus the people who didn't receive as much ibrutinib, they were trying to do a little better. It's something that definitely called for the fact that these drugs really, really decrease significantly the amount of the disease.

And this has an impact on how the T cells are maybe coming back in a better way. So, the expansion of these T cells after the patient has been taking ibrutinib for a certain amount of time is much more successful. And it's possible that it is one of the reasons that why we start to see better responses. This is, for sure, the BTK, we don't know what's going to happen with the drugs, but definitely, it's something exciting to see, in the future.

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