Looking Ahead: What Treatments Are in Development for CLL?

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Andrew Schorr:
So you're working on something new, in early trials, called cirmtuzumab to try to get at the CLL cell in a new way, and maybe that could lead to yet another combination. And you have trials like that.

Dr. Kipps:
I think that's very important, and, as you mentioned, this antibody targets another protein which we and now others have found on the leukemia cells. It's a protein that we ordinarily don't have in our body. It's usually expressed during the time when we were an embryo, and it's very useful for developing organs in the embryo, and we dispense with it because it's no longer necessary because we have already have a liver and a heart and what have you.

So I think that it's still an unanswered question of why this leukemia and now we find other cancers, re-expressing this protein. And so we have to ask the question what's it doing, what does it mean, why do tumor cells go out of their way to re-express something. I always have used the rule of thumb at that if you find something that distinguishes a cancer cell from a normal cell that difference could potentially be important, not only as a target but lead to understanding of differences in how the tumor works in contrast with a normal cell.

And so we've been doing a lot of times to try and spend looking at how ROR1 is actually working. And this antibody does target ROR1, and it seems to block some of the signaling pathways that's governed through ROR1. And what's exciting is that this clinical trial done by Dr. Michael Choi and Dr. Kent Jamieson has completed, one, patients tolerated it very well, because it's finding this new approach. It's not on your B cells or other cells of the body, it's found on the tumor cells.

The second thing is it seems to be able to block the signaling pathway. We see this by examining the leukemia cells from patients as they're being treated. And it seemed to stop the disease in its tracks. So patients did not have progression on therapy. We saw are reductions in the leukemic cell counts, and in the few instances where we looked we saw reductions in the marrow infiltration by the leukemia cells. And the time, average time it took from patients stopping therapy to requiring additional therapy was comparable to what we'd seen with a drug called ofatumumab (Arzerra), as you know, that was approved for patients with CLL.

Andrew Schorr:
Wow.

Dr. Kipps:
Now, I think that that's important, but the bar for therapy is higher now. We just can't have this because I think that we need to understand how this might fit in to the current landscape of therapy. When you look at patients who have treatment with ibrutinib (Imbruvica) you have to ask the question, why aren't the cells going away? Why are they sticking around? What's governing that? And that's the important question we're not asking.

Now, it may be true that you can have patients on therapy for years and years and over the years you might see eking out a response, but what's keeping the cells alive if it's so effective in taking them out of the lymph nodes in the microenvironment. And we actually looked at patient cells when they're treated with ibrutinib and found that the signaling pathway we're trying to figure out before one is in overdrive, and we think that might be adding a lifeline.

I always call attention to this movie called "The Terminator," and, as you know, the Terminator was crushed at the end of the movie, and then he rewires his circuits and then finds a way to rise up again and walk again. And so you have to think of these tumors as finding alternative pathways that they can adapt to, and they become then lifelines when you block other pathways.

Andrew Schorr:
Cut all the cords. So the concept might be to combine this cirmtuzumab, which goes after ROR1, with a drug like ibrutinib to cut out the sustenance, the escape route, etc., the way to rewire itself.

Dr. Kipps:
That's exactly right. That's the basis of a clinical trial which is starting not only at UCSD but at a number of other centers in the United States. So we're hopeful that patients will do well with this, and I think that we'll be very interested to see how that data actually unfolds. But these are strategies we think are very important because we have to try and figure out more about what makes the leukemia cell tick, and if we can develop tools that are very specific for taking out things that are helpful to the leukemia they could be very helpful to the patient.

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