



Checkpoint Inhibitors and CLL: An Update

Michael Keating, MB, BS

Professor of Medicine, Department of Leukemia
The University of Texas MD Anderson Cancer Center

Nicole Lamanna, MD

Associate Clinical Professor of Medicine
Columbia University Medical Center

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Andrew Schorr:

Here in the U.S. and some people are watching from abroad, but if you are in the U.S., you could turn on your TV and see ads for a couple of lung cancer drugs that fit in this next category of checkpoint inhibitors. There are two. The brand names are pembrolizumab (Keytruda) and nivolumab Opdivo, but they are out there, and they're being tested along with others from other companies to see do they work for our blood cancer. So, Nicole, checkpoint inhibitors, my understanding of it is what they're trying to do is get your immune system to recognize the cancer and do its job, right?

Dr. Lamanna:

Yeah. Absolutely. So these are also similar to what we were talking about in a different way but similar to what we were talking about with cars. Another way to sort of enhance your body's ability to fight your cancer cells, and so this is basically approved in some of the solid tumor cancers. And as actually Andrew mentioned earlier, sometimes many of these drugs can cross over into other disease states.

And so we're looking at different ways to harness your immune system, and it may be applicable to many different cancers, and so these drugs are also being looked at in CLL and other hemanologic malignancies, AML, so on and so forth. And so this is also a targeted way to have your immune system try to kill off your leukemia cells. And so in CLL, I think the data's young and may need to be combined with other agents. So I think stay tuned.

Andrew Schorr:

And you tried it.

Dr. Lamanna:

I'm gonna let you...

Andrew Schorr:

You tried it with Allen.

Dr. Lamanna:
...speak about that.

Andrew Schorr:
Allen is in a trial with nivolumab being combined.

Dr. Keating:
It appears when the disease is in the regular form of CLL, that it really doesn't do very much but one of the surprising things that was reported from the Mayo Clinic was that in a trial with a different drug, pembrolizumab, they had three patients with Richter's transformation that responded.

Dr. Lamanna:
Right. That's...

Andrew Schorr:
That responded?

Dr. Lamanna:
Yeah.

Andrew Schorr:
That Richter's transformation...

Dr. Lamanna:
Richter's.

Andrew Schorr:
Is not good. Do you wanna just define Richter's for one second and come back?

Dr. Lamanna:
Sure.

Andrew Schorr:
What's Richter's?

Dr. Lamanna:
So when you hear—so this is the disease can transform in a small proportion of patients to a more aggressive lymphoma, and so actually it looks differently when you actually take a piece of tissue. It doesn't look like CLL, these small mature lymphocytes. It looks like these large, ugly lymphoma cells. Diffused large cell lymphoma is the most common type.

And so we've traditionally given therapies in those situation that are for patients with diffused large cell lymphoma, a different disease. And unfortunately, those treatments are usually unsuccessful in patients with this form of Richter's syndrome and so the traditional lymphoma treatments do not work well in patients with Richter's syndrome but essentially haven't had very good therapies until...

Andrew Schorr:
So you're talking about...

Dr. Lamanna:
This is an exciting data that perhaps in this subset of patients, this is an area that we need to explore, because we absolutely need new therapies for the patients who develop Richter's.

Andrew Schorr:

So if I get it right, you're looking at using one of these immunotherapies combined with other medicines for people who have developed Richter's.

Dr. Keating:

Yes and usually, they combine with an antibody and it appears to enhance it. There's actually some experimental evidence that if you prepare the animals with lenalidomide (Revlimid), it makes it much more effective. And seeing as CLL lenalidomide works on enhancing the immune system, it might be a very nice partner for the nivolumab to bring it into the mainstream CLL population as well.

Andrew Schorr:

One of the things I want you all to get is there's a whole arc to this, right? So Michael's been at this how many years?

Dr. Keating:

40.

Andrew Schorr:

Okay. So there's a lot of wisdom...

Dr. Keating:

Twelve I was when I started.

Andrew Schorr:

Yeah. Lot of wisdom with this and his peers around the world and the CLL Global Research Foundation, you get people together and they're discussing all this. So there's a whole arc to this and particularly related to these clinical trials with newer agents. Well, what could work for which patient? Maybe in a clinical trial at a place like MD Anderson, at Memorial Sloan Kettering where we used to be, at Columbia, at City of Hope, wherever it may be or around the world, the research center, could it be combined for greater effectiveness?

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