ASH 2014 Coverage: The Promise of Immuno-Oncology to Treat CLL

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Andrew Schorr:
One area that's investigation now is this CAR T-cell therapy, and the whole idea of immjunocology—can your immune system be sparked to fight the cancer that it missed the first time. How do feel about? 'Cause there's been a lot of buzz about that.

Dr. Kipps:
That's exciting, too. As you know, this has been something that's been very attractive to us. We've been working to bolster the immune system with even gene therapy to jack up the immune system. One of the features of CLL in particular is the fact that patients have immune suppression. The leukemia can suppress the immune response, so therefore patients are more prone to infection. There are features of that immune suppression, which can be targeted. There's a whole category now of new therapies called immune checkpoint inhibitors. What these are are antibodies that bind to proteins that are involved in that immune suppression. And once that immune suppression is removed, then T cells may awaken and discover the tumor cell and be able to fight back that tumor cell.

The use of immune checkpoint inhibitors actually has been approved in various cancers, such as in metastatic melanoma, where there can be some dramatic regressions in cancer by just waking up the immune system. There's very good evidence that the same will be true in blood cancers and CLL in particular. Some of the work that we and actually John Gribben has done most recently to identify some of the features that account for the immune suppression are related to the fact that the CLL cells may amplify these immune checkpoints. And so using immune checkpoint inhibitors may be unleashing the immune response against the leukemia. That would be truly fabulous. Because if you talk about a treatment that could help prevent recurrence, this seems to be a great formula to combine perhaps with these other modalities of treatment.

Andrew Schorr:
Wow.

Dr. Kipps:
Now you mentioned the CAR T cells. This is quite an exciting thing. I'm very attracted to this. We have been I guess one of the first groups to introduce genes into cells and give them back to patients, as you know, over a decade ago, trying to induce a patient's immune response by generating a cellular vaccine against the leukemia. This is a bit different. What it is is that you have antibodies which are very specific for the cancer cell or antigens that might be shared by B cells, for example, like CD-19. And then you have an antibody that can do that very specifically. And then you take the binding part of the antibody, and you link it onto proteins that the T cell normally expresses. So it fools the T cell. It's sort of like putting an antenna on your roof, and you can receive maybe satellite TV. And you're fooling the TV set, getting the signals to the cell that tell it to respond, tell it to go after the cell, tell it to kill the cell. So what you do is you make what's called a chimeric

receptor. The chimera is half the antibody-binding portion and half of the portion that can help stimulate the T cells. And the gene that encodes that chimera is actually then inserted into the T cells of the patient they removed from the patient. And then you put that gene in there, and then the T cells begin to express this chimeric antigen receptor, and they become chimeric antigen or CAR-T cells.

Now there have been some dramatic responses in patients. Some of them have been associated very vigorous inflammatory response as you can imagine. The T cells have an attitude. They're armed against the tumor. You have a lot of tumors. You can expansion of the T cells, and some patients required admission into the ICU and treatment with inhibitors of the inflammatory response. But that being said, the T cells in some cases have been quite effective in going after the tumor cell and eradicating the tumor cell. There have been a few cases in CLL where it appears there's no evidence of the CLL left, and that's quite exciting. Now the overall response rate in studies that have been done at the University of Pennsylvania, studies that are ongoing at Sloan Kettering, we're working with other sites too with also MD Anderson, the results have not been as high as we would like to have them in chronic lymphocytic leukemia. There may be a number of reasons for that. We have to work out what are the best T cells to be able to do the job? Are those T cells in adequate numbers as we get more advanced in age? Are the T cells up to the challenge?

But it's clear in the case of childhood leukemia, acute lymphocytic leukemia (ALL), kids who have failed treatment are responding to this CD-19 CAR therapy. And the complete response rate has been over 80 percent, approaching 90 percent. So this is quite exciting. So for kids and young adolescents, this may be a winning formula. Obviously, it's complicated. You have to take your T cells out, get them genetically modified. That can't be done at your county—your community physician's office, and then it has to be re-administered. And during the time that the T cells are expanding, you have to be under close observation, may require hospitalization, may be quite sick during that time and have to be attended to by well-trained clinicians who can keep you from having consequences. But if we can marshal that effect, then we can potentially eradicate the clones of leukemic cells.

So think about all these possibilities here—having antibodies to awaken the immune system, have the ability to activate the T cell to go after the tumor, having new antibodies that may eradicate the stem cells of our disease, and having drugs which might be able to mind the store and get us ready so we can maybe apply some of these approaches either alone or in combination plus drugs that might be able to attack an important protein that keeps even the stem cells surviving like the ABT-199, it's truly exciting. And I don't think this is a thing that we have to treat like hypertension. This is something that we need to treat like maybe a community-acquired pneumonia.

Andrew Schorr:
Hint: eradicate it.

Dr. Kipps:
Exactly.

Andrew Schorr:
End of story. Okay, that's what we want to hear, Dr. Tom Kipps. Thank you once again for begin with us on Patient Power.

Dr. Kipps:
Thank you so much for all you do too.

Andrew Schorr:
Thank you. All right. That's where we're going to get to is to a cure. In the meantime, isn't it great that so much is in research? Of course, I always say consider being in a clinical trial. Have a discussion with maybe your specialist physician. Consult with a center where they're doing trials to see if any of this applies to you, so that we can move the ball forward. And you may get the benefit in the process. On location in San Francisco, I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.