An Update on CAR T-Cell Therapy for Myeloma

Sagar Lonial, MD, FACP
Professor, Chair and Chief Medical Officer, Department of Hematology & Medical Oncology
Winship Cancer Institute

Krina Patel, MD, MSc
Assistant Professor, Department of Lymphoma/Myeloma, Division of Cancer Medicine
The University of Texas MD Anderson Cancer Center

Jack Aiello:
Where are we in the world of CAR T’s? How fast are these CAR T’s going?

Dr. Patel:
Sure. So, CAR T—obviously, what I tell my patients is when we collect your stem cells, we’re collecting a different type of cell here. We’re collecting T cells. These are lymphocytes that we all have in our body that help us fight viruses and bacteria and all those kinds of things. They have receptors.

So, each of our T cells is made when we’re born and things we’re exposed to, they have kind of like night vision. They’re made for something specific. What we can do is actually take those cells out and unlike stem cell transplant, where the stem cells are just to make sure you have a normal immune system again after melphalan (Evomela).

Here, we can actually put a new receptor in. We genetically modified the genetics of that cell, that T cell and then we grow them to bigger numbers. Then we give it back after a different type of chemo to help knock your immune system down just for a little bit. Those cells go in and now, you can imagine these are like little army men with night vision.

They can go in and kill just the myeloma because that new receptor we put in is a flag that’s on the myeloma cell. So, it can differentiate between your own normal cells versus the myeloma cells. So, now, they’re going into the bone marrow. They’re going into the other places that myeloma is and they can actually kill. It’s like a lock and key.

Once it seems that flag with that receptor, it turns on, it’s activated and it kills. It actually dies too and it brings all the other immune cells there through those mechanisms.

So, we’ve had great data with one of the trials that’s gone the farthest. I think there are 47 trials right now between the US and China looking at CAR T. The main flag that we look at right now is called BCMA, B-cell maturation antigen. And the BB2121, that’s through Celgene, has kind of gone the farthest. Potentially, we have our first standard of care, which doesn’t have to be on trial next year, early next year. So, we’ll find out in the next six months or so. But of course, we want to make it better.
So, as of right now, that’s not the cure that we were hoping for, but it has shown really impressive results in patients who have already gone through everything in multiple other clinical trials and the other nice thing so far right now is that once you get the CAR T, you don’t get any other therapy. So, the average was about a year that patients were on no therapy after seven lines of therapy, where they felt better and everything was going well.

So, we’re hoping that bringing that up sooner might make that longer. The other part is we have a lot to learn still. Everyone’s T cells are different based on what we’ve been exposed to, what T cells we were born with. So, we’re trying to figure all those things out to make the best T cells.

So, the allo part she was talking about is the trial we have hopefully opening soon where a lot of folks—we can’t make CAR Ts necessarily for them because there are not enough of them because of the therapy we’ve had or for other reasons. So, for those patients—or they can’t wait four weeks to make them—so, if we have something that we can just pull, like a drug—we’ve actually found normal donors who seem to have what we want in T cells and made those already and we actually used genetics to knock out the things that can cause what’s called graft-versus-host disease.

So, we don’t want these cells to go in and say, “Wait, this is not my body. I’m gonna start attacking the liver or the skin.” So, we can actually knock that out. It’s a little bit science fiction, but it’s really exciting that we can do that and then actually give these cells so that we don’t have to worry about making them or potentially have to wait so long to give them.

Jack Aiello:
It is exciting. While folks might think average one year before you relapse, you have to again remember that these are patients that these are patients that have been heavily pre-treated, as you indicated, and what will happen when it moves further up in the treatment protocol.

Dr. Patel:
And we’re looking at new antigens too and then combining antigens. So, how can we kill the myeloma so it doesn’t get smart on us? It’s really exciting.

Jack Aiello:
Dr. Lonial, anything to add on CAR Ts?

So, we’ve had great data with one of the trials that’s gone the farthest. I think there are 47 trials right now between the US and China looking at CAR T. The main flag that we look at right now is called BCMA, B-cell maturation antigen. And the BB2121, that’s through Celgene, has kind of gone the farthest. Potentially, we have our first standard of care, which doesn’t have to be on trial next year, early next year. So, we’ll find out in the next six months or so. But of course, we want to make it better.

So, as of right now, that’s not the cure that we were hoping for, but it has shown really impressive results in patients who have already gone through everything in multiple other clinical trials and the other nice thing so far right now is that once you get the CAR T, you don’t get any other therapy. So, the average was about a year that patients were on no therapy after seven lines of therapy, where they felt better and everything was going well.

So, we’re hoping that bringing that up sooner might make that longer. The other part is we have a lot to learn still. Everyone’s T cells are different based on what we’ve been exposed to, what T cells we were born with. So, we’re trying to figure all those things out to make the best T cells.

So, the allo part she was talking about is the trial we have hopefully opening soon where a lot of folks—we can’t make CAR Ts necessarily for them because there are not enough of them because of the therapy we’ve had or for other reasons. So, for those patients—or they can’t wait four weeks to make them—so, if we have something that we can just pull, like a drug—we’ve actually found normal donors who seem to have what we want in T cells and made those already and we actually used genetics to knock out the things that can cause what’s called graft-versus-host disease.

So, we don’t want these cells to go in and say, “Wait, this is not my body. I’m gonna start attacking the liver or the skin.” So, we can actually knock that out. It’s a little bit science fiction, but it’s really exciting that we can do that and then actually
give these cells so that we don’t have to worry about making them or potentially have to wait so long to give them.

**Jack Aiello:**
It is exciting. While folks might think average one year before you relapse, you have to again remember that these are patients that have been heavily pre-treated, as you indicated, and what will happen when it moves further up in the treatment protocol.

**Dr. Patel:**
And we’re looking at new antigens too and then combining antigens. So, how can we kill the myeloma so it doesn’t get smart on us? It’s really exciting.

**Jack Aiello:**
Dr. Lonial, anything to add on CAR Ts?

**Dr. Lonial:**
No, I think that’s a great description on the premise and the concept here. I think that BCMA, which is the target that most of the CAR-T cells are going after right now to me is the best target in myeloma because it’s most narrowly expressed of anything else that we used, more narrowly expressed than CD38, which is the target for daratumamab (Darzalex), more narrowly exposed than CS1, which is the target for elotuzumab (Empliciti).

There are many different ways to get to BCMA. I think CAR-T cells are the ones that we are most optimistic and hopeful for if we can figure how to make those cells live longer. The longer the cells persist, the more likely you are to have disease control. In my guess, you probably need to be a little bit longer than six months to really have the optimal long-term outcome with CAR-T cells alone.

But the BiTE antibodies that was discussed earlier, that to me is another way to get to BCMA. That’s looking very exciting and promising in early trials as well, as well as an antibody drug conjugate, which means you take the antibody targeting BCMA, but you put a piece of chemotherapy on the back of it. That selectively delivers chemotherapy to the myeloma cell. That we’ll hopefully see some data on in the next few months as well because that’s another way to get to BCMA.

So, I don’t think that one is mutually exclusive of the other. I suspect we’re gonna use all of them and we might use one as a bridge to get to another. I think these are all really exciting approaches that target that best antigen, which is BCMA.

*Please remember the opinions expressed on Patient Power are not necessarily the views of our sponsors, contributors, partners or Patient Power. Our discussions are not a substitute for seeking medical advice or care from your own doctor. That’s how you’ll get care that’s most appropriate for you.*