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Selecting High-Risk Mantle Cell Lymphoma Patients for CAR T-Cell Therapy

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Kite Pharma. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss how we can identify patients with high-risk mantle cell lymphoma who would most likely benefit from CAR T-cell therapy is Dr. Tara Graff. She is a medical oncologist who leads a community-based clinical trial program at Mission Cancer + Blood in Des Moine, Iowa.

Dr. Graff, thanks for being here today.

Dr. Graff:
Thanks for having me.

Dr. Turck:
Well, to start us off, would you tell us about CAR T-cell therapy and how it's used to treat patients with high-risk mantle cell lymphoma?

Dr. Graff:
Yeah. So CAR T is a type of immunotherapy that uses genetically altered T-cells. These T-cells are taken from a patient's blood and modified in the lab to bind to and kill cancer cells. The T-cells are given a new receptor called the chimeric antigen receptor, or CAR, that recognizes and attaches specific proteins on the surface of cancer cells, and in this case, the mantle cell lymphoma cells.

Dr. Turck:
Now with that background in mind, let's focus on how we can identify appropriate patients for CAR T. First, how do you approach stratification to determine whether a patient has high-risk disease? And how does treatment refractoriness fit into your assessment?

Dr. Graff:
So if a patient has relapsed to their prior therapy, especially relapsed quickly, so they didn't really have a long-term remission, that's a poor prognostic marker. This is really indicating that this disease trajectory is very quick, right? Also, if a patient were to harbor what's called a TP53 mutation in mantle cell lymphoma—well, really in all cancers, but we're speaking on mantle cell—that's a really poor prognostic sign, and usually these patients don't respond well to chemotherapy and will need more aggressive therapy, such as CAR T-cell therapy.

Dr. Turck:
So then once you determine that one of your patients has high-risk disease, are there any clinical indicators to suggest that they may be an ideal candidate for CAR T-cell therapy?

Dr. Graff:
So, again, that quickness in which they've relapsed and also if they've relapsed to a prior covalent BTK inhibitor—this is a good indicator that it's time to get them to CAR T-cell therapy and quickly. But it's more important not to stop the BTK inhibitor while awaiting CAR T. So if you're not at a CAR T center, you're going to need to refer them. And so you want to make that referral fairly quickly, but you don't want to stop their current therapy in that process.

Dr. Turck:
And are there any other factors that might impact a patient's candidacy for CAR T-cell therapy?

Dr. Graff:
You can think of high disease burden. Again, if a patient's relapsing quickly and relapsing on a BTK inhibitor, that's a sign that it's time. But also with high disease burden, we talked about the TP53 mutation; those all have to come into account when deciding if a patient is a CAR T-cell candidate as well as their overall health, right? Their age—chronically, age is just a number, but you have to also take into account their social factors. Can they travel? Can they be away from home for said period of time? Will their health even allow CAR T-cell therapy? So all of those, it's not just a matter of do they need a CAR, but also, can they tolerate it?

Dr. Turck:
And are there any ways that a patient's prior treatments and their response to those prior treatments can inform how we might predict treatments success with CAR T?

Dr. Graff:
Well, we're looking at that, right? How different initial therapies may affect the tumor microenvironment. How the T-cell population will expand, if you will, when a patient received a CAR. It's kind of called sequencing. What's the proper treatment sequencing to make the CAR T-cell therapy the most effective? A patient's prior chemotherapy can cause mobilization failures, meaning these patients can't get the cells that they need to go on and have the CAR made, if you will. And you also want those new and improved T-cells to be able to expand. And if prior therapy has prevented that, that can make a major impact.

So we really have to think about the treatments we are using today and how they may affect tomorrow because it's not, "Oh I'm going to use this now and worry about that later." It's sort of a continuum. So you really have to kind of be thinking long-term, almost like a foreshadowing, if you will.

Dr. Turck:
For those just joining us, this is *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Tara Graff about which patients with high-risk mantle cell lymphoma might benefit the most from CAR T cell therapy.

So, Dr. Graff, now that we have a better understanding of how to select appropriate patients for CAR T-cell therapy, do you have any advice or best practices for applying some of the criteria you mentioned to clinical practice?

Dr. Graff:
Yeah. So I can't stress enough that it's crucial to always remember that the treatment we give today can truly affect what happens to our patient tomorrow. A lot of these patients are with oncologists in the community setting. They're not used to doing CAR T or maybe thinking about CAR T, and so it's really important that we educate about where a CAR T therapy falls into the treatment landscape in mantle cell lymphoma. And if a patient relapses, it's crucial that a non-CAR T site reach out to a CAR T-treating physician right away before second-line therapy is even selected to ensure that that next line of therapy doesn't impact the possibility of CAR. And then we can sort of do this multi-disciplinary approach where we're working together to get the therapy that's really needed, the safest and best effective method to get that patient onto CAR T. The disease trajectory for high-risk mantle is different than our other forms of non-Hodgkin's lymphoma, and when these individuals relapse, a lot of times, it's quick, and the disease just multiplies and really starts to take over. So get patients referred quickly; timing is everything.

Dr. Turck:
And what are some barriers to care that you notice in the use of CAR T-cell therapy for high-risk mantle cell lymphoma?

Dr. Graff:
Barriers really are about patients getting to where they need to be. Timely identification is crucial to getting a patient to a CAR T site and getting product. You can say I want my patient to have CAR T, but there's time. The patient has to be seen. The product has to be made. All these things take time, like insurance approval.

So we have to think about the manufacturing time and insurance, so the sooner you identify the patient and communicate with a site, the process can begin immediately. Again, I cannot harp or focus on that timing identification being so crucial to the referral and breaking down those barriers and the things that we can't control. The clock starts with identification, and it's a race, not a marathon, for this disease. You need to sprint if you can.

Dr. Turck:
Well, with those final thoughts, I want to thank my guest, Dr. Tara Graff, for joining me to discuss how we can optimize treatment outcomes in high-risk mantle cell lymphoma with CAR T-cell therapy. Dr. Graff, it was great having you on the program.

Dr. Graff:

Yes, thanks for having me. This was fun.

Announcer:
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