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Treating R/R Diffuse Large B-Cell Lymphoma: Who's Eligible for CAR T-Cell Therapy?

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

Dr. Turck:
This is *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss best strategies when selecting patients for CAR T-cell therapy who have relapsed or refractory diffuse large B-cell lymphoma, or DLBCL, is Dr. Nilanjan Ghosh. He's a Clinical Professor of Hematology and Oncology at Atrium Health Levine Cancer Institute Wake Forest University School of Medicine in North Carolina. Dr. Ghosh, thanks for being here today.

Dr. Ghosh:
Thank you for having me.

Dr. Turck:
So to kick us off, Dr. Ghosh, what criteria do you use to identify suitable candidates for CAR T-cell treatment in the setting of relapsed or treatment-refractory DLBCL?

Dr. Ghosh:
That's a very important question. The first thing to remember is CAR T eligibility is broader than transplant eligibility. So let's start with age. Patients above the age of 70 to 75 are often not considered as transplant candidates, but older patients can receive CAR T-cell therapy. There have been trials conducted for those who would not be good candidates for transplant. For example, the PILOT study was conducted where liso-cel was used as a CAR T product, and this was for patients who were not considered as good candidates for transplants, and that included patients who were either age above 70 or had other comorbidities which would preclude them from getting a transplant. Similarly, the ALYCANTE study was performed in Europe with the axi-cel product. The outcomes for these studies were excellent in this patient population. However, age does impact various aspects of CAR T-cell therapy in lymphoma, from things like treatment tolerance and quality of life. So while older patients may face higher risks and challenges, many can still benefit from this therapy, particularly if you are careful with selection and use tailored treatment approaches and comprehensive support care.

The other thing beyond age is performance status. So this is a very important consideration for CAR T-cell therapy. We do know that patients who have poor performance status do not do really well with CAR T-cell therapy. Those with better performance status are often better equipped to handle the intensive monitoring and management required during CAR T-cell therapy. And we also know that overall survival and progression-free survival tend to be better for patients with lower ECOG performance status. So those who have a better performance status as well as overall health and functional status derive more benefit from CAR T-cell therapy.

Dr. Turck:
So digging a little deeper into these treatment decision-making factors, are there any other reasons why they're important in the management of relapsed or refractory DLBCL?

Dr. Ghosh:
The prior treatment history is a very important one. So we know that initially, CAR T-cell therapy for DLBCL was approved after two prior lines of therapy. And after seeing the benefit in later lines of therapy, there were trials which were conducted to compare CAR T-cell

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therapy to transplant in the second-line setting. So now you're talking about lesser prior lines of therapy, just one prior line of therapy, and that showed superiority over autologous transplant for axi-cel and liso-cel. So those two are approved in the second-line setting. So any patient who is primary refractory to frontline therapy or have relapsed within 12 months of frontline therapy as well as those who are not considered to be transplant candidates, that's where CAR T-cell therapy would be approved in the second-line setting in DLBCL. But in terms of prior therapy, one important point is I would caution the use of bendamustine, which is an alkylating agent with prolonged lymphotoxic capacity, has been discouraged prior to leukapheresis given the deleterious impact on T cell fitness and CAR T-cell outcomes in B-cell lymphoma.

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Nilanjan Ghosh about navigating patient selection for CAR T-cell therapy in relapsed or refractory diffuse large B-cell lymphoma, or DLBCL.

So now that we've discussed the factors that go into selecting patients who would benefit most from CAR T-cell therapy, Dr. Ghosh, would you address some common questions that clinicians may encounter when considering this form of treatment for their patients?

Dr. Ghosh:
The first question which comes to mind is, how soon can the patient be seen for the CAR T consultation? We want to be able to give rapid access to these patients because this is a disease which is a fast-growing disease. It's an aggressive type of lymphoma. So the first thing is, how can we make sure that they have quick access to a center where CAR T-cell therapy can be performed? Then the other questions they have is, how long will it take after the patient is seen to actually receive the CAR T-cell therapy? Because there is a time between consultation to actually leukapheresis that is often not captured on clinical trials, but that's a significant amount of time because that's a time when people have to get financial clearance and get a date for the leukapheresis. And then after that is obtained, the next period of time, which is known as the “vein-to-vein time,” is from the leukapheresis to actual administration of the CAR T product.

The other question which comes up from referring physicians is, while the patient is waiting to get CAR T-cell therapy, what should they use for bridging therapy? If the patient does need something for bridging therapy or therapy before even collection of the T cells, then avoid bendamustine at that time. Other questions I often get is, what product will be used? And also what kind of monitoring may be needed? When the patient goes back to the referring physician, what do they need to look out for? Things like cytopenias, B-cell aplasia, infection monitoring, and those kind of things. So those are the usual questions I receive from referring physicians.

Dr. Turck:
Now would you mind sharing a real-world patient case that applies some of these considerations that we've been discussing into practice?

Dr. Ghosh:
Yeah, so I wanted to discuss a patient who was referred to me a few years ago. And the referring physician was a little bit hesitant because this patient was in his 60s and was not a candidate for transplant. So he had had two prior lines of therapy, and he initially had presented with indolent lymphoma, and he had several lines of therapy, including radiation to the chest for an indolent lymphoma, which had led him to then develop cardiomyopathy, and so his ejection fraction was low in the 30s. But he then transformed into aggressive B-cell lymphoma, and he had received a couple of different treatments for that aggressive B-cell lymphoma. When those treatments failed, he was referred for CAR T-cell therapy. And the reason I say that the referring physician was hesitant is because they didn't know with his cardiac condition whether he would be eligible for CAR T-cell therapy.

So I assessed his disease status and his comorbidities, and he seemed to be a very compliant patient with excellent social support. And also, had been following with our cardio-oncology team to optimize his cardiac function, so even though his ejection fraction was in the 30s, he didn't have any clinical signs of heart failure; he was euvolemic, and his exercise tolerance was quite good. So with that, we discussed the pros and cons of CAR T-cell therapy with him. After a good discussion and involvement with the cardio-oncology team, we decided to proceed to CAR T-cell therapy. And he ended up getting CAR T-cell therapy and got a really nice remission. He actually tolerated the treatment really well and enjoyed the benefits from having this aggressive B-cell lymphoma, which was not cured by chemotherapy, go into a long-term remission with CAR T-cell therapy.

Dr. Turck:
Now shifting focus just a bit, what tools or resources would you recommend to clinicians for making informed decisions when selecting CAR T-cell therapy?

Dr. Ghosh:
So for those who are delivering CAR T-cell therapy, there are apps which can easily help you calculate, based on patient symptom

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ontology, the grade of cytokine release syndrome or the ICANS, or immune cell effector associated neurotoxicity. And they are very good tools where you can decide when to use tocilizumab, when to use steroids, when to use both, and other things which may be needed. So very good guidelines are available from published manuscripts as well as apps for that. And also very good information about the CAR T-cell product, the timing for CRS, and timing for neurotoxicity so that you know when to monitor for these and things like that.

Now for the referring physicians, there are other web tools which are available. So when I talk to referring physicians who want to know more about this, I direct them to websites where they help you find the closest CAR T site. Some of those tools may be available from foundations, and then some are available from things like Kite Konnect. There's also Let's Chat CAR T, which is another website which has good CAR T education. So there's a lot of tools out there, which are available on the web. And I often talk about those to physicians who are interested to learn about this topic.

Dr. Turck:
Now before we end today, Dr. Ghosh, when we incorporate all these strategies into practice from a high-level view, how could they influence our patients' outcomes or qualities of life?

Dr. Ghosh:
Yeah, so that's actually the most important thing, right? So DLBCL is a very aggressive disease. It's a disease which is difficult to live with. It's either: it can be cured, or if it persists, then quality of life can go down pretty fast, and patients can succumb to this disease. CAR T-cell therapy, which is a one-and-done treatment right now—no maintenance, nothing, so it's a one-time therapy—can offer long-term remission for patients with relapsed or refractory DLBCL. So it is an intensive therapy, and for that period when they are getting the CAR T-cell therapy, that is intense monitoring and frequent visits after they finish the treatment, so it can impact the quality of life while getting it. But over time, the side effects profile is such that some of the side effects like CRS or ICANS are very early side effects. Over time, these side effects are usually not an issue. There can be other things like prolonged cytopenias or a need to get immunoglobulin because of B-cell aplasia. But if the disease gets controlled and the disease gets into a long-term remission, then that can lead to a significant improvement in the quality of life and lower the level of suffering for these patients.

Dr. Turck:
Well, with those final insights in mind, I want to thank my guest, Dr. Nilanjan Ghosh, for joining me to discuss strategies for selecting CAR T-cell therapy in patients with relapsed or refractory diffuse large B-cell lymphoma. Dr. Ghosh, it was great having you on the program.

Dr. Ghosh:
Thank you for having me. It was a real pleasure.

Announcer:
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