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B-Cell Lymphoma Care: Overcoming Challenges in the Second-Line Setting

Announcer:
You're listening to *Project Oncology* on ReachMD. On this episode, sponsored by Kite Pharma, a Gilead company, we'll hear from Dr. Matthew Lunning, who's an Associate Professor in the Division of Hematology and Oncology and the Medical Director of Cellular Therapies at the University of Nebraska Medical Center. Today, he'll be discussing various challenges in the management of patients with relapsed or refractory large B-cell lymphoma in the second-line setting. Here's Dr. Lunning now.

Dr. Lunning:
When we start treating large B-cell lymphoma, it's often with curative intent with anthracycline-based therapies. In that setting, about 10 to 15 percent of the patients will have primary refractory disease, meaning that their lymphoma will either progress during induction therapy or will still be there at the end of therapy, often manifested by PET positive disease. And I think it is important to get a biopsy of the lesion if that is occurring.

This happens about 10 to 15 percent of the time, otherwise patients do relapse. And those relapses often occur within the first year from completion of their induction chemotherapy. So again, that's about 75 percent. And then those relapses that occur after one year are at about 25 percent. And why do I talk about this timeframe as an important point? Because I think we've seen some evolution in the therapeutic landscape around either primary refractory disease or those patients who have relapsed within one year of completing their induction therapy or those who have relapsed after one year. And that comes from the introduction not only of CAR T-cells in two lines or greater, but also CAR T-cells in those high-risk populations for second-line relapse or refractory large B-cell lymphoma that again relapsed within one year of completion of their therapy or are primary refractory or primary progressive.

There were two trials. There was the ZUMA-7 trial as well as the TRANSFORM trial that were randomized trials in this population looking at second-line chemotherapy and then followed by an auto transplant if a response was amenable to going to an autologous stem cell transplant or receiving CAR T-cell therapy. And in both trials, they met their primary endpoint for event-free survival in favor of CAR T-cell in lieu of second-line chemotherapy and autologous stem cell transplant. So I think that that now raises CAR T-cell up into that space.

But what about those patients that relapse within or after a year from their induction therapy? I still think you have to have the question of are they transplant eligible? And even in that population, the biggest barrier to transplant eligibility is often their disease. These patients are now almost all rituximab exposed or CD20 monoclonal antibody exposed. And so after two to three cycles of second-line, platinum-based chemotherapy, often a response is performed.

And if they achieve a response amenable to transplant, then BEAM or other transplant myeloablative strategies can be used. And I still believe that is the standard of care. Now transplant eligibility and CAR T-cell eligibility I think is taking a little bit of different approaches. I think we've continued to see data after datasets showing that there probably isn't an upper limit to CAR T-cell. I think with the lysis cell pilot, exposure and advanced age over the age of 70 as well as individuals with comorbidities, whether or not it was pulmonary comorbidities or cardiac or renal comorbidities, that you can have the opportunity for success, meaning CRs with durability with the lysis cell in a transplant-ineligible population. And that data continues to mature. So there are patients who would be considered transplant ineligible based upon comorbidities or potentially even advanced age that still may be CAR T-cell candidates.

So I think you have to be mindful about the depth of response in order now to go to an autologous transplant. And that does prevent some challenges because not all partial remissions to chemotherapy are created equal. And I think we see that in practice. And if those partial remissions aren't acceptable to go to transplant, then I would deem that as refractory disease. So even in the second-line setting

in the relapsed arena if a response isn't amenable to going to a transplant, then I think CAR T-cell does still remain an option in that population.

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