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Panel: Selecting and Sequencing CD19-Targeted Therapy in the Third-Line Treatment of R/R DLBCL

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Dr. Riedell:
Hi, my name is Peter Riedell, from the University of Chicago. And today I'm joined by my colleague Paolo Caimi, from Cleveland Clinic. And today we'll be discussing selecting and sequencing CD19-Targeted therapies in relapse refractory, diffuse large B cell lymphoma. And specifically for this section, we'll be focusing on therapy beyond the second line. And so, I'll start by just presenting a case to you, Dr. Caimi and then we can kind of discuss how you would approach it. So, my patient's a 76-year-old gentleman who presents to medical attention with some right neck swelling. He has a past medical history, significant for atrial fibrillation, hypertension, hypothyroidism, and some reflux. Additionally, in pertinent to note, he also does, in terms of his social history, have a wife who's currently suffering from Alzheimer's disease and he's sort a primary caregiver and the patient lives approximately three hours from a major medical center. On physical exam, he has a palpable mass in his right neck and his performance status is one. Some pertinent labs include an elevated LDH and his IPI score is four, consistent with high-risk disease. His PET imaging shows multi-station adenopathy including involvements both above and below the diaphragm. And he undergoes a biopsy of his right cervical lymph node, which reveals evidence of diffuse large B cell lymphoma, non-germinal center type, and his FISH analysis is negative for MYC, BCL2, and BCL6. And so initially this patient's treated with standard-of-care therapy with six cycles of R-CHOP and his end-of-treatment imaging, unfortunately, reveals some persistent disease in his left inguinal region. He then undergoes a biopsy which confirms persistent disease and he's then treated with a couple cycles of R-GemOx with unfortunately some residual disease persistent after that, at this point in time, he still has a preserved performance status at one. And so my question for you is, you know, we have a 76-year-old gentleman now who's failed two prior lines of therapy. And how would you kind of approach management in this patient?

Dr. Caimi:
Well, I think the case that you described is not an uncommon presentation of something that we need to approach in our clinical practice. I think you're seeing a patient with chemo refractory disease. Who's shown not to respond to first and second-line therapy. I think somebody who's failed the first-line therapy. You already know they're going to have difficulties in responding to a subsequent line. And I think that's where now we'll discuss in a separate episode what to do for a patient at that stage. But I think somebody who's at third line, with chemo refractory sees, you, I think switching modalities is reasonable, moving on to immunotherapy would be the best choice. I think if I could offer him CAR Ts, would be probably my preferred method of treating a patient like this. However, there's some pitfalls I think, included in the description of the case that make it a little bit hard to administer. And I think that's why not every patient that's eligible for CAR Ts received CAR Ts, I think because A, access is far away from the center, B, his patient care, or his caregiver liability seems to be limited with having to care for a wife with Alzheimer's, so I think in that scenario, I think choosing for alternatives would be probably what I would go for, I think of the options that you present there, definitely, I think the two preferred choices for me would be either loncastuximab tesirine and something that's been used in patients refractory disease and including the treatment, but also considered Pertuzumab, rituximab ad bendamustine, also included patients with high-risk disease, although not all were refractory

in the trial. I think that the one limitation probably will be the travel to back and forth to a center. So, I think that would probably be a limitation for including patients with tafasitamab and lenalidomide treatment with that.

Dr. Riedell:
Yeah, those are very good points. And I certainly think, you know, to echo your sentiment, it, CAR T-cell therapy is a very impactful therapy in patients in the third-line setting. We now have, you know, data, mature data from three trials, the Juliet transcend and ZUMA-1 study demonstrating CAT T's efficacy in that setting. But yeah, absolutely, in this case, there are some impairments that, you know, that preclude that therapy likely for this patient, given the distance and so forth. So, I think, you know, the options that you outlined are really reasonable. A lot of times in my clinical practice, you know, because none of these therapies have really been compared head-to-head, it is sometimes challenging for us to figure out what is always the best treatment for each patient and so in many of these situations, it is individualized. And I think the points that you raised in terms of logistics really are probably going to be one of the things that is going to dictate which therapy might be the best for this patient. You know, as you mentioned, zylonta or loncastuximab tesirine is every three-week infusion. And so that does, you know, provide some convenience factor to this patient that has, you know, some caregiver needs along with BR Pola also provided on an every four-week basis is another very reasonable option. And then, you know, for the reasons that you mentioned, I think probably tafasitamab and lenalidomide might be not the preferred choice in this setting, just because there's not a lot of data to back, you know, its utilization in patients with primary refractory disease.

Dr. Caimi:
I agree. I think logistics will be probably the predominant thing. Eligibility will be the other one, certainly tafasitamab and lenalidomide has a very frequent infusion schedule, which is the additional limitation. I think that, you know, that at the point of the third line, the choice of treatment will also be impacted by the adverse events you would expect of somebody who's got in six cycles of R-CHOP and two cycles of GemOx will have a little bit of a higher risk of neuropathy or will have had other side effects that will make you choose one of the other, their remaining options of either Pola BR or loncastuximab tesirine whether you would choose somebody who has no neuropathy for more any lung can, somebody who has other comorbidities to choose maybe Pola BR also for the schedule hematologic toxicity as well.

Dr. Riedell:
Absolutely, and you know, one of the other things I always think about when I'm determining therapy in patients in this setting is kind of what's the pace of their disease and how urgently they may need a response, you know, in patients that have failed two prior regimens, a lot of times they can be very symptomatic. And so, trying to choose a therapy that has a short time to response is also something important. And, you know, we have data to support that with BR Pola along with loncaT, where generally, responses are relatively early on.

Dr. Caimi:
Yeah, I think that's true. And I think that's one of the, you know, besides the limitations of logistics for CAT Ts is the time to treatment and what to bridge them with. Many people are using some Polatuzumab-containing agent maybe not always with the addition of bendamustine but I think understanding what you can give a patient before CAR T or understanding that a patient that is rapidly progressing may preferably be treated with something else, like you mentioned, to control the diseases. And so sequently, maybe consider CAR Ts would be a reasonable option as well.

Dr. Riedell:
Absolutely and you know, certainly in this case, if this patient were to, you know, receive next-line therapy in the third-line setting, and then, you know, not fare well with that, then if things were to change, CAR T could certainly be an option in the future. If, you know, logistics were to be improved if you were to be able to get caregiver support or other things like that. So, these aren't necessarily mutually exclusive

Dr. Caimi:
Fully agree, I think in a patient who has the capacity to access CAR-Ts, it would be my choice. If I had somebody of the same age, I probably, you know, seems to be somebody who has some comorbidities. If I was able to give CAR-Ts in that scenario, I would probably lisocabtagene for treatment. Whereas if, as a younger patient, with more tolerability of adverse events, probably at that point, which is oxycaptodene.

Dr. Riedell:
Excellent, all right, well, thank you very much for all your insight and thoughts, Dr. Caimi. This has been a great session and I appreciate

the audience's time and attention, take care.

Announcer:
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