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Late-Stage Bispecifics and ADCs in DLBCL

Announcer:
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On May 19, 2023, the FDA granted accelerated approval to epcoritamab-bysp (Epkinly) for relapsed or refractory diffuse large B-cell lymphoma not otherwise specified, including diffuse large B-cell lymphoma arising from indolent lymphoma, and high-grade B-cell lymphoma after 2 or more lines of systemic therapy.

On June 15, 2023, the Food and Drug Administration granted accelerated approval to glofitamab-gxbm (Columvi) for relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) or large B-cell lymphoma (LBCL) arising from follicular lymphoma after 2 or more lines of systemic therapy.

Dr. Rutherford:
Hello. This is CME on ReachMD, and I'm Dr. Sarah Rutherford from Weill Cornell Medicine and New York-Presbyterian Hospital, here with Dr. John Leonard, also from the same institution. And we're looking today at the rationale and evidence for late-stage bispecific antibodies and antibody-drug conjugates for diffuse large B-cell lymphoma, DLBCL. There's been so many new drugs available and being studied, so this is an exciting time for our patients.

Dr. Leonard, what does our audience need to know about these drugs?

Dr. Leonard:
Well, I think that this is a really important area, I agree. For a long time, we had very few options for patients with recurrent diffuse large B-cell lymphoma, and now the categories of bispecifics and antibody-drug conjugates are quite important. We have several approved drugs as well as agents that are in clinical trials, and so for a patient who's been through a chemotherapy-based regimen and had a relapse, they may get more chemotherapy and an autotransplant, they may get CAR T-cells, but we have a group of bispecific antibodies. These are antibodies that with one arm bind CD20 typically on the tumor cell, and with the other arm, CD3 on a T-cell. And these include epcoritamab, mosunetuzumab, glofitamab, odronextamab. These are all investigational for diffuse large B-cell lymphoma. [Epicoritamab-bysp (Epkinly) and glovitamab-gxbm (Columvi) are no longer under investigation. On May 19, 2023, the FDA granted accelerated approval to epcoritamab-bysp (Epkinly) for relapsed or refractory diffuse large B-cell lymphoma not otherwise specified, including diffuse large B-cell lymphoma arising from indolent lymphoma, and high-grade B-cell lymphoma after 2 or more lines of systemic therapy. On June 15, 2023, the Food and Drug Administration granted accelerated approval to glofitamab-gxbm (Columvi) for relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) or large B-cell lymphoma (LBCL) arising from follicular lymphoma after 2 or more lines of systemic therapy.] Mosunetuzumab is approved for follicular lymphoma in certain settings. And the bottom line is that in aggressive lymphoma or DLBCL, they have response rates in the range of anywhere from really 60% to 80% with CR [complete response] rates in the range of 30% to around 50%, and in some cases, these can be quite durable with median responses over a year or so. And so these are important drugs. I would say that they are more tolerable than CAR T-cells. They

don't have quite the same immune reactions but probably more effective – or less effective than CAR T-cells, so kind of an intermediate option.

And I'm going to turn over the discussion to you, Dr. Rutherford, to perhaps cover some of the other agents in this category.

Dr. Rutherford:
Thank you so much, Dr. Leonard. That was really interesting to hear. I wanted to mention specifically, I was impressed by some of the data that I saw at ASH 2022 meeting on epcoritamab, in their study looking at relapsed and refractory diffuse large B-cell lymphoma patients, quite a large group of over 150 patients. And I think that while there may be inferior efficacy compared to CAR T-cell therapy, there are many advantages of this type of drug, one of which, especially in diffuse large B-cell lymphoma, is that it's readily available off the shelf, as we often say, whereas CAR T-cell therapy will take sometimes 3 weeks and even longer and even can fail in production, whereas we know this type of drug will be immediately available for our patients who often need therapy right away as their disease is progressing quickly. And I do think that the rates of CRS [cytokine release syndrome] and some of the neurotoxicity appears to be lower as a class with bispecific antibodies in comparison to the CAR T-cell therapy. So I'm very excited about this type of agent coming as a possibility for our patients, and I think it will be interesting for us to learn how to sequence them best with so many novel agents available now.

We also have some other antibody-drug conjugates that target CD19, for example, that's loncastuximab tesirine, and we have tafasitamab, which also targets CD19, and there actually even could be a role for brentuximab vedotin, which targets CD30, which is expressed sometimes in diffuse large B-cell lymphoma. So I think it'll be interesting for us all to move forward with these treatment options hopefully available for our patients in the future.

Thank you so much. This has been a great few minutes of discussion. Our time is up. We appreciate you listening today.

Announcer:
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