

Transcript Details

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First-Line ADCs in Metastatic Triple-Negative Breast Cancer

Announcer:

You're listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. Here's your host, Dr. Alexandria May.

Dr. May:

This is *On the Frontlines of Metastatic Breast Cancer* on ReachMD, and I'm Dr. Alexandria May. Joining me to discuss the treatment of metastatic triple-negative breast cancer is Dr. Heather McArthur. She's the Clinical Director of Breast Cancer and Komen Distinguished Chair in Clinical Breast Cancer Research at the University of Texas Southwestern Medical Center in Dallas. Dr. McArthur, welcome to the program.

Dr. McArthur:

Thank you so much for having me. It's a pleasure to be here with you.

Dr. May:

So, let's jump right in, Dr. McArthur. This year brought two major first-line approvals for metastatic triple-negative breast cancer, sacituzumab govitecan and datopotamab deruxtecan. How have these shifts changed the way you plan treatment for a newly diagnosed patient?

Dr. McArthur:

So, I think the context is incredibly important here. When we depended on conventional chemotherapy, the life expectancy for patients with metastatic triple-negative breast cancer was 12 to 18 months. And we saw an incremental benefit for patients who had PD-L1 positive disease with the KEYNOTE-355 study. That improved overall survival by seven months, which, on the surface doesn't seem like a huge incremental benefit. But when you think about the context—survival of 12 to 18 months—that was a huge incremental benefit. But it was relevant to the minority of patients. Only 30 to 40 percent of patients have PD-L1 positive tumors. So there was a huge unmet need.

So, it was incredibly exciting this year, when we saw the antibody-drug conjugates that had been very successful in more heavily pretreated disease move up into the first-line setting. Two drugs are now both in the first-line space, with very different clinical trial designs, which we can absolutely talk about. But that really shifted the needle away from conventional chemotherapy and gives patients and providers much more exciting outcomes. We can actually change the long-term outcomes for patients with metastatic triple-negative disease, which has been a very difficult space in which to innovate.

Dr. May:

How much does tolerability factor into your first-line choice for a given patient, and what does managing those side effects look like in practice?

Dr. McArthur:

Sacituzumab govitecan, which outperformed conventional chemotherapy in ASCENT-03, is given days one and eight of every three-week cycle, so it's two weeks out of three, whereas TROPION-Breast02 showed the benefit of datopotamab deruxtecan, which is given less frequently. However, it does require more management on the part of patients. So they have to do the mouthwash, they have to do the eye drops four times a day. So it's a little bit more engaging for patients. So these become nuanced conversations.

And in ASCENT-03, they allowed for crossover to access sacituzumab govitecan if you progressed on conventional chemotherapy,

which was the right thing to do, because that was the standard of care in the United States and other geographic locations. On the TROPION-Breast02 study offering datopotamab deruxtecan, it wasn't approved in that setting, and so there wasn't the same crossover. So you can't really do a cross-study comparison there, because the survival data is influenced by the access to subsequent lines of therapy. And so that's a consideration.

So all things being equal, they both had incredible progression-free survival in the first-line setting. And, in my practice, it's become a more nuanced discussion. If patients live at a geographic distance, that's a consideration. If they're not willing to do the eye drops four times a day and mouthwash, with the Dato-Dxd, that's a consideration. So they really are becoming much more nuanced conversations than we had a couple of years ago.

Dr. May:

For those just tuning in, you're listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. I'm Dr. Alexandria May, and I'm speaking with Dr. Heather McArthur about the management of metastatic triple-negative breast cancer.

Dr. McArthur, an important question that's been raised in light of these recent approvals is what to do when a patient progresses on a first-line ADC. What are your thoughts on the situation?

Dr. McArthur:

So there's been a lot of conversation around ADC after ADC because, obviously, there's a lot of excitement about ADCs in general. Retrospective datasets and emerging data indicates that ADC after ADC isn't a particularly successful strategy, so put your best foot forward and get the drug most likely to benefit upfront.

And right now, we are—after ADC—dependent on conventional chemotherapy or clinical trials. And there are a lot of very exciting clinical trials available to patients with TNBC. So patients can access drugs that have bispecific antibodies that have multiple payloads. So all the drugs that we've been talking about have topoisomerase one inhibitor payloads. They now have drugs that have multiple different payloads and multiple different targets, and the best way to access the future is through participation in clinical trials.

Dr. May:

Now, we know that roughly half of patients with metastatic triple-negative breast cancer unfortunately never make it to a second line of therapy. Given that reality, how do you talk with patients early on about goals of care, and does that fact change how aggressively you sequence therapy from the start?

Dr. McArthur:

I mean, how heartbreaking is that statistic? It's terrible. I would say to put your best foot forward. My job is not to dictate to my patients how to live their life. It's to present to them the best menu of options that I can offer them, which is usually standard of care versus clinical trials. I think clinical trials, especially for triple-negative breast cancer, are so important, because even despite recent innovations, the life expectancy is not what we would hope for, and we need further innovation. And the only way to innovate is access through clinical trials. It is the only way that we move the field forward, and it takes brave men and women to take a leap of faith.

Engagement in research and early access is super important, especially in patients who have triple-negative disease, which often affects our younger patient population. These are my pregnancy-associated breast cancer patients. These are the patients who have early recurrence. These are patients where we desperately need to innovate, and the only way to do that is through research.

Dr. May:

Dr. McArthur, as we come to the end of our program, what are the most important takeaways for clinicians to remember when treating patients with metastatic triple-negative breast cancer?

Dr. McArthur:

So I think it's very clear that you have to put your best foot forward. So accessing the best available drugs, which currently are antibody-drug conjugates in the first-line setting, is critically important. That definitely improves progression-free survival and maybe improves overall survival. But I also think that referring your patients to centers that have clinical trials where we can, in the second-line setting and beyond, do better than conventional chemotherapy is critically important.

Dr. May:

With those final thoughts in mind, I want to thank my guest, Dr. Heather McArthur, for sharing her insights on treating metastatic triple-negative breast cancer. Dr. McArthur, it was great having you today.

Dr. McArthur:

Thank you so much. I appreciate it.

Announcer:

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