Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/project-oncology/mtnbc-first-line-strategies/36349/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Staying Ahead in mTNBC: First-Line Strategies for an Evolving Standard of Care

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Gilead Sciences. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
Welcome to *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and joining me to discuss how we can address unmet needs in the first-line management of metastatic triple-negative breast cancer is Dr. Alexis LeVee. She's a breast medical oncologist and clinical instructor at UCLA Health.

Dr. LeVee, thank you so much for being here today.

Dr. LeVee:
Thank you so much for having me.

Dr. Caudle:
So, to start us off with some background, Dr. LeVee, why is early decision-making so critical in first-line metastatic triple-negative breast cancer?

Dr. LeVee:
Early decision-making is so critical because of how poorly these patients do. Prognosis is poor for metastatic triple-negative breast cancer with a median overall survival of around one year, and studies show that about half of patients who are diagnosed with metastatic triple-negative breast cancer don't make it to see second-line treatment. They can only receive first-line therapy, and that's often because patients develop disease progression and disease complications and pass away before being able to see subsequent treatment.

And when the disease progresses, it often also becomes more difficult to treat and more resistant to standard therapies. And so it's really critical that we give our best treatments first in the first-line treatment setting.

Dr. Caudle:
And how does disease heterogeneity play a role in shaping treatment decisions for these patients?

Dr. LeVee:
Triple-negative breast cancer is a very heterogeneous disease. First of all, there's different histologies, so you can have ductal, lobular, or even metaplastic triple-negative breast cancer, and they all behave pretty differently. There's also underlying molecular subtypes within triple-negative, such as the more basal-like, mesenchymal, and luminal androgen receptor. And all of these respond to chemotherapies and standard treatments differently. So we have to understand that triple-negative breast cancer is not just one type of breast cancer, but really a very heterogeneous type of breast cancer.

And within these different histologies and molecular subtypes, you can have different mutations. So, for example, BRCA status can impact how we treat triple-negative breast cancer. Patients who do have BRCA1 and 2 mutations, and even patients who have somatic BRCA1 or 2 as well as PALB2 mutations, may respond to PARP inhibitors.

And then patients may also respond to immunotherapy depending on their PD-L1 status. So PD-L1 is a biomarker that can show response to immunotherapy, and the biomarker is not a great test. There's lots of various tests that can test PD-L1. And there's also PD-L1 heterogeneity too, whether you test a lymph node versus the liver versus the bone, and so the outcomes of the testing may differ.

And so it is sometimes difficult to tell when a patient will respond to immunotherapy in triple-negative breast cancer.

Lastly, there's different presentations of triple-negative breast cancer. So there's a patient who may have relapsed after already receiving standard of care neoadjuvant chemoimmunotherapy, or there's a patient who's presenting with de novo metastatic disease in the liver versus someone who's presenting with de novo leptomeningeal disease.

So all of these types of triple-negative breast cancer presentations must be handled really differently with the use of chemotherapy, immunotherapy, targeted agents, PARP inhibitors, and now antibody-drug conjugates. So we have various treatments for triple-negative breast cancer, and how we decide on those treatments is based on all of these different molecular subtypes and presentations.

Dr. Caudle:
For those of you who are just joining us, this is *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Alexis LeVee about unmet needs in the first-line treatment of metastatic triple negative breast cancer.

So, Dr. LeVee, I'd like to shift over now to implementation challenges. Can you tell us about the barriers that prevent clinicians from translating guideline-recommended regimens into real-world practice, especially in community settings?

Dr. LeVee:
Yeah, I think one of the biggest barriers—and one of the best things too—is how quickly treatment guidelines are changing for triple-negative breast cancer. So it's sometimes difficult to be able to understand and learn how to implement the new data for our patients so quickly and be able to get the new treatments approved.

So just from the last year alone, first-line treatment of metastatic breast cancer will be changing, most likely. So at ASCO this past year, we saw data for ASCENT-04, which looked at sacituzumab govitecan plus pembrolizumab in PD-L-positive metastatic breast cancer, showing that an antibody-drug conjugate plus immunotherapy—so SG plus pembro compared to chemo plus pembro—improved outcomes. And so it looks like that will be our new standard of care.

And then at ESMO just a couple months ago, we saw data in which two different antibody-drug conjugates showed to be superior to chemotherapy in the first-line metastatic setting—that also will likely be new standard of care. So that was ASCENT-03 looking at sacituzumab govitecan compared to chemo. And then TROPION-Breast02 looked at Dato-DXd compared to chemo in the first-line setting.

And so I think being able to interpret all of this data and then being able to learn how to use this data for our patients will be one of the bigger hurdles when the guidelines are changing so quickly. And then, because we have so many ADCs too, understanding how to sequence these ADCs is difficult to understand.

Other implementation difficulties are getting insurance approvals, getting approval and reimbursement and coverage for all the NGS testing, and then being able to manage a patient with a multidisciplinary team given so many kind of disease-related complications that can occur with metastatic triple-negative breast cancer. So it’s a tough disease to take care of—it really needs a full multidisciplinary team with pharmacists, chemo nurses, and financial counselors to help.

Dr. Caudle:
Given those challenges, what tools or strategies could help close that gap between guidelines and patient care?

Dr. LeVee:
I think because first-line treatment of metastatic triple-negative breast cancer should involve automatic testing of PD-L1 status, as well as BRCA1 and 2, there should be some signal or automatic test to try to get more providers to perform those tests.

For example, if a patient gets a biopsy that shows metastatic triple-negative breast cancer, then there should be perhaps a protocol in which the pathologist automatically reflexes PD-L1, and then perhaps some other type of EMR or other way to reflex for our providers and for our patients to test for BRCA1 and 2 because that is necessary in the first-line setting.

I think other tools to implement these new treatments for our patients are also just increasing awareness, both on the provider level and the patient level, given how much treatment is changing and rapidly evolving. And so more peer-to-peer discussions with providers as well as more educational opportunities for patients to be able to know about these new therapies will be really important.

Not only is knowing about the therapy important, but also, each of these newer therapies comes with their own unique toxicities, whether it be significant neutropenia or stomatitis, diarrhea, or an ocular toxicity with Dato-DXd. So I think being able to know about how to manage these newer toxicities will be really important in order to try to maximize duration on therapies too.

Dr. Caudle:

Now, before we wrap up, Dr. LeVee, do you have any key takeaways that you'd like to share with our audience?

Dr. LeVee:
Metastatic triple-negative breast cancer, as we know, has a poor prognosis, but I think there has been a good amount of developments in the field just in the last year alone. And so I'm optimistic that there will be even more developments. There's newer antibody-drug conjugates. There's newer bispecific antibodies that we're testing in clinical trials and combination strategies as well. And so even though these patients overall have a poor prognosis, I'm hopeful in the future there'll be even more development.

I think more studies need to look at newer agents and therapies that can target the brain—that have CNS penetration—as well as for patients who have leptomeningeal disease. These patients have really poor prognoses given a limited number of these therapies can enter the CNS. And as we know, with metastatic triple-negative breast cancer, it can go to the brain quite often. So that is an area of need as well as lots of studies looking at biomarker strategies—so how we can either escalate therapy for those who appear to need it and even de-escalate therapy, for example, for a patient who might have a luminal androgen receptor-type triple-negative breast cancer who may not need as aggressive of a chemotherapy regimen.

There are studies looking at TILs—spatial transcriptomics of what the tumor microenvironment looks like—so that we can really optimize the treatment strategy for each individual patient as each of these triple-negative breast cancers does behave quite differently.

Dr. Caudle:
Well, that's a great way to round out our discussion. I'd like to thank my guest, Dr. Alexis LeVee, for joining me to discuss how we can improve our approach to the first-line treatment of metastatic triple-negative breast cancer.

Dr. LeVee, it was great having you on the program today.

Dr. LeVee:
Thank you so much for having me and for listening.

Announcer:
This episode of *Project Oncology* was sponsored by Gilead Sciences. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!