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/a-look-at-whats-new-in-invasive-lobular-carcinoma/16355/

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

A Look at What's New in Invasive Lobular Carcinoma

Dr. Chalasani:
Invasive lobular carcinoma is a subtype, which occurs in about 10 to 15 percent of breast cancers but is known to be harder to be detected by imaging. So how do we approach diagnosing and treating this subtype?

Welcome to *Project Oncology* on ReachMD. I'm Dr. Pavani Chalasani, and joining me today to talk about invasive lobular carcinoma is Dr. Jason Mouabbi, who is an Assistant Professor of Medicine at the University of Texas MD Anderson Cancer Center and Chair of the Lobular Breast Cancer Alliance. He'll also be presenting a session on this topic at the 2023 San Antonio Breast Cancer Symposium.

Dr. Mouabbi, thanks for joining me today.

Dr. Mouabbi:
Thank you. Happy to be here.

Dr. Chalasani:
All right. To set the stage for our conversation, Dr. Mouabbi, can you give us some background on the invasive lobular carcinoma on its biology and presentation?

Dr. Mouabbi:
Yes, I'd be happy to. Lobular breast cancer is an important understudied subtype of breast cancer. In fact, it is the second most common subtype of breast cancer after the subtype of ductal carcinoma, also known as NST, or non-specific or special subtype. So lobular carcinoma differ greatly from ductal carcinoma. It's because mainly of a loss of a certain protein called E-cadherin. E-cadherin is known as the anchoring protein of cells in our body, and so it plays a vital information to give a geographical location for our cells in our body, so it makes the cell attached to the cytoskeleton of the body and cells attached to one another. However, lobular cells lose E-cadherin due to multiple different ways, and because of that, those cells are just in suspension, and they tend not to form a mass, whereas ductal carcinoma tend to form a mass.

Now because of that, the lobular breast cancer tend to present at the more advanced stages compared to ductal carcinoma, and it's much harder to detect in the metastatic setting unless there is symptoms that may present. So historically, it's been very challenging for imaging to detect it, and mammography and ultrasound, which are commonly used to diagnose breast cancer, do a poor job with lobular carcinoma. There's a very high false-negative rate with mammography on ultrasound, about 40 percent.

So something that I'm going to be discussing in my presentation here are contrast-enhanced mammogram. So those are mammogram that we give a little bit of contrast with to enhance the breast better, and those have shown to be excellent for lobular carcinoma. They have excellent sensitivity close to that of MRI. They have very little false negativity, and very importantly, they have very little false positivity and that their size concordance at this time of surgery are very accurate compared to what they have shown.

Dr. Chalasani:
Oh, that's great. With all the new technologies and modalities available, and hopefully, soon we can leverage them for screening, both

for early stage and also in the metastatic setting too. So aside from the diagnosis, are there challenges in the treatment of lobular cancers that you encounter?

Dr. Mouabbi:
Yes. Historically, lobular cancer has been grouped with the more common ductal carcinoma and treated as one subtype of breast cancer or one type of breast cancer, which really didn't do any justice for patients with lobular carcinoma because now we know by using retrospective data, that lobular cancer tend to respond differently to ductal carcinoma. And one example is if we look at chemotherapy; lobular cancer tend to be less responsive to chemotherapy compared to ductal carcinoma, yet those patients always receive chemotherapy because some studies that group both of them showed that there was a trend to benefit to use chemotherapy, so it's very important to study lobular separately than ductal carcinoma. They are different cancer. They respond differently to therapies.

The majority of lobular carcinomas are hormone-positive, 95 percent of them, and they do respond well to endocrine therapy in combination with targeted therapy. Now the targeted therapy, this is with the area of high importance, and this is the one that a lot of people are working on right now in lobular. So we showed a year ago that when combining endocrine therapy in combination with CDK4/6 inhibitor, a patient with lobular cancer benefited in the same magnitude compared to those with ductal carcinoma, which was great because before that we didn't know if both of them benefited the same way or did one of them do better than the other. So the combination of endocrine therapy, CDK4/6 inhibitor, is viable for both subtypes of breast cancer.

Dr. Chalasani:
For those just tuning in, you're listening to *Project Oncology* and ReachMD. I'm Dr. Pavani Chalasani, and I'm speaking with Dr. Jason Mouabbi about invasive lobular carcinoma.

So now I want to turn your attention to your session at this year's San Antonio Breast Cancer Symposium, Dr. Mouabbi. What are some of the innovative approaches to ILC that you'll be discussing?

Dr. Mouabbi:
There was a study that I'm going to highlight in my presentation, called the SUMMIT trial, that showed that using the neratinib, which is a HER2 tyrosine kinase inhibitor, in patients after they were treated with endocrine therapy CDK4/6, that it worked really well for lobular, and it has a very impressive objective response rate of 41 percent in lobular patients. So this is very encouraging, and it will be highlighted in my presentation, but the interesting part is there is a lot of other promising targets coming. One of them is in HER2. Also, there is another tyrosine kinase inhibitor, called tucatinib, that are also being looked at HER2 mutation.

Other than that, there is also another very interesting target for lobular is we found through research both in the preclinical models and in the clinical setting that the patient with lobular carcinoma have activation of their P10 PI3 kinase AKT pathway irrespective of a mutation in that pathway, which is really interesting. It's interesting because we just got recent FDA approval of a drug, called capivasertib, for a patient with an altered pathway of the P10 PI3 kinase AKT pathway, and it's an AKT inhibitor. So it's really interesting because it does have a huge potential to be a game-changer for lobular breast cancer patient because if you look at lobular breast cancer patient, about 70 percent of them will have an alteration in that pathway. It's interesting also to study this drug in the early setting. Maybe it can also help shrink those tumors before surgery, so that's another thing that's interesting for us as clinician working on lobular cancer.

Another mechanism that we were interested in is we found that there is signature inside lobular cells that predispose those cells to DNA damage, and using a PARP inhibitor have been shown in preclinical model to be of great promise. So this is another thing that right now is being worked on is to treat the lobular breast cancer patient with a PARP inhibitor irrespective of having a BRCA1 or BRCA2 mutation. And also, we're going to highlight another target is the Interleukin-6 STAT3 pathway, which seems to be very active in lobular carcinoma.

Interestingly, we're going to talk about targeting other biomarkers that are present in lobular breast cancer, like HER2, using a drug, called Enhertu, that's been shown great efficacy in patients with HER2-low breast cancers. Also, we're going to talk about another biomarker, called Trop2, which we also have two targeted therapies now for. One is called sacituzumab govitecan, which is already FDA-approved, but there is also recently—and in this San Antonio Breast Cancer Symposium, we will get updated data on—the datopotamab deruxtecan, another Trop2-targeted antibody-drug conjugate. And lastly, we're going to talk about another biomarker, called HER3. So there is an interesting drug that's been coming, called HER3 DXd, or patritumab deruxtecan, and lobular breast cancer

tend to overexpress HER3, which is a very interesting target that also I'm going to be highlighting in my presentation.

So hopefully, by looking at all of those different targets we can get a full picture about how to treat lobular carcinoma in the next 10 to 20 years.

Dr. Chalasani:
This has been a fantastic review of invasive lobular carcinoma, and I would like to thank my guest, Dr. Jason Mouabbi, for joining me to share his insights.

Dr. Mouabbi, it was a pleasure speaking with you.

Dr. Mouabbi:
Thank you so much. This was an amazing opportunity.

Dr. Chalasani:
I'm Dr. Pavani Chalasani. 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.