

Questions and Answers from Panelists of *What's New in Screening and Treatment for Lobular Breast Cancer Webinar*

Q&As re: ILC and Treatment

1. Can you say any more about any immunotherapies coming or currently in use for invasive lobular carcinoma (ILC)?

There are no specific immunotherapies coming up for ILC at this time. The GELATO Study that looked at immune therapy specifically for metastatic ILC showed limited activity. Unfortunately, the Keynote-756, a randomized study of > 1000 patient with early stage, high risk, ER+ breast cancer of chemotherapy +/- pembrolizumab, included invasive ductal breast (IDC) cancers only.

2. Can you share any updates on what is known about pleomorphic ILC?

Pleomorphic cancers have higher proliferative cancers and are more aggressive cancers. Recently, it was shown that they are enriched in ERBB2 mutations when compared to classic ILC, and treatments that target these mutations could be a potential therapeutic option.

3. What does an ER1 mutation mean? What do you think about checking CA 27-29?

ESR1 mutation is a common mechanism of resistance to endocrine therapy that was primarily acquired in metastatic disease. CA 27-29 or CA15-3 are tumor markers that are used in metastatic breast cancer and can help to monitor treatment response or disease progression; however, they do not replace imaging such as CT scans or PET-CTs.

4. How does the presence or not of LCIS when you have ILC affect your prognosis? (Dr. Jason Mouabbi presented a poster at SABCS on this)

In one retrospective observational study from MD Anderson, the absence of LCIS was associated with worse outcomes in ILC. Additional studies are needed to validate this finding.

5. Does ILC have a distant recurrence at the same rate as IDC?

The differences in long term outcomes (distant recurrence) in ILC and IDC has been controversial. Some studies have shown worse outcomes and others have shown no difference. There are studies showing that late recurrences (at least 5 years from the diagnosis of early-stage disease) are more common in ILC.

6. Is there one preferred aromatase inhibitor (AI) for ILC?

Larger studies have shown that there are no significant differences between specific AIs in hormone receptor positive breast cancer. Since their activity is very similar, this is likely true for ILC as well.

7. Is metformin considered useful for long-term cancer suppression?

The addition of metformin does not reduce the risk of breast cancer recurrence. A large phase III randomized study of more than 3,000 patients showed that the addition of metformin did not improve outcomes.

8. Are there any studies or new approaches of treatment for pre-menopausal patients?

Recent large studies have shown the efficacy of the addition of ovarian suppression as part of adjuvant endocrine therapy in early-stage disease. There are multiple efforts to study the unique biology of premenopausal breast cancer.

Q&As related to imaging/detection and ILC

9. What is the current thinking about the effectiveness of thermography in detection of ILC?

Currently, thermography is not considered to be an effective modality for detecting early-stage breast cancer.

10. How common is it for screening to miss the cancer in a person with dense breasts?

There are two ways in which we can answer this question. Firstly, we can discuss the false positive rate, which is the number of screening mammograms that fail to detect breast cancer when breast cancer is present, per 1,000 screens. The false positive rate of digital breast tomosynthesis (DBT, or 3D mammography) in dense breasts is 0.14 per 1,000 screens (Durand et al, False-Negative Rates of Breast Cancer Screening With and Without Digital Breast Tomosynthesis, Radiology, Dec 2020).

Secondly, we can discuss the sensitivity of mammography (which is the percentage of people who have cancer in whom mammography correctly detects the cancer). In women with dense breasts, the sensitivity of DBT (3D mammography) ranges from 84-90%. In other words, for every 100 women who have breast cancer, mammography correctly detects cancer in about 84-90 of those women. Conversely, 10-16 women out of those 100 women with breast cancer will have a falsely normal mammogram.

11. Can you recap what the surveillance can be for women who have had mastectomies?

There is insufficient literature to support the use of mammography (2D or 3D/DBT) in women after they have had mastectomy (on the mastectomy side). Mammography is recommended on the opposite side (if the patient has a native breast).

12. Do you think molecular breast imaging (MBI) is recommended for detecting recurrence of ILC in dense breasts?

There is limited data regarding the use of sestamibi MBI for screening women with a history of invasive lobular carcinoma in dense breasts. Some studies have demonstrated that the addition of MBI to mammography can increase cancer detection rates, including those with a personal history of breast cancer and/or dense breasts. (Wang L, Strigel RM. Supplemental Screening for Patients at Intermediate and High Risk for Breast Cancer. Radiol Clin North Am 2021).

Q&As related to ILC and Surgery

13. Is there data on rate of recurrence when negative margins are not achieved with a DMX followed by radiation?

Data on rates of local recurrence is limited in this specific scenario. However, a few points worth noting: if mastectomy is performed appropriately (i.e., following anatomic planes with removal of all of the evident breast tissue), the presence of a "positive" anterior or posterior margin does not necessitate additional surgery or removal of skin (unless there was evident involvement of the skin by tumor). Additionally, apart from margin status, rates of recurrence are also greatly impacted by other tumor features such as tumor size, lymphovascular invasion, tumor grade, nodal status, etc. Your physician would be able to provide a more individual estimate of risk of recurrence by taking all of these factors into account.

14. Does flap reconstruction make it difficult to identify early chest wall recurrence?

Fortunately, reconstruction (either flap or implant-based) does not usually make it difficult to identify chest wall recurrence. When chest wall recurrence occurs, it typically takes place right below the skin and will be identified by the presence of a nodule on exam. The presence of a flap or an implant underneath does not usually impede the ability to examine and identify such an issue.