Patient Stories and Provider Advice Mark Invasive Lobular Breast Cancer Awareness Event

Fred Hutch experts discuss invasive lobular breast cancer's hormonal risk factors, screening recommendations and new research.

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Lobular breast cancer patients gathered at Fred Hutch Cancer Center last week for a two-hour program featuring patient stories, epidemiological findings and new developments in screening and clinical trials for this common breast cancer subtype.

The event, held October 15, was in recognition of Global Lobular Breast Cancer Awareness Day, selected by patient advocates to represent the 15% of breast cancer patients diagnosed with invasive lobular carcinoma, or ILC, every year. Patient and provider events were held across the U.S. — and the world — with 24 state governors filling official proclamations recognizing the day. The American Cancer Society, in tandem, released its first report on ILC's occurrence and outcome, which showed a steep rise in rates over the last several years.

"Invasive lobular carcinoma is the second most common breast cancer subtype," said Fred Hutch breast cancer radiologist Diana Lam, MD, during her talk on the imaging challenges of ILC. "Unfortunately, it does present at more advanced stages and with larger tumor sizes and lymph node involvement."

Why are lobular cancers found at later stages? What are the biological hallmarks of this disease? Are there ways to reduce the risk of lobular? And what about new research? Fred Hutch experts provided answers to these questions and more.

An often 'lumpless' breast cancer

One reason ILC is often found at later stages is because it doesn't usually form lumps or masses, so it's not easily felt upon exam or seen on imaging. And when it is found, it can still be underdiagnosed.

Stefanie LeJeunesse, diagnosed with metastatic lobular breast cancer, or mILC, at age 39, found

this out the hard way after going to her local rural hospital to have them check out dimpling in one of her breasts.

“I had a mammogram, an ultrasound-guided biopsy, an MRI and a bone scan,” said the educator and mother of three from Mt. Vernon, Washington, who shared her story during the event. “And I was told I had stage II breast cancer with a couple of iffy lymph nodes that were probably nothing to worry about.”

Despite these reassurances, LeJeunesse came to Fred Hutch for a second opinion.

“I still feel sorry for the team who had to tell me at that appointment that my two-centimeter primary tumor was actually 14 centimeters of cancer with extensive lymph node involvement and metastases to several spots in my spine and ribs,” she said. “I actually asked my oncologist ‘Should I stop off to get a coffin on the way home?’”

‘In terms of lobular cancer, there are a lot of opportunities here. I’m really hoping for a time when patients who have ER+ tumors never see chemotherapy because we have so many other things we can use. We have better endocrine manipulation and even endocrine therapy additives that are molecularly targeted and have way less toxicity.’
— Fred Hutch clinical researcher and lobular breast cancer expert Dr. Hannah Linden

Lobular’s hallmark — and what sets it apart as a distinct biological subtype — is its lack of E-cadherin, a protein encoded by the CHD1 gene that acts as molecular glue, clumping cancer cells into a lump. Without it, ILC cells grow in a straight line or branching pattern, which makes it much harder to see on mammograms, especially in dense breast tissue.

Other ILC characteristics:

- ILC tends not to disrupt the normal “architecture” of the body with a tumor mass.
- It tends not to have microcalcifications, another way breast cancers are seen on imaging.
- Lobular tumors are often multi-focal; there can be more than one tumor in a breast.
- Lobular is commonly bilateral; patients are diagnosed with cancer in both breasts.
- ILC’s biological differences make it difficult to image when the cancer becomes metastatic and spreads to other organs.
- ILC’s metastatic spread is also unique, often invading the peritoneum, gastrointestinal (GI) tract, ovaries, etc., in addition to more common sites like bone.

“Mammograms are imperfect, but they’re the only screening test available proven in randomized clinical controlled trials to reduce breast cancer mortality,” Lam said, going on to explain that cancer may appear white on mammograms, as does dense breast tissue. “Trying to find ILC can be like looking for a polar bear in a snowstorm.”

As a result, mammogram sensitivity rates for ILC are lower than those for the more common ductal type, IDC, and “only around 34% to 83% across all densities.”

“For people who have dense breast tissue, it might only be around 10%,” Lam said. “But digital breast tomosynthesis or 3D mammograms are pretty standard now — it’s what we have here at Fred Hutch — and they have improved sensitivity for detecting ILC. We can see through dense breast tissue better.”

Also new, the 2025 National Comprehensive Cancer Network (NCCN) guidelines now recommend MRI screening for average-risk women with extremely dense breasts.

“You don’t need to have additional risk factors to get supplemental screening,” Lam explained.

Contrast-enhanced breast MRI has the highest sensitivity for supplemental breast cancer screening, she said, as neither it nor contrast enhanced mammography are hindered by breast density. The high sensitivity, however, also means this screening modality can have more false positives.

A highly hormonal disease

Fred Hutch’s Christopher Li, MD, PhD, who holds the Helen G. Edson Endowed Chair for Breast Cancer Research, shared an epidemiological perspective. A longtime public health researcher, Li wrote his doctoral dissertation on lobular after collaborating with a University of Washington breast surgeon, the late Roger Moe, MD, who’d noted a rise of ILC rates in his practice.

“He wanted someone to see if it was random or if it was happening more broadly,” Li said. “We documented that the increase in ILC was being seen nationally and that there had been a 65% increase of ILC over a short time period of time versus a 4% increase for all breast cancers.”

Why were ILC rates rising? Li said he and others had found in 2000 that there was an association between the use of hormone replacement therapy, or HRT, and lobular risk.

“What we didn’t expect was that the risk would be so markedly different between lobular and ductal cancers,” he said. “We found women who used HRT had a 2.6-fold higher risk of developing ILC.”

Other small studies showed a similar effect with women’s use of combined HRT.

Li drilled down further with his SHARE Breast Cancer study (Seattle-area Hormones And Reproductive Epidemiology), a first-of-its-kind investigation into ILC risk factors. His team interviewed more than 1,000 menopausal ILC patients and found that longer use of combined HRT, that is estrogen plus progestin, meant a higher risk of lobular — sometimes four times higher.

“About 30% to 40% of women in the U.S. were using HRT at the time,” he said. “And many of these women, once they started, they didn’t stop. Today, we don’t have the frequency of use or the long-term users we had at the time.”

But combined hormone therapy isn’t the only risk factor for ILC. Alcohol use bumps it, as well.

“Alcohol is the most consistent dietary risk factor associated with breast cancer risk,” he said. “It’s also hormonally related. Women who consume alcohol have higher internal levels of estrogen.”

In studies, Li said, alcohol was shown to be more of a risk factor for lobular than ductal. A large Women’s Health Initiative study found “no relationship between alcohol and ductal risk but a very high risk of lobular, particularly for women consuming about two drinks per day.”

Li pointed to combined HRT and alcohol consumption as the two strongest risk factors for ILC, calling it an “exquisitely hormonally sensitive form of breast cancer.”

To that end, he cautioned against using combined HRT for longer than three years as it “substantially” bumps the risk for ILC — and offered that certain types of birth control, like the progesterone-only contraceptive DMPA (known as Depo-Provera), also increase breast cancer risk.

Hopeful new directions

Fred Hutch physician-scientist Hannah Linden, MD, brought the clinical research perspective.

The clinical director of the Fred Hutch Breast Cancer Program and holder of the Athena Distinguished Professorship of Breast Cancer Research at UW Medicine, Linden was instrumental in

bringing a new imaging tracer agent to FDA approval.

The FES-PET tracer, which binds with estradiol rather than glucose, has been a game-changer for lobular patients, particularly those hoping to join clinical trials. But traditional tracers like FDG-PET — which picks up altered glucose metabolism such as that found in tumors — still serve, Linden stressed.

“Patients with bone metastasis are excluded from clinical trials frequently because they don’t have measurable disease and we’re trying to crack that nut,” she said. “FDG-PETs can help monitor the lytic [or bone] lesions so we can modify the criteria ‘RECIST measurable’ to ‘PERCIST, or PET, measurable.’ That will help us enroll bone dominant patients in clinical trials.”

RECIST, or Response Evaluation Criteria in Solid Tumors, criteria require measurable disease, so trial investigators can see whether a treatment is working or not. PERCIST (PET Response Criteria In Solid Tumors) criteria, capable of capturing ILC, would allow for more participation.

Linden also did a bit of lobular myth-busting.

“Because of the screening issue, everybody thinks that you can’t find lobular cancers,” she said. “But in the metastatic setting, we can see metastasis in the bone, lung, lymph nodes, brain, retroperitoneal, uterus and ovaries.”

Liver “mets” can frequently be identified, but Linden said a diffuse involvement of the biliary system — which includes the gall blader and bile ducts inside and outside the liver — can be masked by lobular spread. Unfortunately, the FES-PET is not as helpful for identifying liver mets, as the liver is where the tracer is cleared from the body, causing this area to “light up” with background uptake.

“The problem with lobular is one its favorite sites for cancer is the peritoneal cavity and all our modalities are terrible at that, including FES-PET,” she said. “It’s frustrating for some patients because we can’t estimate the extent of the disease.”

Other tidbits: P13K pathway mutations are seen more frequently in ILC but there are a few good drugs that target it. And new data should be available soon regarding an OncotypeDx genomic assay that includes lobular.

Linden also expressed concern over the lack of proper diagnostic workup in lobular patients.

“Most of our patients are underdiagnosed,” she said. “It’s standard of care to perform a metastatic biopsy, however, Fred Hutch research shows it’s not done 50% of the time here in Washington state. Lobular patients are at risk of not getting an accurate diagnosis because ILC spreads like a net. Better imaging will help get better biopsies.”

A FES-PET scan showing ER+ bone mets might be a way to provide a “virtual diagnosis” in the future, she said.

What's coming down the research pipeline? Linden shared several new clinical trials relevant to ER+ lobular patients:

- The Evangeline trial will look at endoxifen for ER+ premenopausal patients
- A FFNP PET/CT trial will research a radiotracer that looks for progesterone receptor-positive tumors
- Multiple KAT6 inhibitor trials are looking at promising drugs, with two clinical trials opening soon at Fred Hutch.
- A FAPI trial (LuMIERE) will look at fibroblast activation protein inhibition in breast and other cancers.

Linden said she was particularly excited about the FAPI trial, which analyzes the tumor microenvironment for a potential target using a tracer. Eligible patients will then get a theranostic — the tracer paired with a radioactive payload — which Linden called the "way of the future in precision oncology."

"FAPI can be tethered to a radionuclide and we're doing a trial where you get a FAPI scan, see if your tumor takes up this target and if it does, we can treat you with this theranostic," she said. "FAPI is probably the best way to look at lobular and may conquer the peritoneal cavity problem."

She also emphasized the sea change happening overall in cancer care.

"In terms of lobular cancer, there are a lot of opportunities here," she said. "I'm really hoping for a time when patients who have ER+ tumors never see chemotherapy because we have so many other things we can use. We have better endocrine manipulation and even endocrine therapy additives that are molecularly targeted and have way less toxicity."

A Q & A session after the presentations provided additional context, with Linden emphasizing how "very risky" combined HRT is for people who've been diagnosed with ER+ breast cancer, as well as offering context on alcohol's harmful effects.

"Alcohol is not a health food — it's a toxin," she said. "But it's not the same kind of carcinogen as tobacco."

Patients also shared hard-won wisdom.

"When I went to that rural hospital, I was under the impression that all mammograms were equal and all hospitals used the same standard of care," said LeJeunesse. "In the five years since I was diagnosed, I've learned that the machines, the expertise, the knowledge and the trials that are available are not equal everywhere. It can make a huge difference in outcomes to find an NCI-

designated hospital.”

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