SABCS25: What's New in Breast Cancer Research?

Advances include a new endocrine therapy, antibody-drug conjugates, using ctDNA to predict response and tracking bone metastasis.

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From smart pill bottles that help people remember to take their meds to calls for better menopausal symptom relief for women with breast cancer to intriguing hints at what drives dormant tumor cells to reawaken and form metastasis, the 2025 San Antonio Breast Cancer Symposium, held December 9-12, brought plenty of data and bold new ideas to the thousands of clinicians, researchers and patient advocates in attendance.

Fred Hutch/University of Washington/Seattle Children's Cancer Consortium physician-scientists were featured in a number of poster sessions, oral presentations and main stage lectures, sharing brand-new data and proposing tweaks to clinical practice, imaging methodology and clinical trials inclusion criteria to better serve patients with breast cancer.

Fred Hutch News followed it all. Read on for a handful of SABCS 2025 highlights.

'Naked chemo' vs. 'smart chemo'

Sara Hurvitz, MD, FACP, holder of the Smith Family Endowed Chair in Women's Health, spoke on a new class of cancer drugs known as antibody drug conjugates, or ADCs, in a session on translational controversies. Hurvitz is senior vice president of the Clinical Research Division at Fred Hutch and head of the Division of Hematology and Oncology at the University of Washington.

These new combinations — a monoclonal antibody that binds to a specific protein expressed on tumor cells, a cancer-killing chemotherapy drug and a "linker" that connects them and triggers the drug's release in the cell — have changed treatment for many patients with breast cancers.

"ADCs have really transformed the treatment of breast cancer," she said, sharing a slide with half a dozen new ADC drugs. "It's clear they have significantly improved efficacy over naked chemotherapies, [chemotherapies without an attached targeted agent]."

Next-gen ADCs, she said, like those trialed in the recent DESTINY-Breast 03 study, have also led to

significant improvements in terms of progression-free survival over the very first breast cancer-specific ADC, T-DM1, or trastuzumab emtansine, used to treat HER2+ breast cancer.

But these antibody drug conjugates, sometimes referred to as “smart chemo” or “smart bombs” are not without serious side effects.

“There can be substantial gastrointestinal toxicity, cytopenias [low levels of blood cells] and interstitial lung disease with some of these agents,” Hurvitz said. “ADC toxicity is significant and reflects for the most part that of the chemotherapy payload.”

Overall, Hurvitz noted “clear evidence” of improved efficacy of these drugs but said there was definitely room for improvement as they don’t spare healthy cells and they don’t eliminate or substantially reduce toxicities experienced by patients, with the exception of T-DM1.

“The improved efficacy associated with ADCs is likely due to serving as a pro drug, [a drug that becomes fully active after the body metabolizes it], slowly releasing chemo over time and serving as a chemo reservoir,” she said.

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> — Fred Hutch’s head of breast oncology Dr. Heather Parsons

ctDNA for early prediction of ER+/HER2- mets

Fred Hutch’s head of breast oncology and holder of the Maudslien Endowed Chair in Breast Cancer Oncology Research, Heather Parsons, MD, MPH, presented data on a cohort of patients within the

large international PALLAS trial, which tested the benefit of two years of CDK4/6 inhibitor palbociclib (Ibrance) plus endocrine therapy versus endocrine therapy alone in early-stage ER+, HER2- breast cancers after surgery and treatment.

While the PALLAS trial itself showed no survival benefit from the addition of palbociclib, initial translational results using the PALLAS biobank point to a potential new clinical tool for predicting metastatic recurrence, or mets, in early-stage patients after surgery and treatment.

The first author of this TransPALLAS study, Parsons and her team analyzed data from seven-year follow-ups of a cohort of 420 PALLAS patients to determine how many patients had detectable circulating tumor DNA, or ctDNA, before their first trial treatment, at a treatment midpoint and at their last treatment.

The team used Signatera's whole genome sequencing-informed assay, which tracks molecular residual disease, or MRD, by analyzing the blood for bits of ctDNA. The prime study objective was to determine the association of ctDNA status with distant recurrence in order to better identify patients at higher risk.

"ctDNA has emerged as one of the most promising biomarkers in early-stage breast cancer, and the TransPALLAS collaboration gives us a uniquely powerful opportunity to study ctDNA in the adjuvant setting," Parsons said in a press release from Natera, maker of Signatera. "We are excited to share these findings with the breast oncology community and advance a better understanding of ctDNA in patients with HR+/HER2- disease."

In the trial, 8% of post-treatment patients had detectable ctDNA at day one, cycle one, while 92% had no detectable ctDNA.

"The ctDNA positivity was low as expected with these patients with stage 2 and 3 breast cancers," she said, adding that 83% of the study population had already started endocrine therapy prior to the baseline blood draw.

Further analysis is being done, Parsons said, and future presentations will include data in all arms of the study.

The bottom line? "ctDNA status is highly prognostic in HR+/HER2- early breast cancer," Parsons said.

A better way to 'measure the unmeasurable'

Fred Hutch clinical research director of breast oncology Jennifer Specht, MD, presented findings from the ECOG-ACRIN Cancer Research Group's FEATURE trial (1183), which used modified FDG-PET/CT scan criteria to predict whether or not patients with metastatic ER+/HER2- breast cancer that's spread to the bone are responding to treatment or not.

The multi-center study evaluated the efficacy of FDG-PET/CT, which tracks metabolic activity in cancer cells (including those in the bone) by using a radioactive sugar (fluorodeoxyglucose) which lights up tumors that are metabolically active.

The study team, which included Fred Hutch's Hannah Linden, MD, who holds the Athena Distinguished Professorship of Breast Cancer Research at UW, modified the standard criteria for PERCIST (PET Response Criteria in Solid Tumors), theorizing that by lowering the metabolic uptake in bone lesions they could better track their progression (or clearance) after systemic therapy.

The FEATURE trial included 138 patients from 35 sites, mostly in the United States, all of whom were scanned with FDG-PET/CT before starting any treatment and again at 12 weeks. They were then scanned at regular intervals (using standard imaging) and tracked for three to five years.

Results showed FDG-PET/CT scans that found no metabolically active bone lesions after 12 weeks of therapy predicted a better response, with the chance of the patients' cancer getting worse dropping by 83%, a highly statistically significant finding. The scans were also able to stratify patients into different groups: complete metabolic response, partial metabolic response, stable metabolic disease and progressive metabolic disease.

"Our study provides the first prospective validation of FDG-PET/CT and PERCIST response criteria in patients presenting with bone-only or bone-dominant metastatic breast cancer," Specht said in a press release from ECOG-ACRIN, the cancer research group that sponsored the trial. "They support the hypothesis that serial FDG-PET/CT can be used to predict progression-free survival in patients with bone-only or bone-dominant metastatic breast cancer. The results also support adopting FDG PET/CT with mPERCIST as a robust response assessment tool in patients with bone-only and bone-dominant metastatic breast cancer."

Specht noted that current clinical trial inclusion criteria — RECIST 1.1, short for Response Evaluation Criteria in Solid Tumors — effectively excludes many patients with bone-dominant breast cancer from participating in clinical trials.

"Patients with bone-only or bone-dominant metastatic breast cancer represent a significant patient population who are generally excluded from clinical trials using RECIST 1.1 because bone lesions are classified as non-measurable and non-target lesions," she said during her SABCS25 presentation. "Incorporating this approach into clinical trials could standardize response evaluation, enhance endpoint accuracy and accelerate the development of effective therapies for our patients."

Specht, who co-led the study with Dana-Farber Cancer Institute nuclear medicine physician Heather Jacene, MD, said their study showed that FDG-PET/CT with mPERCIST is not only feasible, but "clinically meaningful for assessing treatment response in this historically understudied group."

Or as Jacene put it: "We can now measure the unmeasurable."

Specht, who holds the Jill D. Bennett Endowed Professorship in Breast Cancer at UW, said that in addition to more accurately gauging a patient's disease status, helping inform future treatment decisions and opening the door for more clinical trial inclusion, the data from the study may also lead to change in guidelines for assessing response in this patient population.

New concerns and questions

Additional highlights from SABCS 2025 included results from the large WISDOM study, which proposes moving away from annual mammograms based on age to breast cancer screenings that are based on risk.

Also shared, strong Phase 3 trial data on a new, but not yet FDA-approved, endocrine therapy, the first offered in 25 years. There was also more evidence that eating cruciferous vegetables like broccoli "may reduce the risk of breast cancer, especially those that are more likely to be aggressive tumors." Read more about the benefits of broccoli here.

Finally, new research shared during a session on the reactivation of dormant breast cancer cells showed that inflammation from respiratory infections like COVID-19 or the flu have both been confirmed by research to cause dormant disseminated breast cancer tumor cells in the lungs to wake up and begin forming metastases.

Another researcher shared data showing that chronic stress does the same thing.

"Well, I am feeling very stressed about the risk of COVID and chronic stress right now," joked Fred Hutch patient advocate Lynda Weatherby before going on to share her patient perspective on the new findings.

Weatherby was a 36-year-old new mother of two when she was diagnosed and treated for stage 0 breast cancer, or ductal carcinoma in situ (DCIS). Then 12 years later, she was blindsided to learn she had extensive stage 4 metastatic disease in her bones and brain. Since then, she's worked with researchers at Fred Hutch and elsewhere as a patient advocate, representing the patient voice and pushing for more inclusive research.

She attended SABCS25 specifically to raise awareness about the incidence of young onset breast cancer, particularly among young mothers.

"Young women are still being told, 'You're too young for breast cancer' or 'You're past your five-year window — it can't be breast cancer!'" she said. "We have a lot of work to do in primary care and OB-GYN with regard to these old wives' tales that women are hearing. Stage 0 DCIS recurs, but it doesn't necessarily recur as stage 1. The majority of patients I've met who were diagnosed with DCIS recurred as metastatic, not earlier stages."

Weatherby said she was encouraged that SABCS25 recognized the incidence of breast cancers in young women and included a special session on Epidemiology and Biology of Young Onset Breast

Cancer.

“I’ve learned a post-partum diagnosis has a two to three times higher risk of becoming metastatic,” she told the audience. “Does stress influence dormancy? Is there interplay there? We need more research in the dormancy field and more research in the post-partum field.”

“What would we learn if we started asking women, ‘How old is your youngest child?’ That’s a biomarker we could start collecting tomorrow,” she said. “I’m asking the question, and I hope you will ask this question, too.”

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