What's New in Breast Cancer Research? SABCS24 Looks at ctDNA, AI and 'Right-Sizing' Treatment

Annual conference highlights liquid biopsies, new drug combos, shifts in surgical practice and, yes, patient voices.

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More than 11,000 researchers, clinicians, patient advocates and drugmakers gathered earlier this month to share the latest treatments, tricks and tools to take down breast cancer, which continues to kill about 43,000 Americans and thousands more globally each year.

The San Antonio Breast Cancer Symposium (SABCS) draws participants from around the world every December to learn, share, evaluate and discuss the latest developments in breast cancer. This year, panels and presentations covered everything from new immune biomarkers and imaging agents to drug dose optimization and racial disparities. There was even a panel on "Sex, Drugs and Rock and Roll" with insights on cancer treatment's sexual side effects and a breakdown of harms and benefits of dietary supplements and cannabis.

New drug combinations and promising new agents raised hope for patients, along with legitimate concerns about adverse side effects. Hot topics included epigenetics, ESR-1 mutations and AI. That's artificial intelligence, by the way, not aromatase inhibitors.

"For metastatic breast cancer [MBC], the PATINA and EMBER data bring meaningful progress for patients with ER+ and triple-positive breast cancer," wrote patient advocate Julia Maues on social media. Maues and other patient advocates were included as experts on many SABCS24 panels. "Exciting strides [are] being made."

Promising new directions

Late-breaking data from the Phase 3 PATINA trial showed that patients with estrogen-receptor positive (ER+) and HER2-positive metastatic breast cancer who added palbociclib (Ibrance) to their current standard of care therapy (in this case, anti-HER2 therapy plus endocrine therapy), had a median progression-free survival, or PFS, of 44.3 months, 15 months longer than patients who didn't receive the added kinase inhibitor.

“This is pretty cool,” said Fred Hutch Cancer Center’s Sara Hurvitz, MD, who took the main stage to discuss the findings. Hurvitz is senior vice president and director of the Clinical Research Division and holds the Smith Family Endowed Chair in Women’s Health.

“The median PFS in the palbociclib arm is incredible and, I would argue, historic,” she said. “This is very important data although we’re still awaiting patient reported outcomes, which will be part of the future analysis.”

EMBER 3 offered data on the efficacy of a new endocrine therapy, a selective estrogen receptor degrader (SERD) known as imlunestrant.

“This isn’t immediately practice-changing since imlunestrant is not yet FDA-approved,” Hurvitz said in an interview with OncLive. “But it will be interesting to see whether an approval will be forthcoming for mono therapy or combination therapy. It might be a new option for patients, but it’s unclear whether it’s restricted to those with an ESR1 gene mutation [which causes resistance to hormone therapy] or if all patients can receive it when approved.”

In the realm of molecular imaging, breast cancer clinician-researchers Hannah Linden, MD, and Jen Specht, MD, working with biostatistician Dan Hippe, MS, presented results from retrospective studies on the new estrogen-based imaging agent, FES-PET. The team helped bring the FES-PET agent to FDA approval four years ago.

Linden also shared initial findings from a cooperative group trial (EAI 142) in a spotlight poster presentation. The multi-center trial, sponsored by the cancer research group ECOG-ACRIN, confirmed that FES-PET predicts clinical benefit from endocrine therapy in newly diagnosed metastatic cancer patients.

“The trial found high fidelity and reproducibility of quantitative imaging,” Linden said. In other words, the FES agent was able to provide good, clear, accurate imaging of ER+ tumors. There was a wide range in uptake but the “negative predictive value” could not be assessed due to few FES-negative scans and a low rate of progressive disease, an unexpected result.

“Most patients had poly-metastatic disease with five lesions or more, mainly in the bone,” said Linden, who holds the Athena Distinguished Professorship of Breast Cancer Research at UW Medicine. “The FDG-PET, which uses a glucose tracer, was also useful. While each can be used alone, FES- and FDG-PET are both useful in staging metastatic disease.”

In the retrospective analysis of multiple patient cohorts on endocrine treatment (not chemo), Linden said the findings showed that “if all metastatic sites were positive by FES, patients did well, but if one or more sites were negative by FES, patients experienced disease progression sooner.”

Bottom line? “The FES PET is useful for demonstrating extent of disease and for treatment selection,” Linden said.

‘Right-sizing’ surgery and treatments

SABCS24 wasn’t just about new drugs and new agents, though. Researchers also presented findings about safely reducing the effects of breast cancer surgery and treatment.

Results from the INSEMA trial, which followed patients for six years, showed low-risk early-stage breast cancer patients over 50 can safely skip sentinel lymph node biopsies (and any resulting lymphedema) when they undergo breast conserving surgery, often referred to as lumpectomies.

And the COMET study showed that patients diagnosed with low-risk ER+ ductal carcinoma in situ, or DCIS, can safely choose “active monitoring” for invasive disease over aggressive treatment, much like certain low-risk prostate cancer patients who undergo “active surveillance” in lieu of standard therapies.

EUROPA results also pointed to de-escalation or “right-sizing” of treatment, with improved quality of life for patients over 70 who chose radiation therapy rather than endocrine therapy after lumpectomy.

Obesity and cancer risk reduction

Fred Hutch principal staff scientist Catherine Duggan, PhD, discussed obesity and the epigenetic changes that drive both it and diseases like breast cancer in her session on “Mechanisms of Obesity-Related Risk for Breast Cancer and Approaches to Risk Reduction.”

Duggan, who researches obesity, weight loss and exercise and their role in cancer development and progression, said that epigenetic changes — that is, changes in gene expression driven by diet and environmental exposures — can be inherited from your parents.

These changes can also be passed along to future generations.

“Pollution, the built environment, exercise quantity and quality and other aspects of the lived experience can dynamically alter the cellular processes,” she said. “These epigenetic changes are also influenced by mechanisms such as persistent inflammation associated with obesity and can contribute to breast cancer development. In addition, environmental exposures in one generation appear to influence the health and epigenome of subsequent generations.”

The good news is some epigenetic changes can be reversed, which, she said, “opens interesting possibilities for clinical interventions that target diseases influenced by these modifications.”

Can weight loss and exercise reprogram these epigenetic markers and reduce cancer risk?

Duggan said it’s possible, but also acknowledged it’s complicated. Researchers have found that “adipose tissue maintains an epigenetic ‘memory’ of obesity even after weight loss,” she said, explaining that this doesn’t mean weight loss is impossible.

Researchers have used CRISPR technology to edit the epigenome, she said, adding or removing epigenetic marks in target promoters without altering primary DNA sequences.

“They were then able to switch off gene expression in mice,” she said. “Because this doesn’t alter primary DNA sequences, it’s theoretically reversible which is very exciting for targeted, reversible epigenetic interventions in cancer prevention and therapy.”

Duggan also pointed to “epigenetic clocks” developed using artificial intelligence and machine learning. These tools allow clinicians to estimate a person’s biological age — different from their chronological age — using data from high-throughput DNA methylation arrays.

“Researchers have found that comparing chronological age with the epigenetic clock age can provide important insights into aging and disease,” she said. “And different clocks have shown increased age acceleration in cancer cases compared to controls, suggesting that it might be useful as a way to stratify breast cancer risk.”

Cannabis, supplements and side effects

Fred Hutch Director of Integrative Medicine Heather Greenlee, ND, PhD, MPH, shed light on the good, bad and ugly of dietary supplements and cannabis during cancer treatment in the popular “Sex, Drugs and Rock and Roll” panel discussion.

“We know that many if not most breast cancer survivors seek a holistic whole person approach to cancer care — beyond treating the disease,” she said. “And there’s very high interest in and use of dietary supplements. There’s also an increasing use of cannabis.”

The problem is dietary supplements are not regulated as drugs by the FDA. Instead, they’re categorized as food. As a result, Greenlee said, “there are many misleading health claims.”

There’s also a lot of pressure on patients to use them, often as a result of well-meaning friends and family who simply don’t know better. If patients use dietary supplements — research has found 50 to 85% of breast cancer survivors do after diagnosis — Greenlee said it’s crucial to share that information with the care team since many supplements can interfere with cancer treatment.

Greenlee pointed to the following as the biggest offenders:

- Multivitamins, some of which can cause absorption issues. There’s also concern regarding antioxidant and estrogenic properties (that is, mimicking estrogen, which is often a cancer’s “fuel”).

- Fish oils and omega-3a, said to provide anti-inflammatory support, can cause bleeding.

- Turmeric, a much-touted “anti-cancer therapy” can also cause bleeding, as well as estrogenic activity and CYP interactions (often implicated in drug-drug interactions).

- Melatonin, often taken to help with sleep, can also cause bleeding, CYP1A2 interactions (linked to cancer risk). It also has estrogenic properties.

- Medicinal mushrooms (including turkey tail, lion’s mane, reishi) are taken for immune support, but they can cause bleeding, CYP interactions, liver damage and more.

One supplement that is important to take, if needed, is Vitamin D, which she said is low-risk and has few interactions. Vitamin D levels can be measured with a simple blood test.

“I routinely recommend it in my practice,” she said. “It has multiple benefits — bone health, blood sugar regulation, immune function, even mood. And we have strong data from observational studies that breast cancer patients with sufficient vitamin D have better clinical outcomes.”

Cannabis use is also common among cancer patients, Greenlee said, with up to 30% or more of cancer patients using it for pain, insomnia, mood/stress, appetite stimulation or for recreational use. A survey of use among cancer patients found that 65% perceived a risk associated with cannabis while a whopping 85% perceived a benefit to using it.

Unfortunately, the jury is still out on the true harms and benefits of cannabis since it’s still a Schedule 1 drug — though legal in many states. That means there’s very limited research.

Greenlee said there are currently low levels of evidence regarding potential medication interactions between cannabis and common breast cancer drugs such as tamoxifen, paclitaxel, palbociclib, cyclophosphamide, exemestane, letrozole, etc. (mostly from pre-clinical, or animal studies).

But the American Society for Clinical Oncology, or ASCO, does offer some evidence supporting the use of cannabis for chemo-induced nausea and vomiting. Long-term outcomes of cannabis use in breast cancer patients, however, is not known.

“Just because something is natural doesn’t mean it’s safe,” Greenlee emphasized.

Where does this leave patients? Weighing yet another big decision with their providers.

“It’s important for clinicians to be having conversations with their patients to understand if they’re using cannabis and if there’s a case for interactions,” she said. “For instance, it can change the way cancer therapy drugs are metabolized, potentially slowing it down so a drug could stay in your

system much longer and cause more side effects."

Insights from circulating tumor DNA

Several studies used circulating tumor DNA (ctDNA), often referred to as liquid biopsies, to follow patients after treatment and assess their response to drugs.

Though not currently standard of care in breast cancer oncology, clinicians, scientists and patients are keen to identify how to use this technology in a way that won't exacerbate current health inequities and/or financial toxicity for patients.

For now, studies are using it to follow patients and assess the efficacy of new treatments.

Analysis from the postMONARCH trial, for instance, showed ctDNA to be valuable for providing insights into the "baseline genomic landscape following disease progression on a CDK4/6 inhibitor and endocrine therapy." The SUMMIT trial, though small, also used serial ctDNA sequencing for patients with HER2-mutant metastatic triple negative breast cancer to evaluate treatment response.

Circulating tumor DNA is also being used to test tumor evolution and minimal/molecular residual disease, or MRD, a term used to describe the remaining cancer cells after treatment.

Many in the cancer community are curious whether it can replace tissue biopsies, which are crucial but sometimes hard — and often surgically invasive — to acquire. Others wonder whether it can be used to monitor early-stage patients for metastatic recurrence. Currently, asymptomatic early-stage breast cancer patients do not receive surveillance scans to look for metastatic disease after going through treatment.

"We're all waiting for the ball to drop on ctDNA," said patient advocate Joan Mancuso in a podcast with BreastCancer.org. "But it's not ready for prime time, although it seems to be getting closer. We'd love to be able to have ctDNA in place of tissue biopsies which could potentially get more information from liquid than tissue since breast cancer is so heterogenous."

One trial, ZEST, was designed to use ctDNA to guide treatment in high-risk early-stage TNBC or BRCA-positive ER+ breast cancers, positing that it could identify patients with MRD whose cancer was still too small to be found on imaging. The trial ended early due to low enrollment — out of nearly 2,000 people recruited, only 8% had positive ctDNA tests.

Still, ZEST findings did seem to indicate ctDNA can detect early cancer metastasis before it can be captured on scans.

The big question, of course, is what do clinicians do with that information? Stay tuned for answers.

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