What's New in Breast Cancer Research? SABCS 2023 Takeaways

New drug combos for metastatic breast cancer and a strong focus on toxicities were highlights of the San Antonio Breast Cancer Symposium.

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Scientists, oncologists, patient advocates and a host of others dedicated to stopping the second leading cause of cancer death in the U.S. gathered in Texas [December 5 to 9] for the 46th San Antonio Breast Cancer Symposium.

The world's leading breast cancer research meeting, SABCS 2023 drew approximately 10,000 attendees, with researchers sharing more than 1,700 new scientific abstracts and, hopefully, far fewer germs.

Physician-scientists and others from Fred Hutchinson Cancer Center presented via podium and poster, with findings on everything from new drug combinations to help patients with HER2 positive metastatic disease live longer to new ways to identify which patients are most likely to skip their helpful but often unpleasant anti-hormone medications.

Precision treatment and de-escalation were ongoing themes, with researchers and patients both advocating for individually tailored treatment and a "less is more" mindset when it comes to financially and physiologically toxic therapies. As usual, researchers shared a raft of results from several large clinical trials including monarchE, PROSPECT, KEYNOTE and IDEA, the latter looking at anti-hormone therapy alone after lumpectomy for post-menopausal women.

Hope for patients with HER2+ brain mets

Sara A. Hurvitz, MD, FACP, senior vice president and director of Fred Hutch's Clinical Research Division and professor and head of UW School of Medicine's Division of Hematology and Oncology, presented new data from HER2CLIMB-02 during one of the first general sessions.

The trial looked at a new drug combo for metastatic HER2+ breast cancer patients. It was noteworthy for its large recruitment of patients with metastasis to the brain and received wide media coverage.

"This is the first time that tucatinib [Tukysa] has been evaluated with an antibody drug conjugate in a phase 3 randomized trial," Hurvitz said. "And nearly half of the patients had brain

metastases."

The first HER2CLIMB trial resulted in the 2020 approval of the drug combination tucatinib, trastuzumab and capecitabine (also known as Xeloda, a chemo agent) by the U.S. Food and Drug Administration.

"HER2CLIMB showed that the use of tucatinib, which has the ability to penetrate the blood brain barrier, was associated with an improved survival for all patients including those with brain metastases," Hurvitz said.

Investigators then went on to try additional tucatinib-based combinations.

The phase 3 trial HER2CLIMB-02, which included more than 450 patients with locally advanced or metastatic HER2+ breast cancer, looked at the efficacy of combining tucatinib and trastuzumab emtansine, sold as Kadcyla or T-DM1. Trastuzumab (Herceptin) was one of the first targeted treatments for HER2+ breast cancer.

Patients received either tucatinib plus T-DM1 or placebo plus T-DM1. Median progression free survival for those in the combo arm was 9.5 months; those in the placebo plus T-DM1 arm had 7.4 months. Median progression-free survival for patients with brain mets who received the combo was 7.8 months; patients with brain mets in the other arm had 5.7 months.

Hurvitz said the findings showed a "statistically significant" improvement in progression free survival in overall patient population and a strong trend in improvement in the patient population with brain metastases.

"Combining HER2+ directed therapies can improve patient outcomes in this disease setting," she said. "HER2-positive breast cancer has a predilection for spread to the brain and when this occurs, prognosis is poor. Few options exist for the successful management of breast cancer brain metastases, making this an area of unmet need."

Watch Dr. Sara Hurvitz share trial results in this ASCO Post video.

The HER2CLIMB trials, which are ongoing, are funded by Seagen, Inc. in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.

Promising drug combo for triple positive mets

Hurvitz and Fred Hutch breast oncologist Hannah Linden, MD, FACP, associate program director of the Medical Oncology and Hematology Fellowship Program at Fred Hutch and UW Medicine, were also part of a phase 2a investigation of the bispecific monoclonal antibody Zanidatamab in combination with the CDK4/6 inhibitor palbociclib (Ibrance) and the anti-hormone drug fulvestrant (Faslodex) in patients with HER2+ and ER+, or triple positive, metastatic breast cancer, or MBC.

Added as a late-breaking abstract, the trial enrolled 51 participants and accepted previously treated patients with stable brain metastases, according to Hurvitz, senior author.

“We’re looking at zanatatinab, which targets HER2 at two different locations, in combination with a CDK4/6 inhibitor and anti-hormone therapy, and the efficacy results are exciting,” she said. “The responses we’re seeing and progression free survival are pretty good for patients who’ve had a median of four lines of therapy.”

The trial, which is ongoing, found the drug combo offered a median progression-free survival of 12 months in the overall population and 15 months in those with centrally confirmed HER2+ disease, with a median duration of response lasting 15 months.

Researchers charactered the drug combo as “well-tolerated with an easily manageable safety profile.” Most adverse events were mild. The most common moderate to severe treatment-related adverse effects included neutropenia, anemia and low platelets — side effects known to be associated with palbociclib (Ibrance).

Researchers believe the results support further development of non-chemotherapy treatment regimens for this group of patients.

“I think these are very promising data,” Hurvitz said.

Sponsor for this trial is Jazz Pharmaceuticals.

Who is more likely to stop anti-hormone therapy?

Health services researchers Scott Ramsey, MD, PhD, and Joe Unger, PhD, MS, from the Hutchinson Institute for Cancer Outcomes Research worked with lead author Dawn Hershman, MD, MS, of Columbia University Irving Medical Center, and others on a SWOG Cancer Research Network study that created a risk model to predict which breast cancer patients will likely stop taking their anti-hormone medications.

Presented by Hershman in a poster spotlight discussion session, the study focused on ER+ breast cancer patients who are prescribed anti-hormone medications as part of their regimen. Research shows many women stop taking the daily pills — mainly due to unpleasant side effects like joint pain and hot flashes — increasing their risk of recurrence.

Researchers looked at non-clinical factors associated with non-adherence such as demographic and socioeconomic factors, creating a risk model with data from a previous SWOG trial. A total of 724 patients were registered from 40 institutions. More than half (64.5%) had been on aromatase inhibitors, also known as AIs, for less than a year before registration. Observed adherence after three years was 35.9%.

Non-adherence was associated with an urban environment, especially living in a large city; a younger age; a lack of college education and minimal out-of-pocket cost for the medication. Race and ethnicity data were not associated with non-adherence.

“These findings provide further evidence that an individual’s social and economic background can contribute vital information in predicting the course of their treatment,” said Unger, senior author

on the study. “This recognition is important for establishing early on which patients are at much greater risk of non-adherence to long-term AI therapy, which could allow more effective targeting of interventions.”

Funding came from the NCI and in part by the Conquer Cancer Foundation and the Breast Cancer Research Foundation.

Creating trusted messages with community partners

Researchers on the FOR ME project, aimed at “Fostering Opportunities in Research through Messaging and Education,” also presented a poster update. Investigators on the study include Fred Hutch public health researcher Vida Henderson, PhD, PharmD.

Launched in 2022, FOR ME is developing, optimizing and testing out a narrative decision aid — in this case, a web-based video, for Black women diagnosed with breast cancer. Its end goal is to produce a video promoting shared decision-making and clinical trial participation, based on information gleaned from interviews and story circles with community members.

Researchers have conducted interviews with patients and advocates, community members, clinical trial office personnel and others, identifying what helped and what hindered people to join trials. Next steps include creating a culturally sensitive script and set of storyboards, testing them out on focus groups and then incorporating their feedback. The video will then be produced and test piloted with patients newly diagnosed with cancer.

Henderson said community-based participatory research was crucial to the project.

“Underrepresentation of Black patients in cancer clinical trials slows scientific advancements,” Henderson said. “The involvement of community partners in protocol development, data collection and dissemination — including Black women with breast cancer, the end-users of this video/decision aid — resulted in more culturally responsive, sensitive, impactful and relevant interventions.”

Funding came from the American Cancer Society and the V Foundation, among other sources.

Understudied breast cancers and better communication

Additionally, Fred Hutch patient research advocate Lynda Weatherby and collaborators presented a poster calling attention to the risk young mothers face if they are diagnosed within 10 years of having a child. Postpartum breast cancers are more likely to become metastatic, so adherence to treatment — and clear communication and education — is key.

Other highlights from the annual conference included new research on lobular breast cancer, a subtype that affects up to 15% of patients and presents special challenges due to its tendency to grow in strands, rather than clumps (making it difficult to image). The subtype was highlighted in a long-awaited mainstage educational session as well as dozens of posters, including one highlighting a new genomic driven artificial intelligence system that can detect mutations that

drive this disease.

SABCS 2023's many patient advocates also provided crucial reminders about clear communication between patient and provider.

"Doctors should listen to their patients," said MBC patient advocate Sheila McGowan during a session on side effects. "Make sure you're asking about the side effects. Make sure your patients know what a side effect is — some patients don't even know!"

Patients may also be afraid to tell their doctors about side effects, she added, because they're worried they'll be taken off the treatment.

"Make sure patients know that dose reductions are a possibility," she urged.

Is it safe to de-escalate treatment?

The de-escalation of toxic treatments (and/or their equally toxic price tags) was the subject of several posters and presentations including the following:

- Certain early breast cancer patients can safely skip radiation after lumpectomy, or breast-conserving surgery (BCS), per results from PROSPECT, an Australian precision therapy trial that used presurgical MRI and postsurgical tumor pathology to rule out toxic treatment and boost quality of life.

- The Patient-Centered Dosing Initiative, led by MBC patients, presented survey data from 1,200+ patients and 119 U.S. oncologists highlighting the need for tailored dosing. The poster, shared in an education session, concluded "patient-centered dosing discussions should be part of routine care and may consequently improve quality of life."

- Fred Hutch patient research advocate Teri Pollastro and collaborators shared the design for STOP-HER2, a phase 2 clinical trial investigating whether HER2+ MBC patients can stop taking trastuzumab (Herceptin) in a poster spotlight presentation. Currently recruiting "exceptional responders" to anti-HER2 therapy at 10 U.S. cancer treatment centers, the trial will follow (and evaluate) patients who continue and patients who stop anti-HER2 therapy.

- Oncologists also shared both pro and con arguments for the use of anthracyclines, a common chemotherapy drug for breast cancer. On the plus side, they're affordable and efficacious (especially in developing countries); on the other hand, they have serious (but rare) toxicities including heart damage, congestive heart failure and leukemia.

Throughout the five-day event, patient advocates and physician-scientists alike shared reminders about not using subjective or minimizing language when presenting clinical trial results, particularly when relaying the tolerability of side effects.

"While attending SABCS 23, please beware of the terminology 'manageable and tolerable' when it comes to side effects," the non-profit Advocates for Collaborative Education, or ACE, posted on social media mid-conference. "Please ask yourselves, 'Manageable and tolerable to WHOM?'"

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