By Joni Venticinque, Patient Advocate and TSO Information Specialist January 21, 2023

In its 45th year, the annual San Antonio Breast Cancer Symposium was held on December 6-10, 2022, in San Antonio, Texas. This symposium brought together basic scientists, researchers, clinicians, patients, and patient advocates from around the world to hear about new and late-breaking research in breast cancer and pre-malignant disease. The five days included poster presentations, special sessions, and lectures covering translational research, clinical trial updates, imaging, treatments, data and health equity issues, and quality of life for patients.

There were many important study updates from the symposium important for treating breast cancer and I have included a few here. All presentations and abstracts and posters will be available at https://www.sabcs.org/ after March 1, 2023. I included the general session number after each section for your reference. If you'd like more information before March 2023, please contact me at joni@thesecondopinion.org.

ER+ HER2- Breast Cancer

TAM-01

DCIS is a pre-invasive cancer, which may or may not progress to invasive cancer. It is a prevalent and confusing diagnosis for women. To reduce the risk of invasive disease, many women are recommended to take 20mg of Tamoxifen for five years. Many women have difficulty due to side effects remaining on this dose for 5 years. The TAM-01 is intended to find out if a much lower dose was sufficient to protect women. The 10-year results of the TAM-01 phase 3 trial of low-dose Tamoxifen (Baby-Tam) vs placebo for high-risk lesions were presented by Andrea De Censi, MD, PhD.

- On Risk of Recurrence: "There was a significant 42% reduction in recurrence for women with high-risk lesions, including atypical ductal hyperplasia, lobular carcinoma in situ, and ductal carcinoma in situ (DCIS), when receiving three years of low-dose (5 mg) tamoxifen compared with placebo. This is true seven years after treatment, indicating a carryover effect of low-dose tamoxifen. The benefit was seen across all patient subgroups and was significant in postmenopausal women, obese women, women undergoing mastectomy, and those with DCIS—in which there was a remarkable 50%

reduction of recurrence with low-dose tamoxifen for three years, which provides a new standard of care for this group."

- On Standard of Care: "The low risk of death at ten years (0.6%) supports the use of the reduced dose for women with DCIS."
- On Dose: “Although there is not a 5 mg tablet currently on the market, 10 mg every other day is reasonable.”

General Session 4-08

Updated TAILORx trial

Women with an intermediate Oncotype DX Recurrence Score can safely skip chemotherapy. 10,273 women were enrolled in the TAILORx trial who had a recurrence score of 11-25. They were randomly assigned to endocrine therapy alone (n=3,399) or chemotherapy + endocrine therapy (n- 3,3,12). Eleven years of follow-up data from the trial confirms the 2018 results that woman diagnosed with early-stage, hormone receptor-positive breast cancer with a Recurrence Score of 11 to 25 can safely skip chemotherapy and take hormonal therapy alone after surgery. While good news, there were some reservations from attendees about whether premenopausal women under age 40 would have the same outcomes.

General Session 5-05

monarchE trial

The monarchE study looked at adding Verzenio (chemical name: abemaciclib) to hormonal therapy after surgery for early-stage, hormone receptor-positive, HER2-negative breast cancer with a high risk of recurrence. The study confirms the benefits of Verzenio for early-stage, hormone receptor-positive breast cancer. Four years of follow-up validate the initial results, showing that the benefits continue after people complete Verzenio treatment. Read more about the initial study results.

General Session 1-09

EMERALD trial

Elacestrant offers more benefits than Faslodex for metastatic, hormone receptor-positive breast cancer. The latest results from the EMERALD trial show that experimental elacestrant, an oral selective estrogen receptor downregulator (SERD), continues to offer more benefits than Faslodex (chemical name: fulvestrant) for metastatic, hormone receptor-positive, HER2-negative breast cancer that grew during treatment with hormonal therapy and a CDK4/6 inhibitor, including cancers with an ESR1 mutation.

General Session 3-01

SOFT Trial

A genomic assay called the Breast Cancer Index (BCI) was able to distinguish premenopausal patients with early-stage HR-positive breast cancer who benefited from adding ovarian function suppression to adjuvant endocrine therapy, according to new data presented at the meeting.

In the study, investigators analyzed 1717 patient tumor samples from the landmark Suppression of Ovarian Function Trial (SOFT) trial. The BCI identified 58% of women who benefited from the addition of ovarian function suppression to tamoxifen or exemestane therapy. They experienced an absolute benefit of 11.6% (42% did not benefit), compared with those with received tamoxifen alone. The predictive benefit was observed regardless of age, lymph node involvement, and receipt of chemotherapy.

Dr. Virginia Kaklamani, MD highlighted this study's importance: "*Ovarian suppression is associated with severe adverse events for patients. Obviously, the women who will get a benefit should continue, but this research is important because it will hopefully show us who to recommend ovarian suppression to while not exposing patients who are likely to get little benefit to unneeded toxicity*."

General Session 1-06

HER2 Positive Breast Cancer

DESTINY-Breast03

The DESTINY-Breast03 study results confirm the benefits of Enhertu for metastatic, HER2-positive breast cancer. The DESTINY-Breast03 study compared Enhertu (fam-trastuzumab-deruxtecan-nxki) with Kadcyla (chemical name: T-DM1 or ado-trastuzumab emtansine) for previously treated metastatic, HER2-positive disease. These new results underscore earlier results showing Enhertu offers better progression-free survival than Kadcyla and strongly suggest that Enhertu also provides better overall survival.

General Session 2-02

Triple Negative Breast Cancer (TNBC)

I-SPY2 Trial

Results from the I-SPY2 trial evaluated the checkpoint inhibitor cemiplimab in combination with LAG-3 inhibitor REGN3767 for patients with early-stage, high-risk, HER2-negative breast cancer. Both these agents enhance the body’s immune reaction to cancer cells by different mechanisms. Among the 73 patients with HER2-negative disease who received cemiplimab plus REGN3767, 33 had TNBC. The control group included 357 patients with HER2-negative tumors, of whom 156 had TNBC. Overall, the combination of a LAG-3 and anti-PD1 inhibitor resulted in

a pathologic complete response (lack of cancer in tissue removed after surgery or biopsy) rate of 60% for patients with TNBC and 37% for patients with HR-positive disease.

Note: A poster was presented looking at the side-effect profile of cemiplimab. Although the response rate from cemiplimab was higher than with traditional chemo of doxorubicin+cyclophosamide, there was a higher rate of immune-related adverse effects in the cemiplimab group. The takeaway here is not just efficacy but also what the side effect profile is going to be.

General Session 5-03

TMC Neoadjuvant Platinum TNBC Study

This phase 3 randomized controlled trial explored whether adding carboplatin to sequential taxane-anthracycline neoadjuvant chemotherapy for patients with TNBC improved disease-free survival, pathologic complete response, or overall survival. Overall, 365 patients received carboplatin, and 355 did not. At a median follow-up of 67.6 months, the 5-year disease-free survival rate was 70.6% in the carboplatin group, vs 64.5% in the control arm; the 5-year overall survival was also higher in the carboplatin group (74.0% vs 66.7%). This is the first randomized trial to show overall survival advantage. Pathologic complete response (no cancer seen after surgery) occurred in 55.2% of carboplatin patients vs 41.5% of control patients.

Note: The results of this study suggest a benefit to the TNBC population from being treated with carboplatin. However, it was discussed that despite the encouraging results, it remains to be seen whether there is a specific biomarker for selecting patients who may derive the most benefit from treatment with carboplatin.

General Session 5-01

Breast Cancer and Pregnancy

POSITIVE trial

Can endocrine therapy be safely interrupted for women with breast cancer who wish to become pregnant? This prospective trial enrolled over 500 women for whom endocrine therapy had been stopped in the hopes of their becoming pregnant. Almost all (93.4%) had stage I/II HR-positive breast cancer. The primary objective was to determine the risk of breast cancer relapse associated with interrupting therapy for about two years. The authors defined no more than 46 breast cancer–free interval (BCFI) events as the safety threshold. A BCFI event was defined as a local, regional, or distant recurrence or a new invasive contralateral breast cancer.

Among 497 women, 368 (74%) had at least one pregnancy, and 317 (64%) had at least one live birth, for a total of 365 babies born.

"*This trial is more confirmatory but an extremely important step for young women who want to get pregnant after diagnosis and recovery from HR-positive breast cancer*," commented Dr. Virginia Kaklamani. "*It seems that stopping endocrine therapy to become pregnant did not cause any adverse outcomes or increase the risk of reoccurrence of cancer in the women in the study*."
General Session 4-09

Racial Disparities

Despite having a 4% lower incidence of breast cancer, Black women are approximately 40% more likely to die from breast cancer and are diagnosed at later stages and at increased ages compared to white patients. Several abstracts, posters, and educational presentations highlighted various aspects of racial disparities.

RxPonder Trial

A new analysis of data from the RxPONDER trial, which was conducted in more than 4000 women with hormone receptor-positive (HR+) and HER2 negative (HER2-) breast cancer and up to three positive lymph nodes. It showed that 5-year invasive disease-free survival (IDFS) was lower for Black women, at 87.2% vs more than 90% for the other racial groups. Similar results were seen when looking at distant relapse-free survival (DFRS).

Black women had worse outcomes than White women, independent of recurrence score, treatment arm, and grade. However, the study showed adjusting for body mass index (BMI) appears to decrease this effect.

Although the difference in outcomes between Black women and others was significant after controlling for age, menopausal status, grade, treatment arm, and recurrence score, that was no longer the case after adding BMI into the analysis, although a difference remained.

Black women were more likely to have a higher Body Mass Index (BM) than the other groups. BMI over 30 is considered obese. Among these trial participants, 27% of Black women had BMI of 30-34 and 35% had BMI of under 35, compared with only 6% and 2% of Asian women, 21% and 18% of White women, and 22% and 16% of Hispanic women.

RxPonder reported that Black women were more likely to adhere to their endocrine therapy when compared to White women. It was concluded that tumor biology might differ by race, contributing to outcome differences in addition to issues of healthcare access and other social determinants of health. General Session 1-01

TMEM Doorways

Think of the tumor microenvironment as the 'neighborhood' the cancer cells live in. The cells in the neighborhood–fat cells, immune cells, blood vessels, etc.–can interact and influence each other positively or negatively, contributing to cancer development. An important study looked at racial disparities in the tumor microenvironment and outcomes after treatment with neoadjuvant chemotherapy (chemo before surgery).

The researchers identified three cell structures in primary breast tumors. They labeled these "tumor microenvironment of metastasis (TMEM) doorways " as the entry point for tumor cells into the blood circulation. They developed a TMEM score to determine the future possibility of metastatic disease.

The study included patients with invasive breast cancer who received neoadjuvant chemotherapy to determine whether the TMEM score would predict the likely outcome of residual disease after neoadjuvant chemotherapy and whether there were racial differences in the score for residual disease. It was found that Black women with ER-positive/HER2-negative disease had higher TMEM doorway scores for residual disease than white women.

After adjusting for race, age, surgery type, tumor size, lymph node status, and tumor grade and subtype, a high TMEM doorway score doubled the risk of distant recurrence across all participants, suggesting differences in the tumor microenvironment of Black women. Further research is needed, however, to determine why these differences may exist.

General Session 1-02

Surgery

ASCO Z11102 Alliance Trial

With improved imaging and the expanding use of breast MRI there is an increased diagnosis of multiple breast cancers in the breast. The Z11102 phase 2 clinical trial looked at women over age 40 with two or three small cancers in the breast separated by at least 2 cm of normal breast tissue that could be seen on imaging but not felt. The women went on to have breast-conserving surgery (lumpectomy) and whole-breast radiation therapy. These patients were followed for five years. Out of 204 patients, six had a local recurrence, and four developed distant disease. Most patients had ER+ disease. In conclusion, the study found that women with multiple lesions, breast-conserving surgery followed by radiation had a low local recurrence rate of 3.1% at five years. These results suggest that breast-conserving surgery may be a reasonable consideration for women with small multiple lesions of a breast.

General Session 4-01