San Antonio Breast Cancer Symposium

Conference Report

DECEMBER 8-11, 2020 | **VIRTUAL CONFERENCE**

EXPERTS DISCUSS BREAST CANCER TREATMENT UPDATES

WHAT YOU NEED TO KNOW

- Certain Therapies Potentially Improve Survival in Breast Cancer
- Physicians May Miss Some Treatment-Related Symptoms
- Diabetes Risk Reduction Diet May Increase Survival
- Continued Use of Opioids and Controlled Substances May Be a Concern After Mastectomy and Surgery
- And more!

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FOR ADULTS WHO RECEIVED 2 OR MORE TREATMENTS FOR HER2+ METASTATIC BREAST CANCER

HOPEFUL

ENHERTU helped shrink tumors in 60% of people with HER2+ mBC

In a clinical study of 184 women, most people treated with ENHERTU (**60%**) saw their tumors shrink.*

- Some people (**4.3%**) achieved what is known as a **complete response**, meaning their tumor could not be seen on imaging tests
- Most people (**56%**) achieved a **partial response**, which means the **tumor shrank by at least 30%**

In the same clinical study, half of the 111 people who responded to ENHERTU were able to maintain their response for 14.8 months or longer.† However, how long responses lasted varied by person.

Ask your doctor if ENHERTU is right for you and visit **ENHERTU.com** to learn more.

HER2 stands for human epidermal growth factor receptor 2; mBC stands for metastatic breast cancer.
*111 of 184 people saw their tumors shrink, including 8 of 184 people who achieved a complete response and 103 of 184 people who achieved a partial response.
†14.8 months is the median length of time people maintained their response to ENHERTU. This is called the duration of response.
Median is the middle number in a group of numbers arranged from lowest to highest.

What is ENHERTU?

ENHERTU is a prescription medicine used in adults to treat human epidermal growth factor receptor 2 (HER2)-positive breast cancer that cannot be removed by surgery or that has spread to other parts of your body (metastatic), and who have received two or more prior anti-HER2 breast cancer treatments.

ENHERTU was FDA approved for this use based on a clinical study that measured how many patients responded and how long they responded. ENHERTU is still being studied to confirm these results. It is not known if ENHERTU is safe and effective in children.

Important Safety Information

What is the most important information I should know about ENHERTU?

ENHERTU can cause serious side effects, including: Lung problems that may be severe, life-threatening or that may lead to death. If you develop lung problems your healthcare provider may treat you with corticosteroid medicines. Tell your healthcare provider right away if you get any of the following signs and symptoms:

- Cough • Fever • Trouble breathing or shortness of breath
- Other new or worsening breathing symptoms (e.g., chest tightness, wheezing)

Please see additional Important Safety Information and a Brief Summary of full Prescribing Information, including Boxed WARNING, on following pages.

ENHERTU®
fam-trastuzumab deruxtecan-nxki
20 mg/mL INJECTION FOR INTRAVENOUS USE

Important Safety Information

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Tell your healthcare provider right away if you get any of the following signs and symptoms:

- Cough
- Trouble breathing or shortness of breath
- Fever
- Other new or worsening breathing symptoms (e.g., chest tightness, wheezing)

Low white blood cell count (neutropenia). Low white blood cell counts are common with ENHERTU and can sometimes be severe. Your healthcare provider will check your white blood cell counts before starting ENHERTU and before starting each dose. Tell your healthcare provider right away if you develop any signs or symptoms of an infection or have fever or chills during treatment with ENHERTU.

Heart problems that may affect your heart's ability to pump blood. Your healthcare provider will check your heart function before starting treatment with ENHERTU. Tell your healthcare provider right away if you get any of the following signs and symptoms:

- New or worsening shortness of breath
- Coughing
- Feeling tired
- Swelling of your ankles or legs
- Irregular heartbeat
- Sudden weight gain
- Dizziness or feeling light-headed
- Loss of consciousness

Your healthcare provider will check you for these side effects during your treatment with ENHERTU. Your healthcare provider may reduce your dose, delay treatment or completely stop treatment with ENHERTU if you have severe side effects.

Harm to your unborn baby. Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with ENHERTU.

- If you are able to become pregnant, your healthcare provider should do a pregnancy test before you start treatment with ENHERTU.
- **Females** who are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for at least 7 months after the last dose.
- **Males** who have female partners that are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for at least 4 months after the last dose.

Before you receive ENHERTU, tell your healthcare provider about all of your medical conditions, including if you:

- Have lung or breathing problems.
- Have signs or symptoms of an infection.
- Have or have had any heart problems.
- Are breastfeeding or plan to breastfeed. It is not known if ENHERTU passes into your breast milk. Do not breastfeed during treatment with ENHERTU and for 7 months after the last dose.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive ENHERTU?

- You will receive ENHERTU into your vein through an intravenous (IV) line by your healthcare provider.
- ENHERTU is given 1 time every three weeks (21-day treatment cycle).
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider may slow down or temporarily stop your infusion of ENHERTU if you have an infusion-related reaction, or permanently stop ENHERTU if you have severe infusion reactions.
- If you miss a planned dose of ENHERTU, call your healthcare provider right away to schedule an appointment. Do not wait until the next planned treatment cycle.

What are the possible side effects of ENHERTU?

ENHERTU can cause serious side effects. See "What is the most important information I should know about ENHERTU?"

The most common side effects of ENHERTU include:

- Nausea
- Feeling tired
- Vomiting
- Hair loss
- Constipation
- Decreased appetite
- Low red blood cell counts
- Low white blood cell counts
- Diarrhea
- Cough
- Low platelet counts

ENHERTU may cause fertility problems in males, which may affect the ability to father children. Talk to your healthcare provider if you have concerns about fertility

These are not all of the possible side effects of ENHERTU. Call your doctor for medical advice about side effects. You may report side effects to Daiichi Sankyo at 1-877-437-7763 or to FDA at 1-800-FDA-1088.

What is ENHERTU?

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You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see a Brief Summary of full Prescribing Information, including Boxed WARNING, on following pages.

Daiichi-Sankyo | AstraZeneca

Medication Guide
ENHERTU® (en-HER-too)
(fam-trastuzumab deruxtecan-nxki) for injection

What is the most important information I should know about ENHERTU?

ENHERTU can cause serious side effects, including:

Lung problems that may be severe, life-threatening or that may lead to death. If you develop lung problems your healthcare provider may treat you with corticosteroid medicines. Tell your healthcare provider right away if you get any of the following signs and symptoms:
- cough
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- fever
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- feeling tired
- swelling of your ankles or legs
- irregular heartbeat
- sudden weight gain
- dizziness or feeling light-headed
- loss of consciousness

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See **"What are the possible side effects of ENHERTU?"** for more information about side effects.

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ENHERTU is a prescription medicine used in adults to treat human epidermal growth factor receptor 2 (HER2)-positive breast cancer that cannot be removed by surgery or that has spread to other parts of your body (metastatic), and who have received two or more prior anti-HER2 breast cancer treatments.

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What are the possible side effects of ENHERTU?

ENHERTU can cause serious side effects. See "What is the most important information I should know about ENHERTU?"

The most common side effects of ENHERTU include:
- nausea
- feeling tired
- vomiting
- hair loss
- constipation
- decreased appetite
- low red blood cell counts
- low white blood cell counts
- diarrhea
- cough
- low platelet counts

ENHERTU may cause fertility problems in males, which may affect the ability to father children. Talk to your healthcare provider if you have concerns about fertility.

These are not all of the possible side effects of ENHERTU. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of ENHERTU.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about ENHERTU that is written for healthcare professionals.

What are the ingredients in ENHERTU?

Active Ingredient: fam-trastuzumab deruxtecan-nxki.
Inactive Ingredient: L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, and sucrose.

Manufactured by: Daiichi Sankyo, Inc., Basking Ridge, NJ 07920
U.S. License No. 2128

Marketed by: Daiichi Sankyo, Inc., Basking Ridge, NJ 07920 and
AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850

USMG-ENH-C1-1219-r001
For more information, call 1-877-437-7763 or go to http://www.ENHERTU.com.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Issued: 12/2019

Verzenio Regimen Boosts Survival in High-Risk, Early HR-Positive, HER2-Negative Breast Cancer

In a phase 3 trial, Verzenio plus endocrine therapy lowered the risk of invasive disease recurrence and death versus endocrine therapy alone for this population of patients.

By Gina Mauro

THE COMBINATION OF VERZENIO (ABEMACICLIB) and standard endocrine therapy showed a 28.7% reduction in the risk of invasive disease recurrence or death compared with endocrine therapy alone in patients with high-risk, early hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer, according to findings from an analysis of the phase 3 monarchE trial presented during the virtual 2020 San Antonio Breast Cancer Symposium (SABCS) in December.

The results showed that, with 395 events and a median follow-up of 19 months, the invasive-disease-free survival benefit was clinically meaningful. The two-year invasive disease-free survival rates were 92.3% and 89.3% with Verzenio with endocrine therapy and endocrine therapy alone, respectively.

"(Verzenio) combined with standard endocrine therapy continued to demonstrate a reduction in the risk of developing (invasive disease-free survival) and distant relapse-free survival events for patients with hormone receptor-positive, HER2-negative, high-risk early breast cancer and resulted in a statistically significant improvement in (invasive disease-free survival) in patients with high Ki-67 tumors," said senior study author **Dr. Priya Rastogi**, associate professor of medicine at the University of Pittsburgh School of Medicine, during a press briefing ahead of the meeting. "(Verzenio) in combination with endocrine therapy is the first CDK4/6 inhibitor to demonstrate efficacy and tolerability for (this patient population)."

DR. PRIYA RASTOGI

Verzenio is an oral, continuously dosed CDK4/6 inhibitor that is approved by the Food and Drug Administration for the treatment of patients with HR-positive/HER2-negative advanced or metastatic breast cancer in combination with a nonsteroidal anti-inflammatory drug (or NSAID) with Faslodex (fulvestrant) or as monotherapy.

In the monarchE trial, patients with HR-positive/HER2-negative, node-positive, high-risk early breast cancer were enrolled into one of two groups. The first cohort was based on clinicopathological risk factors, which included patients with four or more positive axillary lymph nodes, or one to three axillary lymph nodes and at least a grade 3 histology or a tumor size of 5 centimeters or larger. The second cohort was based on Ki-67 status (a measurement of how quickly cancer cells are dividing and multiplying) and comprised patients with one to three axillary lymph nodes, a centrally tested Ki-67 index of 20% or higher, no grade 3 histology and a tumor size of less than 5 centimeters. The population (5,637 patients) included patients in both groups.

All patients were randomized to receive standard endocrine therapy for five to 10 years as clinically indicated alone or with Verzenio at 150 milligrams twice daily for up to two years. Patients were categorized based on prior chemotherapy, menopausal status and region.

The primary end point of the trial was invasive disease-free survival, and secondary outcome measures included invasive disease-free survival in the Ki-67-high (at least 20%) population (2,498 patients), distant relapse-free survival, overall survival, safety, patient-reported outcomes and pharmacokinetics (how drugs travel through the body).

Data from an earlier interim analysis, which were presented during the 2020 European Society for Medical Oncology (ESMO) Virtual Congress, showed that at a median follow-up of 15.5 months, 323 invasive disease-free events occurred. Results revealed that Verzenio reduced the risk of invasive disease by 25.3% versus endocrine therapy alone. Additionally, the two-year invasive disease-free survival rates were 92.2% in the Verzenio arm versus 88.7% in the endocrine-alone arm.

Ki-67 was evaluated in all study participants who had suitable untreated breast tissue. Additional findings at this current analysis showed that, in the Ki-67-high population, the risk of developing an invasive disease-free survival event was reduced by 30.9% with Verzenio, which

DR. C. KENT OSBORNE speaks during the opening session of SABCS 2019.

was found to be clinically meaningful in this subgroup. The two-year, invasive disease-free survival rates were 91.6% with Verzenio and 87.1% with endocrine therapy alone.

When evaluating for distant relapse-free survival in this population, results showed that Verzenio reduced the risk of distant relapse-free survival by 31.3% versus endocrine therapy, which was a clinically meaningful benefit. The two-year distant relapse-free survival rates were 93.8% and 90.8%, respectively.

The safety data of the Verzenio regimen are consistent with the findings reported in another analysis and the known tolerability profile of the CDK4/6 inhibitor. Most discontinuations due to side effects occurred within the first five months of study treatment. Additionally, most patients who required dose holds or reductions could remain on therapy.

At this analysis, the most common side effects were diarrhea, fatigue and neutropenia (low number of neutrophils, a type of white blood cell), according to Rastogi. Rare side effects included interstitial lung disease and venous thromboembolism, she added.

At the earlier analysis presented at ESMO Virtual Congress 2020, 463 patients (16.6%) discontinued Verzenio because of side effects; 306 of these patients continued on endocrine therapy. The most common reason for discontinuation was diarrhea (5%), which was managed with antidiarrheals and dose adjustments. Dose reductions from 150 milligrams to 100 milligrams twice daily were permitted if necessary.

Dr. C. Kent Osborne, professor of medicine, the Dudley and Tina Sharp Chair for Cancer Research and founding director of the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine in Houston, provided commentary on the phase 3 findings.

"The additional four months follow-up of this trial… continues to show improved invasive disease-free survival (with) the addition of (Verzenio) to standard endocrine therapy in a very high-risk group of patients with hormone receptor-positive breast cancer. I think these results are very encouraging, especially in the subgroup of tumors with high proliferation," said Osborne, who also is a breast medical oncologist at Baylor St. Luke's Medical Center. "Caution in these data is needed, given the still rather short follow-up, (the fact that) estrogen receptor-positive disease is known for its persistent recurrence rate, even past 10 years, and given that this class of inhibitors is largely cytostatic rather than cytocidal, meaning that it blocks cell proliferation rather than killing the cells. An important question remains: Will the invasive disease-free survival curves come together when the drug is stopped? With these caveats in mind, this is still a very important trial."

Chemotherapy Combined With Endocrine Therapy Leads to Improved Survival in Breast Cancer

Premenopausal women with HR-positive, HER2-negative, lymph node-positive breast cancer and a recurrence score of 0 to 25 benefited from chemotherapy plus endocrine therapy, with better results in five-year invasive disease-free and overall survival.

By Caroline Seymour

CLINICAL BENEFIT FROM ADDING chemotherapy to endocrine therapy may be determined by menopause status in women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, lymph node-positive breast cancer and a recurrence score between 0 and 25, according to findings from an analysis of the phase 3 RxPONDER trial. The data were presented virtually during the 2020 San Antonio Breast Cancer Symposium (SABCS) in December.

In particular, the addition of chemotherapy to endocrine therapy led to an improvement in five-year invasive disease-free survival and overall survival in premenopausal, but not postmenopausal, women.

In premenopausal patients, the five-year invasive disease-free survival rate was 94.2% in the chemotherapy/endocrine therapy group versus 89% in the endocrine-alone group. In postmenopausal patients, the five-year invasive disease-free survival rates were 91.6% and 91.9%, respectively.

"Postmenopausal women with one to three positive nodes and recurrence score between 0 and 25 can likely safely forgo adjuvant chemotherapy without compromising [invasive disease-free survival]," said lead study author **Dr. Kevin Kalinsky**, director of the Glenn Family Breast Center and Breast Medical Oncology at Winship Cancer Institute and acting associate professor in the department of hematology and medical oncology at Emory University School of Medicine in Atlanta.

"This will save tens of thousands of women the time, expense and potentially harmful side effects that can be associated with chemotherapy infusions," Kalinsky said in a news briefing. "(However,) premenopausal women with positive nodes and recurrence scores between 0 and 25 likely significantly benefit from chemotherapy."

Patients with HR-positive, HER2-negative, lymph node-positive breast cancer have an increased risk of recurrence and are typically treated with chemotherapy.

To prevent potential overtreatment or undertreatment, the 21-gene Oncotype Dx Breast Recurrence Score is used to identify which patients can omit chemotherapy.

In lymph node-negative patients, exploratory findings from the phase 3 TAILORx trial suggested that women over the age of 50 with a recurrence score of 25 or less derive no benefit from chemotherapy, whereas patients age 50 or under with a recurrence score between 16 and 25 may derive benefit from chemotherapy. However, whether these results were generalizable to the approximately 20% of patients with nonmetastatic HR-positive, HER2-negative disease and one to three positive lymph nodes in the United States had not been previously defined.

DR. KEVIN KALINSKY presents findings during a session at SABCS 2019.

© SABCS/Todd Buchanan

Researchers launched RxPONDER, in which 5,015 patients with a recurrence score between 0 and 25 were randomized to endocrine therapy alone or chemotherapy followed by endocrine therapy. Patients with a recurrence score of more than 25 were treated with chemotherapy then endocrine therapy.

Patients in the randomized portion of the trial were categorized by recurrence score (0-13 versus 14-25),

menopausal status (pre- versus post-) and nodal surgery (axillary lymph node dissection versus sentinel lymph node biopsy).

Eligible patients included women 18 years or older with at least 1% estrogen receptor and/or progesterone receptor expression, HER2 negativity, one to three positive lymph nodes, recurrence scores of 25 or less without distant metastases, and an ability to receive taxane and/or anthracycline-based chemotherapy.

Invasive disease-free survival, defined as local, regional, distant recurrence; any secondary invasive cancer; or death due to any cause, served as the primary end point of the study. Overall survival served as the secondary end point.

Additional results demonstrated that the invasive disease-free survival benefit also translated into an overall survival benefit in premenopausal patients. In this population, the five-year rate of overall survival was 98.6% with chemotherapy/endocrine therapy versus 97.3% with endocrine therapy alone. However, in postmenopausal women, the five-year rates were 96.2% and 96.1%, respectively.

"The results clearly show no benefit to adding chemotherapy to standard endocrine therapy in postmenopausal patients, despite having positive nodes, emphasizing that node positivity, while an important prognostic marker, is not a predictive marker of chemotherapy sensitivity," said SABCS co-director **Dr. C. Kent Osborne**, professor of medicine, the Dudley and Tina Sharp Chair for Cancer Research and founding director of the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine in Houston.

"In premenopausal patients, a different result was obtained. Is the difference in outcome in this subset due to the endocrine effects of chemotherapy? Unfortunately, we may never know the answer to this question," Osborne concluded.

Physicians 'Systematically' Miss Significant Symptoms in Certain Breast Cancer Cases

Study results suggest that patients with breast cancer who are younger than 60 and of Black, Asian or an unspecified race are more likely to have symptoms that go unrecognized by their physician compared with White patients.

By Ryan McDonald

ONCOLOGISTS FREQUENTLY UNDERRECOGNIZE substantial symptoms in patients with breast cancer who received radiotherapy following a lumpectomy, according to data presented at the 2020 San Antonio Breast Cancer Symposium (SABCS). The findings highlight the need to improve symptom detection.

The results from the multipractice consortium also indicated that patients who were younger than 60 and Black, Asian or an unspecified race were more likely to experience underrecognized symptoms compared with White patients.

"I think this is a really important area for future research. One thing that we've done relatively poorly thus far is disaggregated the experiences of our racial and ethnic minority patients and understood what intersections there are between, for example, gender and race or ethnicity (and) how the unique lived experiences of any individual patient will reflect all of the experiences … that they bring with them to the exam room," said lead study author **Dr. Reshma Jagsi** during a press briefing. "We absolutely need to do more research to understand (what the) cultural, societal (and other) experiences (of) groups that are

DR. RESHMA JAGSI speaks during a session at SABCS 2017.

underrepresented in our population might be so that we can tailor our treatments and our support accordingly."

Using a large multicenter consortium of 29 practices in Michigan, Jagsi, deputy chair of the department of radiation oncology at the University of Michigan, and colleagues aimed to compare physician and patient reports of acute toxicity during breast radiotherapy to determine if underrecognition of toxicities was pronounced in certain subgroups.

Between January 2012 and March 2020, 13,725 patients completed radiotherapy at one of the practices included in the Michigan Radiation Oncology Quality Consortium. Of those patients, 9,941 filled out at least one patient-reported outcome questionnaire while receiving treatment.

For physician assessments via Common Terminology Criteria for Adverse Events reporting of patient toxicity that were available within three days of patient-reported outcome evaluations, Jagsi and colleagues compared the ratings of four symptoms: pain, itching, swelling and fatigue. The researchers most wanted to evaluate pain, which was assessed within the past 24 hours as "worst," "least," "average" and "right now," using the Brief Pain Inventory. Patients who reported their pain as a 4 to 6 on a 10-point scale (with 10 being the worst) but whose physician graded it as absent or 0 were considered to have underrecognized pain. Patients who reported severe pain as a score of 7 or more were deemed to have underrecognized pain if their physician graded it as mild, rated as 1 or less.

Based on frequency, itching and swelling were considered underrecognized if graded as absent by physicians when patients reported being bothered often or all the time by those symptoms. Fatigue was deemed underrecognized if a patient reported experiencing it most of the time and the physician said the condition was absent.

Approximately one-third of patients reported moderate or severe pain (34.5%; 3,433 of 9,940 patients) and frequent bother from itching (30.6%; 3,039 of 9,923 patients). Less than one-fourth of patients reported frequent bother from swelling (23.9%; 2,363 of 9,906 patients) or severe fatigue (24.9%; 2,209 of 8,860 patients).

Underrecognition of at least one symptom occurred at least once among 53.2% of patients who reported at least one substantial symptom while receiving radiotherapy. "Understanding whether physicians detect whether patients are experiencing substantial toxicity is important, both because recognition of symptoms is necessary for appropriate supportive care and because clinical trials investigating new treatment options often rely on physician assessments using common toxicity criteria for adverse events," Jagsi said.

DR. VIRGINIA KAKLAMANI addresses the audience during the opening session at SABCS 2018.

The results, according to Jagsi, demonstrate that physicians systematically miss substantial symptoms in certain patients, underscoring the need to improve symptom detection to reduce disparities in radiation therapy, experiences and outcomes.

Following the presentation of the data, SABCS co-director **Dr. Virginia Kaklamani** said it was surprising to see that 30% of cases of what patients reported as issues associated with radiation therapy were underrecognized by physicians. Moreover, she said, it was unexpected to see those cases higher in young women and racial minorities.

"We need to do a better job," said Kaklamani, leader of the breast oncology program at The University of Texas Health San Antonio MD Anderson Cancer Center. "We need to conduct studies where patient-reported outcomes are being reported, and we as physicians need to listen more to our patients."

Eating Plan to Ward Off Diabetes Risk May Also Increase Survival for Patients With Breast Cancer

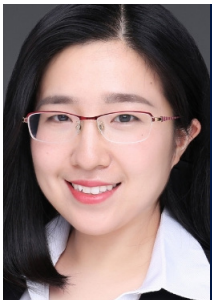
Women who scored higher for diet adherence after diagnosis had reduced risks of 33% for all-cause mortality and 17% for mortality related to breast cancer compared with women who scored lower.

By Darlene Dobkowski, MA

THE SAME DIET THAT HELPS prevent diabetes also improves survival for women with breast cancer, according to findings presented during the 2020 San Antonio Breast Cancer Symposium.

Diabetes can be common in women with breast cancer, especially because 75%, or more than 2.6 million women, are 60 years or older, according to **Tengteng Wang**, a research fellow at Harvard T.H. Chan School of Public Health. "(That) means breast cancer survivorship must be managed in consideration with aging-related comorbidity such as diabetes," Wang said during a virtual presentation of the study results.

Type 2 diabetes, in particular, is a risk factor for breast cancer incidence and may be a predictive factor for breast cancer mortality. In addition, breast cancer increases the likelihood of developing Type 2 diabetes. "Identifying modifiable strategies to prevent Type 2 diabetes among breast cancer survivors may be very important to improve their survival outcomes," Wang said.



TENGTENG WANG

Researchers analyzed data from 8,320 women with stage 1 to 3 breast cancer from two large cohort studies: the Nurses' Health Study (1980-2014) and the Nurses' Health Study II (1991-2015). Validated questionnaires were completed every two to four years to collect information on diet, among other factors.

This study focused on a diabetes risk reduction diet with nine components: higher intakes of nuts, cereal fiber, coffee, polyunsaturated-saturated fat ratio and whole fruits; a lower glycemic index of diet; and lower intakes of sugar-sweetened beverages and fruit juices, trans fats and red meat. "The (diabetes risk reduction diet) has been associated with 14% lower Type 2 diabetes risk in (a) previous publication of the Nurses' Health Study," Wang said.

Researchers calculated an average score of adherence to this eating plan through repeated measures of diet after a diagnosis of breast cancer. Follow-up was conducted for a median of 16 years after diagnosis.

> **"Promoting dietary changes consistent with prevention of Type 2 diabetes may be very important for breast cancer survivors."** —*TENGTENG WANG*

During follow-up, 2,146 deaths occurred, of which 948 were related to breast cancer. Women with higher diet adherence scores had a 33% reduced risk of all-cause mortality and a 17% reduced risk of mortality related to breast cancer compared with women who had lower scores. "Our results did not differ by breast tumor (estrogen receptor) status or stage," Wang said.

During the discussion portion of the presentation, Wang said that she and her colleagues analyzed the potential mechanism for this association. "We looked at how (the diabetes risk reduction diet) influenced gene expression in (the) breast tumor for (a) subgroup of our breast cancer patients," she said. "According to our pathway analysis, the (diabetes risk reduction diet) is more associated with the pathway related to immune regulation and also cell proliferation, so this is, I think, an interesting finding."

Neighborhood socioeconomic status slightly affected the association between diet adherence and mortality risk within the entire cohort, with patients with greater adherence having a 31% lower risk of all-cause mortality and a 14% lower risk of mortality from breast cancer.

"In conclusion, we felt that a greater adherence to the (diabetes risk reduction diet) after breast cancer diagnosis was associated with better survival outcomes, which means (that) promoting dietary changes consistent with prevention of Type 2 diabetes may be very important for breast cancer survivors," Wang said.

Women With Breast Cancer Who Receive Mastectomy and Reconstructive Surgery Face Greater Risk of Continued Opioid, Controlled Substance Use

Younger age, breast cancer diagnosis, Medicaid insurance and treatment type were associated with an increased risk for women becoming chronic users of opioids or sedatives/hypnotics following mastectomy with reconstructive surgery.

By Kristie L. Kahl and Ryan McDonald

WOMEN WHO RECEIVED RECONSTRUCTIVE surgery after a mastectomy, those who received a breast cancer diagnosis, those who received chemotherapy and those who were younger were more likely to have a higher risk of new chronic controlled substance use, according to data presented at the 2020 San Antonio Breast Cancer Symposium.

The data, according to lead study author **Dr. Jacob Cogan**, indicate that more attention is needed for patients with mental health and substance use diagnoses when managing any pain, anxiety and sleep disorders they may experience following breast cancer diagnosis or treatment.

Results from previous studies have demonstrated that chronic opioid use following surgery has increased, with up to 10% of patients filling prescriptions more than three months after surgery. However, according to the researchers, data involving postoperative use of opioids in those who received a diagnosis of cancer, as well as those who did not receive a cancer diagnosis, are lacking. There are also limited data on chronic opioid use patterns regarding benzodiazepine and nonbenzodiazepine sedative/hypnotic use following mastectomy and reconstructive surgery.

DR. JACOB COGAN

"Despite the high rates of psychiatric disorders in the cancer population, there is little research into the rates of persistent sedative/hypnotic use in these cases," Cogan, a fellow in hematology/oncology at NewYork-Presbyterian/Columbia University Irving Medical Center, said during a press briefing.

To determine predictors of developing new, persistent controlled substance use after surgery, researchers aimed to assess rates of new, persistent controlled substance use after mastectomy with reconstructive surgery.

Using a health care claims database, researchers evaluated women over the age of 18 who underwent mastectomy plus reconstruction between 2008 and 2017.

Opioid and sedative/hypnotic drug prescriptions were identified across three time periods:

- Preoperative (365 days to 31 days before surgery; period one).
- Perioperative (31 days prior to 90 days after surgery; period two).
- Postoperative (90 days to 365 days after surgery; period three).

Patients who filled at least one prescription for controlled substances during period one were excluded from the study analysis. Those who did not use controlled substances during period one but filled at least one prescription in period two and at least two prescriptions in period three were considered new chronic users and were compared with the other nonchronic users.

The researchers conducted a separate multivariable logistic regression analysis, a method to look at two or more possible discrete outcomes, to evaluate demographic and clinical factors associated with risk of chronic use for each drug category, including age, insurance, region, breast cancer diagnosis, chemotherapy treatment, radiation treatment, prior mental health diagnosis and prior substance use diagnosis.

In total, the researchers identified 25,270 women who were opioid naive and 27,651 who were sedative/hypnotic naive.

Within each group, 13.1% of opioid-naive patients became new chronic users and 6.6% of those in the sedative/hypnotic-naive group became new persistent users.

Patients who had never filled or received their prescriptions following surgery were then removed from the study. In turn, rates for opioid-naive (18,931 patients) and sedative/hypnotic naive (10,781 patients) individuals rose to 17.5% and 17%, respectively.

Age under 60 years, Medicaid insurance, breast cancer diagnosis, chemotherapy treatment, mental health diagnoses and substance use diagnoses were all associated with higher rates of opioid use.

Moreover, the researchers found that a patient's risk of becoming a new persistent user increased with the number of risk factors identified. For example, those with five risk factors (age, Medicaid, Southern region, breast cancer diagnosis and chemotherapy/radiation treatment) had a 19% increased risk of becoming a new persistent user of opioids and a 10.5% increased risk of becoming a new persistent user of sedatives/hypnotics.

Commenting on the study, former American Association for Cancer Research president **Dr. Carlos Arteaga**, of The University of Texas Southwestern Medical Center, noted that a lot of this information is known, but not all of it. "I wonder if you can tell us which are the types of patients that we might not be paying attention to, that this study is telling you to be particularly aware of for this risk of substance abuse," Arteaga said.

Within each group,
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of opioid-naive patients became new chronic users and
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of those in the sedative/hypnotic naive group became new persistent users.

In response, Cogan explained that the risk factors found in the study necessitate particular attention for certain patients. "It raises the issue that, as a provider, when you're seeing patients in follow-up, this is something you might want to explicitly ask about and not assume that the postoperative opioids were taken and disposed of after," he said. "Ask the patient, 'Are you still taking opioids? Are you still taking your Ambien?' If someone is still taking it, that's something to diligently follow up about and make sure it's disposed of. Or, if someone is still taking it, refer them to the right services to raise a flag across the board as something we should routinely pay attention to postoperatively."

Meditation, Survivorship Classes Significantly Ease Depressive Symptoms in Young Breast Cancer Survivors

Before receiving behavioral interventions, more than half of participating young survivors of breast cancer were considered clinically depressed. That number dropped to 30% after participants received mindfulness meditation and survivorship education classes.

By Kristie L. Kahl

DATA PRESENTED AT THE 2020 San Antonio Breast Cancer Symposium demonstrated that younger women treated for breast cancer experienced a reduction in depressive symptoms after participating in mindfulness meditation and survivorship education classes.

"Younger breast cancer survivors represent a vulnerable population, with well-documented side effects from breast cancer treatments and notable increases in depressive symptoms," lead study author **Dr. Patricia A. Ganz** said during a virtual presentation of the phase 3 results. "These lasting effects of breast cancer treatments can have a negative impact on quality of life in the survivorship period."

Ganz, associate director for population science research at the UCLA Jonsson Comprehensive Cancer Center, presented data from the randomized, multi-institutional phase 3 Pathway to Wellness trial. The authors evaluated the efficacy of mindfulness meditation and survivorship education classes — both aimed to target depressive symptoms in younger breast cancer survivors — compared with a concurrent waitlist control group.

Both interventions consisted of six-week programs conducted for two hours each week. Participants were provided with a series of educational seminars with discussions of life after breast cancer.

The intervention programs had a standard curriculum that was manually documented and recorded throughout the study.

Mindfulness Awareness Practices (MAPs) sessions addressed the following, followed by a wrap-up session:

- "What is mindfulness?"
- "Listening, Embodiment and Obstacles"
- "Working With Pain"
- "Working With Difficult Emotions and Cultivating Positive Emotions"
- "Working With Thoughts and Mindful Interactions"

Survivorship education sessions included the following:

- "Breast Cancer 101: Important Issues for Younger Survivors"
- "Quality of Life in Breast Cancer Survivors"
- "Energy Balance, Nutrition and Physical Activity"
- "Cancer in the Family: Cancer Genetics and Testing"
- "Relationships and Work-Life Balance"
- "Body Image, Menopause and Sexual Health"

Patients were screened by phone and included in the study if they were 50 years of age or younger with a diagnosis of stage 0-3 breast cancer, between six months and five years after their primary treatment, had no metastatic disease, were not already practicing meditation, had a minimum level of depressive symptoms and were willing to be randomized and able to participate in the six-week program.

DR. PATRICIA A. GANZ speaks during a general session at SABCS 2018.

“Interventions significantly reduced depression, with additional reductions in other symptoms only in the MAPs group.” *—DR. PATRICIA A. GANZ*

Measuring depressive symptoms at postintervention (defined as a Center for Epidemiologic Studies Depression Scale score of 16 or greater) served as the study’s main goal. Additional end points included anxiety, fatigue, sleep disturbance and hot flashes. Assessments were conducted before the interventions started, postintervention, and at three- and six-month postintervention follow-ups.

Of the 247 patients (median age, 45.4 years; 82% White), 85 were analyzed under the MAPs intervention, 81 with survivorship education and 81 in the waitlist control group.

Most patients were married (75%) and employed full time (68%). On average, patients were 2.6 years out from their breast cancer diagnosis; more than half had undergone a mastectomy (56%) or had received chemotherapy (57%) or radiation (65%). Moreover, 66% reported receiving endocrine therapy during the study period.

At baseline, all three groups reported mean Center for Epidemiologic Studies Depression scores above 16, with over 50% of participants scoring in the clinically depressed range before the intervention. However, after intervention, the researchers saw a significant decline in depression for both the MAPs and survivorship education groups, with only 30% of women scoring in the clinically depressed range. These scores were sustained at three months in both cohorts and at six months in the MAPs cohort.

Anxiety, sleep disturbance and hot flashes significantly improved in both intervention groups; however, fatigue severity improved significantly only in the MAPs cohort. Of note, improvement in these areas was not sustainable in either group.

“The Pathways to Wellness participants have high levels of depression, anxiety, fatigue, sleep disturbance and other symptoms an average of 2.6 years after diagnosis,” Ganz concluded. “Interventions significantly reduced depression, with additional reductions in other symptoms only in the MAPs group. … Further dissemination and evaluation of these interventions (are) warranted to address the unmet psychosocial needs of young breast cancer survivors.”

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