FOR PATIENTS, SURVIVORS & THEIR CAREGIVERS

WOMEN'S CANCERS

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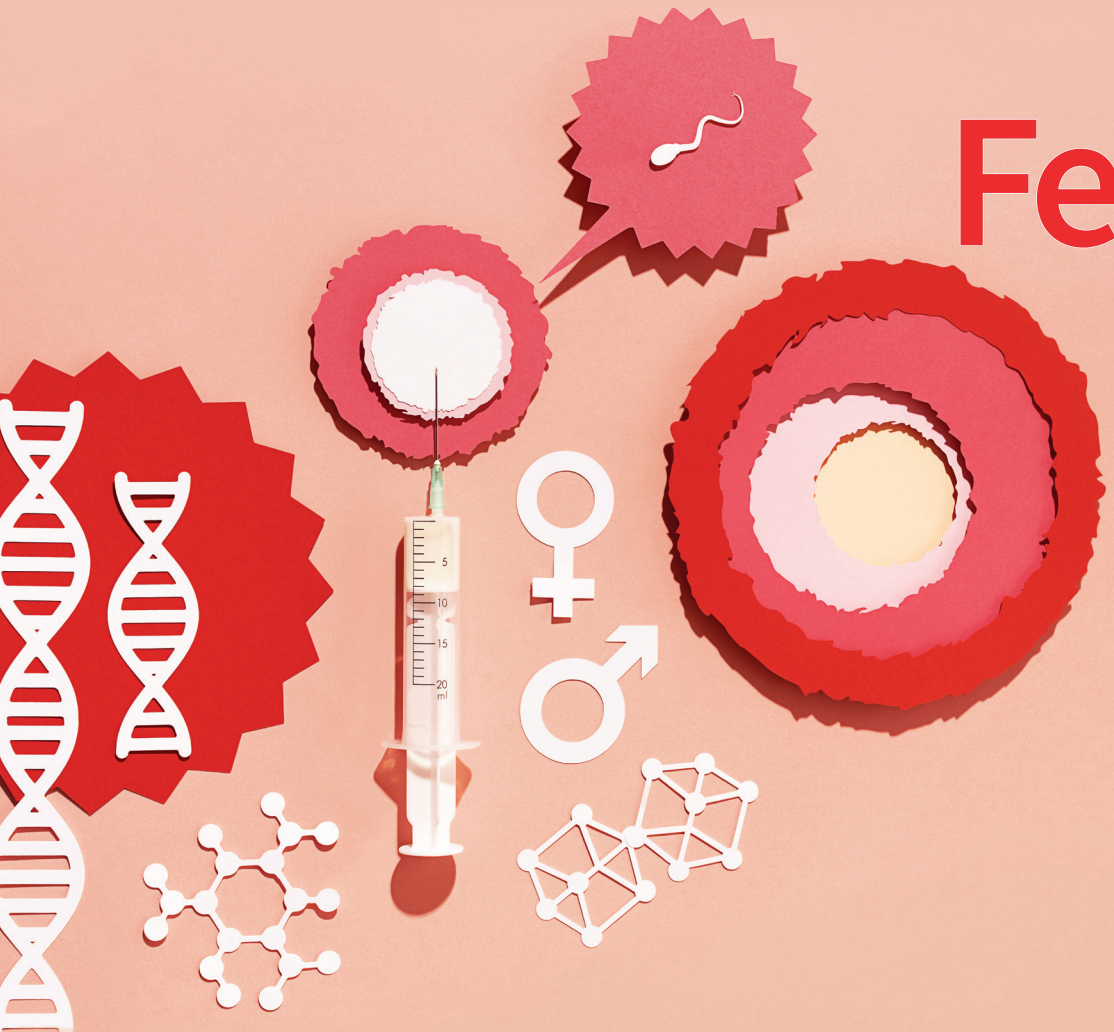
Cancer Updates, Research & Education®



PRESERVING Fertility in Adolescent and Adult Women With Cancer

How should fertility preservation be addressed in patients who may not be thinking about having children yet?

ALSO INSIDE:

CANCER SCREENING
Postponing tests or doctor visits during the COVID-19 pandemic may increase women's risk of cancer

ENDOMETRIAL CANCER
New treatments including targeted therapies are emerging for this disease

HPV
What have we learned about the vaccine 15 years since its FDA approval?

OVARIAN CANCER
Actor Scott Foley discusses the importance of timely action to potentially prevent recurrence

RISK FACTORS
Cardiometabolic conditions may affect survival in postmenopausal women with cancer

curetoday.com

WOMEN'S CANCERS SPECIAL ISSUE · 03.21

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 • Trouble breathing or shortness of breath • Fever
- 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 WARNINGS, on following pages.

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

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
- 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, when used in people with breast cancer, include:

- Nausea
- Low white blood cell counts
- Low red blood cell counts
- Feeling tired
- Vomiting
- Hair loss
- Increased liver function tests
- Low platelet counts
- Constipation
- Decreased appetite
- Diarrhea
- Low levels of blood potassium
- Cough

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?

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.

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 WARNINGS, 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:

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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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- **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.

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

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.
- stomach cancer called gastric or gastroesophageal junction (GEJ) adenocarcinoma that has spread to areas near your stomach (locally advanced) or that has spread to other parts of your body (metastatic), and who have received a prior trastuzumab-based regimen.

It is not known if ENHERTU is safe and effective in children.

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.
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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, when used in people with breast cancer, include:

- nausea
- low white blood cell counts
- low red blood cell counts
- feeling tired
- vomiting
- hair loss
- increased liver function tests
- low platelet counts
- constipation
- decreased appetite
- diarrhea
- low levels of potassium
- cough

The most common side effects of ENHERTU, when used in people with stomach cancer, include:

- low red blood cell counts
- low white blood cell counts
- low platelet counts
- nausea
- decreased appetite
- increased liver function tests
- feeling tired
- diarrhea
- low levels of blood potassium
- vomiting
- constipation
- fever
- hair loss

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 Ingredients: 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-C4-0121-r002
For more information, call 1-877-437-7763 or go to https://www.ENHERTU.com

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

Revised: 01/2021

cure® CONTENTS

WOMEN'S CANCERS · 03.21

EMMA VIVIAN discussed fertility preservation options with her doctor before starting breast cancer treatment.

AMY REA delayed her cancer screening appointment because of fears about COVID-19.

JO ANNE SCHATZ considers the targeted treatment she received for endometrial cancer an "eraser."

Thinking of the Future During Cancer Treatment

CANCER CAN AFFECT WOMEN of any age, but what happens when a woman has to think about her reproductive years before she is ready to have children? If cancer treatment involves the removal of ovaries or the uterus, for example, thoughts of having children — if that's a woman's wish — may occur sooner than expected.

The good news is that adolescents and women with cancer have options if they see children in their future. In this special issue of *CURE*®, we speak with two women who underwent processes, such as freezing their eggs, to ensure they can potentially have children later. Although women sometimes are still able to conceive naturally after cancer treatment, having another option may ease their minds. One woman details her journey when she and her husband were ready to have children and she received a diagnosis of cancer, whereas another woman wanted to wait a few years after treatment before thinking of children. We also spoke with several experts who highlighted the importance of discussing fertility with young patients at the same time treatments are discussed.

> **"Adolescents and women with cancer have options if they see children in their future."**

Also inside, a feature examines the use of targeted therapies for endometrial cancer, which is the most common gynecologic cancer. Although surgery is often the go-to treatment for women with endometrial cancer, some experience recurrence, resulting in the need for a more targeted option. This can include immunotherapy, which utilizes a patient's immune system to destroy cancer cells.

Also meet a woman who was vaccinated for HPV in her 20s when the vaccine first became available, although it was too late, since she later received a diagnosis of cervical cancer. The Centers for Disease Control and Prevention currently recommend vaccinating children starting at age 9 for HPV to potentially obtain the greatest cancer-preventing benefit for cervical cancer, among others. This woman now lobbies in Washington, D.C., and Boston, where she lives with her husband, for greater access to the HPV vaccine, in addition to screening and treatment for minority communities and people who live in rural areas.

This issue also covers a patient's experiences with ovarian cancer, the importance of genetic testing in patients with a family history of cancer and several factors that may affect quality of life during cancer treatment or risk for the disease.

As always, thank you for reading.

MIKE HENNESSY SR.
Chairman and Founder

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Balancing Cancer Screenings and COVID-19 Safety

THE COVID-19 PANDEMIC is an unprecedented situation not only for patients who contract the virus but also for health care as a whole. Over the past year, we've seen declines in cancer screening rates, especially for women's cancers such as breast, cervical and endometrial. We previously saw a version of this decline with prostate cancer, but for a different reason — changes in guidelines. We are now seeing more advanced cases of prostate cancer, but there is still a debate about whether screening or other factors are at play.

Health care pivoted and innovated as the pandemic grew in severity in an attempt to deliver care while protecting providers and patients. Technologic adaptations such as telehealth and video appointments have allowed us to talk through the diagnosis and treatment plans with our patients remotely. Our offices and centers have taken safety precautions for the patients who need to come in, including enhanced cleaning procedures, protective equipment such as masks and shielding, social distancing and limited time in the clinic. These measures both on- and off-site not only provide a safer experience but allow patients to be in a more private environment. Even with these measures in place, patients are sometimes hesitant to come into our centers for tests and treatment.

In February, the federal government reported that life expectancy in the United States fell by one year during the first six months of 2020, which is the greatest decline since World War II. Although this is indicative of the mortality impact of COVID-19, it will be interesting to observe the secondary impacts of the pandemic, such as fewer cancer screenings due to the fear of contracting the virus. Will there be a blip on cancer incidence graphs in future years? Will different types of cancer rates be affected differently, and can we learn something from this?

In this issue of *CURE®*, you will learn how decreased cancer screening rates during COVID-19 may affect women's cancer rates. You will also read about the available data on how many preventive

screenings were missed through the pandemic and why some women decided not to go for their mammograms, for example. It is also important to highlight that this effect on cancer screenings has disproportionally affected minority and rural communities, as COVID-19 has amplified health disparities that existed far before the pandemic.

Although COVID-19 has shaken our lives in so many ways, it's important to keep our health one of our top priorities while also staying safe. We must find widely acceptable ways to screen for cancer in this new era so that we don't turn the clock back on the gains we have made in the past few decades.

DEBU TRIPATHY, M.D.
Editor-in-Chief
Professor of Medicine
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The University of Texas MD Anderson Cancer Center

Preventing Certain Cancers With the HPV Vaccine

We asked readers on *CURE*®'s Facebook and Twitter pages to share their thoughts on the HPV vaccine being given to help prevent certain types of cancer later in life. ***Here's what they told us.***

> It's such a simple, preventive measure. As a parent and (patient with cancer), I would want to do everything possible to help prevent my children from going through what I'm experiencing. I've urged my daughter to consider it for my grandchildren. — *K.I.*

> Yes! It prevents many cancers. I wish it was available when I was younger before being exposed so I wouldn't have had to fight cervical cancer. Isn't a PREVENTION better than a CURE? — *A.A.*

> I wish it was available when I was younger. I would have received it. I was diagnosed with HPV-related cervical cancer just before my 32nd birthday. This is a safe and effective vaccine that prevents cancer. — *T.C.*

> We can try to cheat death, but unfortunately it will catch up to us one way or another. — *O.H.*

> If it had been available when I was young, I would have taken it. — *V.C.*

> I wish it was around when my daughters were young, they would have gotten it. Some people have (a) reaction; most don't to any vaccine. I watched my daughter suffer through cervical cancer (with) surgery, radiation and chemo right after the birth of her second child. I would have gotten the vaccine that would have prevented all that in a heartbeat... — *L.S.*

We want to know what you think about CURE®. *Address your comments to* **editor@curetoday.com**. *If you prefer that your comment not be published, please indicate.*

Cure Magazine **cure_magazine** **CureToday**

GORBACHLENA / STOCK.ADOBE.COM

Many Women Are Satisfied With 'Going Flat' After Mastectomy

Although most patients reported satisfaction after undergoing a mastectomy without breast reconstruction surgery, 20.7% felt that their surgeon was not supportive of their decision to do so. By DARLENE DOBKOWSKI, M.A.

A MAJORITY OF WOMEN — 73.7% — who underwent a mastectomy without breast reconstruction reported that they were satisfied with their outcome, according to results of a study published in the *Annals of Surgical Oncology*.

"For patients, the findings may serve to reinforce their decision and may provide some degree of support knowing that there are others who are making the same choice they are," said Dr. Deanna J. Attai, associate clinical professor of surgery at UCLA David Geffen School of Medicine in Los Angeles, in an interview with *CURE*®. "The findings may also help patients better communicate with their surgeons regarding their surgical choice."

Some studies had shown that women who did not undergo reconstruction with their mastectomy were less satisfied and had a poorer quality of life compared with those who underwent immediate reconstruction. Attai and her team wanted to look at this more closely after seeing contrasting reactions online.

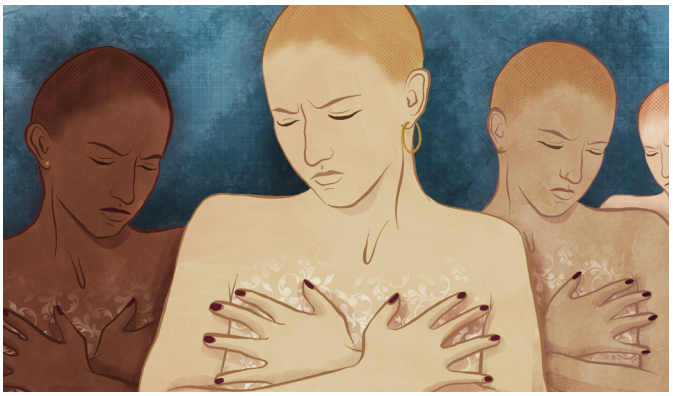
"I was seeing an increasing number of women in the online communities openly discussing their 'going flat' experience, as well as seeing more online support and advocacy organizations for these women," Attai said. "There seemed to be a disconnect between what I was reading in the surgical literature and what I was seeing in the online communities. That's what sparked my interest. I think the findings are important because if surgeons are exposed to studies showing lower satisfaction, they may be less likely to recommend going flat to their patients."

In this study, researchers surveyed 931 women (mean age, 49 years) who had a unilateral (one breast) or bilateral (both breasts) mastectomy to either treat breast cancer or potentially reduce elevated breast cancer risk. None of the women who completed the online survey had undergone breast mound reconstruction. In the survey, women used a 5-point scale to rate their satisfaction of the surgical outcome and the support they received from their surgeon throughout the process.

The decision to proceed with a mastectomy alone was the first choice for 73.7% of women in the study.

"(Although) our respondent population may not be representative of the 'average' patient, it's still a large number of women who were happy with their results," Attai said.

Although 65.2% of patients reported that they received adequate information about their surgical options before making their decision, 20.7% reported that their surgeon did not support or respect their decision to go flat.



MOLLY FERGUSON ART / STOCK.ADOBE.COM

"('Flat denial') is a term I learned from the patients. It includes not initially being offered the option to go flat, being discouraged (by their surgeon) from going flat or the surgeon not performing the agreed-upon procedure — intentionally leaving excess skin and later stating it was done in case the patient changed her mind about reconstruction (and) that the excess skin could be used for a subsequent procedure," Attai said.

Women reported that the main reasons for undergoing only a mastectomy were to avoid the placement of a foreign object in their body and to recover quicker than if they also underwent reconstruction. The mean score for satisfaction after mastectomy in this study was 3.72 out of 5.

The strongest predictor of a satisfaction score lower than 3 was a low level of surgeon support on the decision to go flat. Dissatisfaction with surgical outcome also was seen in patients with a body mass index of 30 kg/m^2 or higher and in those who underwent a unilateral mastectomy. In contrast, patients were more likely to report greater satisfaction if they received adequate information on surgical options and had a surgeon with a practice focused on specialized breast surgery.

There are limitations to this study, including the survey that was used to collect information. "Our study was unique in that we did not use a validated survey tool to measure satisfaction, and the reason was that our patient advocates who partner with us felt that the primary tool was biased toward reconstruction," Attai said. "Of course, that is one of the limitations of our work, and future work should be done to develop and validate a survey tool for this patient population."

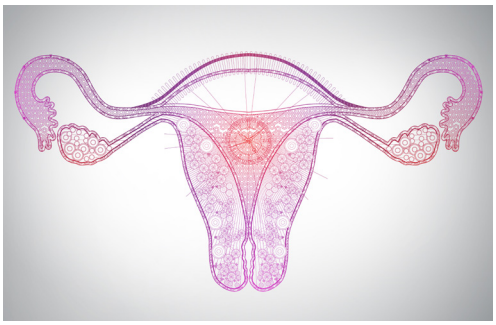
Radiation After Surgery May Lower the Risk for Disease Spread in Uterine Carcinosarcomas

Women who underwent the treatment had improved distant metastasis-free survival rates, but this benefit did not greatly improve their chance of overall survival. By DARLENE DOBKOWSKI, M.A.

RADIATION AFTER INITIAL CANCER treatment in women with uterine carcinosarcomas may reduce the rate of distant metastases (cancer development in another part of the body), according to a study published in the *American Journal of Clinical Oncology*.

Despite this benefit, radiation after initial cancer treatment did not significantly improve survival in these women, regardless of whether they underwent chemotherapy, radiation or a combination of both after surgery.

"This study did not detect survival differences in patients treated with surgery alone compared with surgery and adjuvant therapy (chemotherapy or radiation)," the study authors wrote. "Adjuvant chemotherapy remains a common treatment component even for patients with early-stage (uterine carcinosarcomas), given the high rate of local and distant recurrence. Adjuvant chemotherapy has been demonstrated to improve (overall survival) compared with surgery alone in multiple studies, though many patients (experience) significant (side) effects associated with alkylating and platinum-based therapies."



Uterine carcinosarcomas can lead to 15% of deaths from uterine cancer.

Uterine carcinosarcomas are relatively rare and account for approximately 5% of all uterine malignancies diagnosed annually. They constitute an aggressive cancer that leads to approximately 15% of deaths associated with uterine cancer.

"The optimal treatment algorithm is still debated extensively, as its low incidence has made it impractical to investigate prospectively and difficult to draw conclusions from small retrospective studies," the study authors wrote. "While the benefits of surgery and chemotherapy are widely agreed upon, the utility and efficacy of adjuvant radiotherapy (are) less known."

In the study, researchers assessed 24 patients (mean age at diagnosis, 61 years) with uterine carcinosarcomas who underwent surgical resection to remove cancer-affected areas between 1993 and 2011. Of these patients, all underwent surgical resection, 29% underwent surgery and radiation afterward, 25% underwent surgery and chemotherapy afterward, and 33% underwent surgery and both chemotherapy and radiation afterward.

Several metrics were calculated including disease-free survival at three years (time from surgery to death or three years after surgery), distant metastasis-free survival (time from surgery to cancer recurrence not related to previously affected areas in the body or death), locoregional recurrence-free survival (time from surgery to cancer recurrence in previously involved areas of the body or death) and overall survival (time from surgery to death or last known follow-up). Patients were followed for a median of 22.1 months.

At three years, overall survival did not significantly differ among treatment groups: surgery alone (100%), surgery and chemotherapy (60%), surgery and radiation (100%) and all three treatments (88%). Patients who underwent radiation, chemotherapy and surgery had a distant metastasis-free survival rate of 83% compared with 44% in those who underwent surgery and chemotherapy, indicating that radiation therapy may provide additional benefit.

The eight patients with lymph node involvement had a lower locoregional recurrence-free survival compared with those without lymph node involvement (38% versus 92%).

"The importance of thorough lymphadenectomy (the removal of one or more lymph nodes to assess for cancer) for prognosis and staging has been demonstrated consistently, as this tumor and other endometrial carcinomas spread via the lymphatic system," the study authors wrote. "It is likely that future developments in the surgical management of (uterine carcinosarcomas) will focus heavily on lymphatic monitoring strategies such as sentinel lymph node mapping (locating the first lymph node where cancer is most likely to spread from the primary tumor)."

The study authors added that there were some limitations to their analysis. They wrote, "This study is primarily limited by its small sample size, increasing the chance … of complicating more in-depth analysis. Given the rare nature of (uterine carcinosarcomas), it is difficult to enroll a larger sample size at a single institution, though we hope this study will contribute to the current literature and improve the accuracy of multi-institution meta-analyses."

FORCE
Facing Hereditary Cancer EMPOWERED

Having the Ball in Your Court Helps You Fight Cancer

A three-time cancer survivor discusses the importance of genetic testing, listening to your body and teaching family members about your experiences to potentially protect them from future cancers. By DARLENE DOBKOWSKI, M.A.

THREE-TIME CANCER SURVIVOR Wenora Johnson knows you can never assume you've beaten the disease.

Johnson, 54, lives outside Chicago in Joliet, Illinois, and works as an administrative assistant for a science and engineering research laboratory. She has a large support system that includes her husband, two daughters, four grandchildren and many more friends and family.

When she was 45, Johnson received a diagnosis of stage 3b colorectal cancer, for which she received treatment. In the four years that followed, she had no evidence of disease, but her oncologist consistently asked about her family history. Johnson knew that her mother had died of glioblastoma (an aggressive cancer in the brain or spinal cord). And two years after her initial diagnosis, she learned that her grandfather died at an early age of colorectal cancer. This prompted her oncologist to push for genetic testing to see whether Johnson had Lynch syndrome.

According to the Centers for Disease Control and Prevention, having Lynch syndrome increases a patient's risk of receiving a diagnosis of colorectal, endometrial and other cancers before age 50. Lynch syndrome contributes to approximately 4,000 cases of colorectal cancers and 1,800 cases of endometrial cancers each year.

Johnson was hesitant at first to proceed with genetic testing; she had been free from cancer for four years and thought it would not make a difference. Johnson finally agreed, and in April 2016 the results showed that she had Lynch syndrome and a 60% to 80% chance of developing endometrial cancer. For years, she had had irregular bleeding and cysts but never associated those factors with endometrial cancer, Johnson says.

"That was my biggest indicator: that the ball's in my court now (and) I can do something proactive about my own health," she says.

This led to a conversation with her gynecologist about having a complete hysterectomy, since she was not planning to have more children.

"You can't take for granted that you beat colorectal cancer," Johnson says. "You want to take for granted that you can continue to beat other cancers, especially if you have a (genetic) mutation."

In December 2016, Johnson underwent the hysterectomy, from which a biopsy showed she had stage 1a endometrial cancer. She had a grade 3 tumor, which meant it could grow quickly, and tested positive for the p53 gene, which can increase the rate at which cancer cells grow and spread in the body.

WENORA JOHNSTON and her husband, **JONATHAN**, who has been supportive throughout her cancer journey.

"That was a shocker, and it really showed me the importance of genetic testing to help confirm or … push me in the right direction (to make) the right decisions about my health," Johnson said. "All these little things ahead of time could have maybe helped me make an even firmer decision on getting a hysterectomy when I realized I no longer wanted any additional children … instead of waiting 15 to 20 years."

Johnson did not have to undergo additional treatments after the complete hysterectomy in 2016. But five years later, she still wonders whether the cancer may still be there despite her surgery.

"I still wake up wondering, 'Should I have also had additional chemotherapy, or should I have had radiation?'" Johnson says. "Everything I've read is that usually with (stage) 1a (endometrial cancer), it's total removal of everything, and then being retested again to make sure that you don't have any additional evidence of disease. That's been a little bit of a reassurance for me, but a part of me still wonders whether there's something that may linger there that causes it to reoccur."

The complete hysterectomy started early menopause in Johnson, who was then 50 years old. A week after Johnson

PHOTOS COURTESY OF JOHNSON

returned home from surgery, the hot flashes and night sweats began, which she said were her biggest complaint. Within the past two years, Johnson has started experiencing heart-related issues such as palpitations, which her cardiologist said were associated with early menopause. She now takes a low-dose blood pressure medication to minimize the palpitations.

Johnson added that her love life also was affected by the early menopause; she did not want to be touched nor felt "the urge to feel even somewhat of a woman," she says. She and her husband addressed these issues in counseling and have taken up new hobbies such as dancing.

» During her cancer journey, **JOHNSON** learned how family medical history can make an impact.

» **JOHNSON** with her two daughters and grandchildren at her wedding.

Despite this, she wouldn't trade menopause and its challenges for cancer.

"If I had to weigh which one or the other I would want, I would still opt for the (hysterectomy) because it was lifesaving," Johnson says. "Now (we) have to deal with the emotional impact of that lifesaving measure. I have a great husband; you do some counseling, and you figure it out. We do other things to offset the days that I don't feel my best as a woman. … We're in a really good place, but it can (cause) some emotional damage if you don't recognize that it's all tied to your hormones or how important those hormones are as a female."

Shortly after receiving her diagnosis of endometrial cancer, Johnson noticed what she thought was a small pimple on her back. She visited the dermatologist, who removed it and determined that it was 2 inches of basal cell carcinoma.

"It shocked even (the dermatologist), and she said, 'Wenora, we're just going to send it off to make sure everything is OK,' but in the back of my mind, I already knew what it was," Johnson says.

All the basal cell carcinoma was removed, and Johnson visits her dermatologist every few months to monitor for abnormal skin pigmentations. These visits are in addition to her visits to her oncologist, gynecologist, cardiologist and primary care physician every six months.

"I go to … any doctor in between that they send me to because, to me, survival is important," Johnson says. "I feel if I can stay three steps ahead of Lynch syndrome because of these mutated genes, then I'm doing pretty darn good. I don't look at it as an inconvenience; it's about saving my life."

Johnson emphasizes the importance of staying on top of her health, especially in hopes that it will influence her daughters, who are 36 and 28.

"I've been begging them to be checked," Johnson said. "I hope that maybe the light bulb moment will come for them at some point in their life before it's too late. They have a 50% chance of this happening to them as well. They are what I call walking time bombs."

Johnson also encourages other people, especially minority families, to share their family medical history with each other so that they can act on it sooner.

"A lot of times for minority families, when someone passes away in a family, we're never told what they passed away from," Johnson said. "Be honest with your family members because … had I known that (my grandfather) passed away at the age of 38, I could have been tested at the age of 30 for colorectal cancer instead of 15 years later."

Johnson also advises women to pay attention to signs that may indicate what could be endometrial cancer, such as heavy bleeding and abnormal pains in the pelvic area.

"I encourage (women) to have those yearly Pap smears … and keep that line of communication open with that doctor," Johnson said. "(If) you're having pains, don't lie about it. If you're bleeding in between periods, don't lie about it. Just don't walk away and say, 'It's OK, it's just part of my cycle' or 'I'm so used to it.'" C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PRESERVING FERTILITY in Adolescent and Adult Women With Cancer

How should fertility preservation be addressed in patients who may not be thinking about having children yet?

By JEANNETTE MONINGER

Emma Vivian and her husband were looking forward to 2019. The couple, married for five years, were ready to start a family. But in December 2018, they found themselves sitting numbly at a cancer center as a breast surgeon explained that 29-year-old Vivian had stage 1b triple-positive breast cancer. The recommended treatment plan included a mastectomy, months of chemotherapy and perhaps immunotherapy or biotherapy, followed by years of estrogen-blocking anastrozole plus Lupron (leuprolide acetate) injections. At the end of the conversation, the doctor cautioned that the cancer treatments meant to save Vivian's life could affect her ability to have a baby.

For the first time, Vivian broke down. "It was horrific enough to get a cancer diagnosis when I wasn't yet 30," she says. "To find out that your dream of having a child might be lost was too much to bear." Still, Vivian was grateful that her doctor brought up fertility preservation. "Since starting cancer treatments, I've met other women with cancer who didn't know that they might not be able to have children," she says. »

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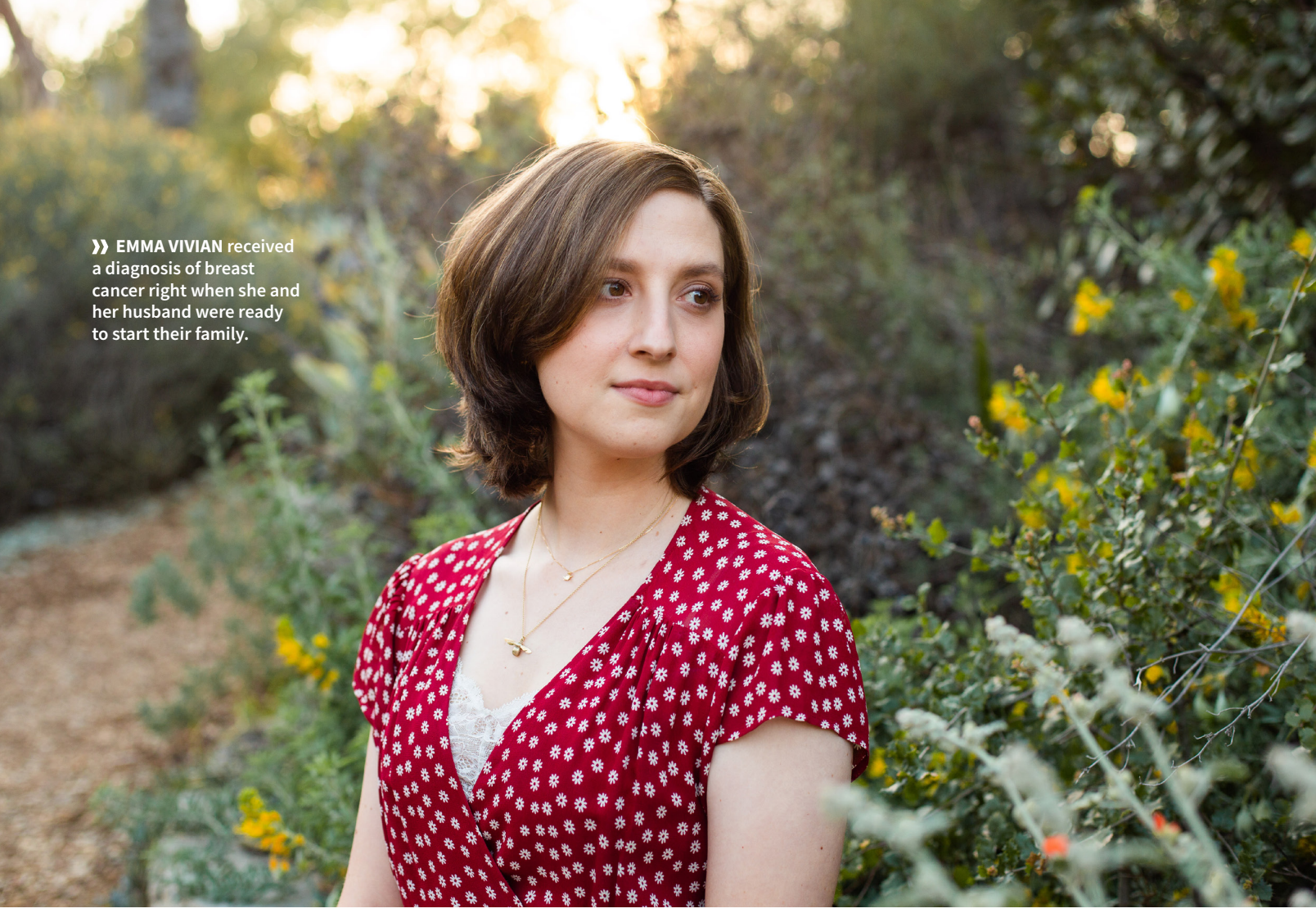

EMMA VIVIAN received a diagnosis of breast cancer right when she and her husband were ready to start their family.

This lack of knowledge can have long-lasting implications for cancer survivors. Research shows that women who find out about infertility risks *after* getting cancer treatments (when the opportunity for fertility preservation has passed) experience more severe depression and grief than those who knew about the risks beforehand.

The good news: More oncologists are discussing fertility with their adolescent and young adult patients, often at the same time they first discuss cancer treatments. The timing is critical. "Depending on the cancer type and stage, there can be a very short window of opportunity for fertility preservation to happen before cancer treatments must start," says Dr. Mahmoud Salama, director of The Oncofertility Consortium at Michigan State University in East Lansing.

But there's still a lot of work to be done in oncofertility, a term coined in 2006 to bring the fields of oncology and fertility medicine together to help children, adolescents and young adults who have cancer. That same year, the American Society of Clinical Oncology issued guidelines urging oncologists to discuss the possibility of infertility as a cancer treatment side effect and to refer patients to fertility specialists when needed. Three years later, a national survey found that fewer than 50% of people with childhood and gynecologic cancers were aware of these infertility risks.

ONCOFERTILITY: HELPING WOMEN WITH CANCER CONCEIVE

Chemotherapy and radiation therapy are commonly used to treat breast and gynecologic cancers. Some of these anticancer therapies are also highly gonadotoxic, meaning they can temporarily or permanently damage a woman's ovaries. "Radiation therapy can (sometimes) cause the ovaries to fail, putting a woman into early menopause," says Kristin Smith, program manager for fertility preservation at the Adolescent and Young Adult Cancer Program at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University in Chicago. "And chemotherapy drugs can't distinguish between rapidly dividing cancer cells and the active cells in ovaries that produce eggs. They go after both."

Egg freezing, or cryopreservation, is the simplest fertility preservation method for women. "A woman gets daily hormone injections for about two weeks to stimulate egg production, and then has an outpatient procedure to retrieve the eggs, which are frozen and stored," says Dr. Elizabeth Constance, a reproductive endocrinologist and fertility preservation specialist at Heartland Center for Reproductive Medicine in Omaha, Nebraska. Egg retrieval needs to happen first, which means there can be a two-week delay in the start of cancer treatments. "We always

ALYSSA STEFEK

work with the oncologist to prioritize the patient's health over fertility preservation," Constance says.

Unfortunately, the hormones that stimulate egg production also can feed the growth of estrogen hormone-positive cancers such as Vivian's triple-positive breast cancer. When Vivian decided to freeze some of her eggs, she took letrozole to keep estrogen levels from surging too high. Letrozole is a nonsteroidal aromatase inhibitor that suppresses the body's natural production of estrogen. Doctors typically use it to treat breast cancer in postmenopausal women.

A woman may need to wait one to five years after finishing cancer treatments to try to conceive. In vitro fertilization (IVF) can be used to fertilize some of the previously frozen eggs. Laboratory clinicians mix sperm from a woman's partner or a donor with the eggs, which have been thawed. Another option is intracytoplasmic sperm injection, which injects sperm directly into an egg. The fertilized egg, now an embryo, is then placed into the woman's uterus where it hopefully implants and starts to develop.

Some women freeze embryos instead of unfertilized eggs, a method that has been in use since the 1980s. Freezing a fertilized egg is more successful in achieving pregnancy than freezing eggs and fertilizing later, although this requires a partner or anonymous donor. Once frozen, embryos and eggs don't age. "Eggs retrieved from a 22-year-old woman remain 22 indefinitely," Smith explains. This means a woman in her 40s can conceive with a frozen egg or embryo that is younger and theoretically healthier. Women older than 40 who conceive naturally have an increased risk of having a child with Down syndrome, autism or other chromosomal problems. Conceiving with a previously frozen young egg or embryo lowers this risk.

For prepubescent girls with cancer who haven't started to produce mature eggs, ovarian tissue freezing is the only option. This method also can help teens and adult women. "Doctors surgically remove part or all of an ovary, leaving the other ovary in place in the hopes of preserving natural hormone production in the future," Constance says. Thin strips of ovarian tissue are frozen and stored. These tissue strips can contain follicles with thousands of immature eggs. At a later date, a doctor surgically implants the thawed tissue back onto a woman's remaining ovary or into the pelvic region. The hope is that the tissue starts releasing eggs on its own for natural conception or can be stimulated to produce eggs through IVF.

The first baby conceived through ovarian tissue freezing was born in 2004 to a Belgian woman who froze tissue seven years earlier before getting chemotherapy to treat Hodgkin lymphoma. She became pregnant naturally 11 months after the tissue reimplantation. In 2005, an infertile American woman (who didn't have cancer) became pregnant after receiving an ovarian tissue transplant from her identical twin sister. »

VIVIAN took letrozole to control her estrogen levels and to potentially prevent cancer growth during the process to freeze her eggs.

PHOTO COURTESY OF VIVIAN

More than 300 babies have started life this way. But it wasn't until December 2019 that the American Society for Reproductive Medicine lifted the experimental label, giving more girls and women with cancer the opportunity to freeze ovarian tissue. Because the procedure is relatively new, many fertility clinics don't offer it yet. In addition, there's a chance that the tissue may have cancer cells that can start to grow when reintroduced into the body. "We think this risk is greatest if you have a blood cancer (such as) leukemia or an ovarian malignancy," Smith says.

Ovarian transposition (or oophoropexy) is another surgical procedure that may protect the fertility of prepubescent girls and young women with cancer who need radiation therapy to the pelvic area. "Usually via laparoscopy, we move one or both ovaries away from the field of pelvic irradiation," Salama says. After the patient finishes her radiotherapy, becomes cancer free and is fit to become pregnant, the ovaries could be placed back surgically into their original anatomical sites to help natural conception. If natural conception does not occur, IVF can be attempted.

When this procedure takes place in children, the ovaries, fallopian tubes and uterus often stay connected. In adults, doctors may disconnect the ovaries and tubes from the uterus. They can't be reattached, but doctors can stimulate egg production and use IVF for conception. Moving the ovaries won't protect them against systemic treatments such as chemotherapy.

Doctors also can take measures during cancer treatments to protect fertility. "Hormone suppression drugs such as Lupron (leuprorelin) or Zoladex (goserelin) can put the ovaries into hibernation during chemotherapy," Constance says. "This may make cells in the ovaries less sensitive to damage because they aren't actively trying to make eggs." Menopausal symptoms are an unfortunate drug side effect. "I had a fan on my desk to help with the hot flashes," says Maggie Davis, who was 24 when she took Lupron in 2013 during chemotherapy to treat stage 1 breast cancer.

The drug may have made a difference. In 2016, Davis, who lives in Marietta, Georgia, gave birth to a daughter conceived naturally. The eggs she froze before starting cancer treatments remain untouched. "My doctor said that I might need to use the eggs in the future," she says. "There's no way to know for sure until I try to get pregnant again."

My doctor said that I might need to use the eggs in the future. There's no way to know for sure until I try to get pregnant again.

— MAGGIE DAVIS

DAVIS had a daughter who was conceived naturally despite freezing her eggs before starting cancer treatment.

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THE HIGH COST OF FERTILITY PRESERVATION

Davis knows she's fortunate to have had the opportunity to freeze her eggs and to not yet need them. "When I learned that egg freezing was going to cost almost $7,000, I didn't think I could afford to do it," she says. Fees for fertility preservation vary depending on the method and even the clinic location and doctor. "The medications to stimulate egg production can run as high as $6,000," Smith says. "And then you still have to pay for the egg retrieval and annual storage fees." The cost can reach $15,000, and there's no guarantee that it will work. IVF with fresh eggs is effective about half of the time. Using frozen eggs or embryos may lower those odds.

Only 10 states have laws that require health insurers to cover some of the costs of fertility preservation procedures. Some fertility clinics offer discounts for people with cancer. Still, these expenses come at a time when women are also facing hefty charges for cancer care.

Vivian received her diagnosis toward the end of the year, which meant she paid two years of insurance deductibles in quick succession. The egg cryopreservation fee was $12,000. The couple borrowed money from family, and friends helped to raise money through a crowdfunding effort.

Davis was in a similar predicament. "I looked into a payment plan, but it cost $150 just to apply," she says. If she was approved for the plan, she was told the interest rate could be as high as 30%. Instead, Davis' mom, Mary Jones, helped out. Wanting to repay her mom, Davis began selling T-shirts emblazoned with "Team Maggie." During a chemotherapy session, Davis and Jones discussed how unfair it was that young people with cancer might forgo fertility preservation because the costs were out of reach. Six months later, Team Maggie's Dream was born.

DAVIS sold "Team Maggie" T-shirts in an attempt to repay her mother for fertility preservation, which then led to the creation of her nonprofit organization.

The nonprofit organization provides fertility assistance grants to people ages 15 to 37 who have cancer.

"My daughter, Layleigh, is the best thing to ever happen to me," Davis says. "She was a bright light after a dark period. It's reassuring to know that I have options if I need help giving her a younger brother or sister. It would be wonderful for every young person with cancer to have this same opportunity."

Get Help for Fertility Preservation

Grants for fertility preservation

- Livestrong Fertility Program
- Team Maggie's Dream
- The Chick Mission
- The Samfund

Free or discounted fertility medications

- Heart Beat
- Livestrong Fertility Program
- ReUnite Oncofertility

Resources

- Alliance for Fertility Preservation
- The Oncofertility Consortium

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Is Delaying Screening Worth the Risk?

Postponing tests or doctor visits during the pandemic may increase women's risk of cancer

By DARA CHADWICK

TERAVECTOR / STOCK.ADOBE.COM

Amy Rea, 58, of Eden Prairie, Minnesota, has always been diligent about attending health care screenings. But last October, she had a decision to make — cancel the scheduled appointment for her annual mammogram or keep it and face potential exposure to the virus that causes COVID-19.

She canceled the appointment.

"There's no family history of breast cancer, and every mammogram I've had has been fine," Rea says. "I thought about it and decided it's too close contact. Your face is in somebody else's face, so I opted to postpone."

Rea isn't the only woman who has delayed cancer screening during the pandemic. Preventive screenings for all cancers, including breast and cervical, dropped in March and April 2020 as health care facilities halted all nonessential services including screening mammograms, and then restarted with modifications after the first wave passed. With protocols in place and a better understanding of risk, many women now feel comfortable going ahead with screenings. But for others, potential exposure to the virus that causes COVID-19 is too big a chance to take.

"During the first few months, we saw a cessation of all cancer screenings and all elective surgeries," says Dr. Melissa K. Frey, assistant professor of obstetrics and gynecology in the Division of Gynecologic Oncology at Weill Cornell Medicine in New York City. "It's undeniable that happened. But even today, we still see women delaying their screenings because they're concerned about exposure to the virus." »

AMY REA originally canceled her mammogram appointment in fear of becoming infected with COVID-19.

According to results from a study published by Epic Health Research Network, preventive screenings for breast and cervical cancer dropped by 94% when COVID-19 was first declared a national emergency. The organization later reported that between March 15 and June 16, 2020, approximately 285,000 breast exams and 40,000 cervical exams were missed. This is a drop of 63% in breast cancer screenings and 67% in cervical cancer screenings from the number expected based on historical averages.

Those missed screenings are concerning, according to Dr. S. Diane Yamada, chief of gynecologic oncology at University of Chicago Medicine and president-elect of the Society of Gynecologic Oncology. Her health care system saw a 17% drop in Pap tests in 2020 compared with 2019 numbers, she says, adding that between March and May 2020, mammograms were down 80% from their typical levels.

"Screenings are an opportunity to catch cancers early," Yamada says. "I'm worried about cancer being diagnosed at later stages with poorer prognoses."

With safety protocols in place, screening appointments at many facilities are on the rise. Still, experts can only speculate on the long-term impact of missed screenings during the initial pause and how it may affect women who continue to put off screenings because of fear of virus exposure. An article in a recent edition of *Science* stated that modeling the effect of COVID-19 on cancer screening and treatment suggests there could be almost 10,000 additional deaths during the next decade from breast and colorectal cancer.

THE IMPORTANCE OF CANCER SCREENINGS

Screenings can help doctors find cancer early, sometimes before symptoms appear. The American Cancer Society recommends annual mammograms for women ages 45 to 54, with women age 55 and older continuing annual mammograms or switching to a mammogram every two years. In addition, the American Cancer Society states that most women who get breast cancer do not have a family history of breast cancer, so it is important to undergo screening in the presence and absence of family history.

Cervical cancer screenings, also known as Pap tests or Pap smears, should be done every 3 years, starting at age 21, according to the American College of Obstetricians and Gynecologists. Experts also recommend testing for HPV every five years, starting at age 30. Annual OB-GYN visits are recommended for all women.

Studies have shown that screening lowers death rates for many of the common cancers, although there is ongoing debate about the extent of mortality reductions for different malignancies. Newer technologies have improved precision and reduced "false alarms."

It's easy to lose sight of the importance of screenings during a pandemic, Frey says. But delaying appointments has led to some patients presenting with more advanced disease.

Dr. Linda Donegan, director of breast imaging at Rhode Island Medical Imaging and assistant professor in the Department of Diagnostic Imaging at Brown University's Warren Alpert Medical School in Providence, says that during the pandemic some patients opted to

REA BY BRIANNA STACHOWSKI

delay appointments for additional imaging even though screening mammograms showed suspicious areas.

"Imaging allows us to detect cancers when they're smaller and at earlier stages, when they're most treatable," she says. "We have seen some cancers that have increased in size."

Donegan says she understands women's concerns about potential virus exposure. "We screen an older patient population, and we're all being bombarded with bad news about COVID-19," she says. "There's a lot of anxiety and fear of the unknown."

Rhode Island Medical Imaging has focused on letting patients know it's safe to come in for screenings.

"We're all patients at some point," Donegan says. "And education is power. The more our patients know about the importance of screenings and the safety protocols we have in place, the more comfortable they'll feel. This might be our normal for quite a while."

PROTECTING PATIENTS

Health care facilities have a variety of protocols to keep patients and staff at minimal risk of viral transmission. Masking, social distancing, hand sanitizing and enhanced cleaning measures between patient visits are now the norm in offices. Prescreening is also a critical part of safety, with many facilities requiring patients to self-screen for symptoms and answer questions about travel and potential virus exposure. Some have implemented patient temperature checks upon arrival.

Rhode Island Medical Imaging texts all patients 90 minutes before their appointment time with a link to an online COVID-19 screening tool. Patients call when they arrive, wait in their car until their appointment time and are brought right into the changing area.

Yamada says University of Chicago Medicine has tried to reduce additional barriers that might prevent people from coming to the office. "We've offered mammograms on weekends and after hours," she says. "At one point, we were also allowing walk-in appointments."

Frey says Weill Cornell is using telehealth for patient discussions when possible, keeping in-person appointments for screenings and physical exams.

"We've been relying on video visits where we can talk through issues and plans," she says. Still, the pandemic has created new barriers to care for some people, such as finding safe transportation to appointments or using technology to access care.

"Many of our patients are 65 and older," Frey says. "Technology is really intimidating for some people."

Frey also notes that COVID-19 has amplified health disparities that existed before the pandemic began. According to a 2018 article in *Health Equity*, the incidence of cervical cancer is typically higher in Black and Hispanic women than in White women. A decrease in cancer screenings during the pandemic could lead to cancers being missed or diagnosed at more advanced stages in these populations.

"We know that there were disparities in cancer screening rates based on race, ethnicity, education level, insurance status and income level," Frey says, adding that missed opportunities to diagnose cancer through screenings can lead to disparities in health outcomes. "Underserved populations have been hit hardest by COVID-19."

EVALUATING RISK

To date, no clear data exist on the risk of COVID-19 infection during a mammogram or cervical cancer screening visit. Ultimately, women must weigh the risk of potential virus exposure against their health history and make their own decisions.

Rea says she has tried to be strategic about avoiding risk. When she saw her primary care doctor this summer, she requested the first appointment on a Monday morning. "They had staff stationed at the front door doing temperature checks," she says. "All staff members were wearing masks and visors, 6-foot spacing was clearly marked and they'd removed some of the seating from the lobby."

Rea spoke with her doctor about the potential implications of delaying cancer screenings. Because she's at higher risk for skin cancer, she chose to keep her scheduled dermatologist appointment. She also kept her annual gynecologist appointment for a pelvic exam and Pap smear test in October.

"My gynecologist was masked and wearing a visor," Rea says. "I felt safe." »

> **"All staff members were wearing masks and visors, 6-foot spacing was clearly marked and they'd removed some of the seating from the lobby."**
>
> *— AMY REA*

TERAVECTOR / STOCK.ADOBE.COM

> **I was OK with the initial delay. If the delay had been much more than (eight weeks), I would have been concerned.**
>
> — *CARA PEPPER*

PEPPER felt somewhat concerned when getting a mammogram despite the safety precautions in place.

Cara Pepper, 51, of Reading, Pennsylvania, says that although her scheduled mammogram and Pap smear test were initially delayed by her health care facility at the beginning of the pandemic, both appointments were rescheduled — and she kept them.

Pepper, who works for a health care system, says she wasn't concerned about virus exposure during her screenings.

She says she's familiar with the protocols and procedures the hospital uses and, as a patient, those protocols helped her feel safe at her appointments. "I was really fine with it," she says.

Still, she admits she felt a "slight" concern about getting a mammogram.

"You do have to get extremely close to the technician while they're manipulating your breast into the machine," she says. "I just looked the opposite way when we were close."

Pepper's original appointments were delayed by about eight weeks at the pandemic's start.

"I was OK with the initial delay," she says, adding that, although she isn't considered high risk, there is a history of multiple types of cancer in her family. "If the delay had been much more than that, I would have been concerned."

PROTECTING YOUR HEALTH

Doctors want women to know that if they choose to delay screening, it's important to get in touch if they experience new or troubling symptoms. "I had one patient with an enormous ovarian mass who delayed an appointment because of (COVID-19) fears," Yamada says. "It got to the point where she couldn't walk anymore and her family finally had to bring her in."

Women who are at higher risk of breast, cervical, uterine or ovarian cancer should arm themselves with knowledge of potential signs and symptoms, Yamada says. If a woman with symptoms is afraid to come in, she should reach out to her doctor or a nurse triage line right away, she adds. "We can't necessarily examine a patient during a telehealth visit, but we can talk about symptoms and decide if you must be seen," Yamada says.

Bleeding after menopause is one symptom that should be evaluated immediately, according to Frey. She also advises women to contact their doctor if they experience bleeding after intercourse, abdominal pain or pain when urinating.

Donegan encourages patients at higher risk of cancer to talk to their doctor about the risks of delaying screening. Patients also can call the facility to talk about safety protocols that have been put in place.

"We've had patients who are fearful and anxious," she says. "We're happy to walk them through our process."

Rea says she hasn't yet rescheduled her mammogram, but she expects to soon.

"If there had been a family history of breast cancer, I absolutely would have gone," she says.

MATTHEW LESTER

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TARGETED THERAPIES Take Aim at *Endometrial* Cancer

As more is learned about the biology of this disease, new treatment possibilities emerge.

By LEAH LAWRENCE

When Jo Anne Schatz, 69, talks about the latest treatment she received for her endometrial cancer, she describes it as an "eraser."

"It was amazing," Schatz says. "It just wiped my cancer out."

The drug, Keytruda (pembrolizumab), is a type of cancer treatment called immunotherapy, designed to harness a person's immune system to identify and destroy the cancer. It is just one of the targeted treatments approved by the Food and Drug Administration (FDA) for or being developed for the treatment of endometrial cancer.

Unlike traditional chemotherapy, which acts against cancer cells and healthy cells alike, targeted treatments are aimed at specific aspects of the cancer cells.

Keytruda hitting its target is what Schatz credits with saving her life. »

« **JO ANN SCHATZ** originally received a diagnosis of endometrial cancer in May 2015 and was recently treated with immunotherapy.

» **SCHATZ** was treated with a targeted therapy for endometrial cancer after it recurred shortly after chemotherapy and radiation.

FIRST SIGNS

Schatz, a former addiction specialist from Philadelphia, received a diagnosis of endometrial cancer in May 2015 after experiencing unexpected vaginal bleeding. She had never heard of the disease.

"My primary care doctor told me to contact my gynecologist; within two weeks, I was seeing a specialist at Fox Chase Cancer Center and headed in for a complete hysterectomy," Schatz says.

Endometrial cancer is a disease in which cancer cells form inside the lining of the endometrium, or uterus. Vaginal bleeding and pelvic pain are common symptoms.

"Endometrial cancer is the most common of all gynecological cancers in the United States," says Dr. Christina S. Chu, professor in the Department of Surgical Oncology at Fox Chase Cancer Center in Philadelphia. "Fortunately, the vast majority of endometrial cancers can be treated surgically with the removal of the uterus, ovaries, fallopian tubes and cervix. Most are cured with this surgery plus or minus radiation."

Some patients — 13% — who receive a diagnosis of endometrial cancer, however, will have their disease recur. After surgery, Schatz underwent several rounds of radiation and chemotherapy to destroy any remaining cancer cells. After a brief remission, her cancer recurred, metastasizing to the peritoneal lining, and her physicians began to look for more targeted treatment options.

FIND THE TARGET

"When we started to get down to the genomic levels of these tumors, we realized that just because some endometrial cancers may look (similar) under the microscope, they may still behave biologically different based on genomic signature," says Dr. Emily M. Ko, assistant professor of obstetrics and gynecology at Pennsylvania Hospital of Penn Medicine in Philadelphia. "Based on that genomic signature, there may be biologic pathways that we can target."

That is what happened to Schatz, who was told that her type of endometrial cancer had a genetic component called MSI-high.

MSI stands for "microsatellite instability." When disease is MSI-high, the cancer cells have a high number of mutations within microsatellites, which are short, repeated sequences of the DNA. These signify abnormalities in DNA repair, which can be targeted with certain drugs.

In 2017, the FDA approved Keytruda for use as a treatment for any solid tumor that was MSI-high, had progressed after prior treatment and had no satisfactory alternative treatment options.

"This was important for patients with endometrial cancer because (approximately) 30% of patients with endometrial cancer will have tumors that are MSI-high," explains Dr. Shannon N. Westin, associate professor in the Department of Gynecologic Oncology and Reproductive

KRISTA PATTON

Medicine at The University of Texas MD Anderson Cancer Center in Houston.

One study evaluating the use of Keytruda in patients with MSI-high tumors showed that among a small group of women with endometrial cancers, more than half saw their tumor respond to the treatment, and the majority had at least some clinical benefit.

"A larger proportion of patients with endometrial cancer will have microsatellite-stable disease," Westin says. "For those patients, there is a newer FDA-approved targeted therapy combining Keytruda with Lenvima (lenvatinib)."

Indeed, in late 2019, the FDA approved the immunotherapy Keytruda with Lenvima for patients with endometrial cancer that is not MSI-high and whose disease has come back after prior chemotherapy. Lenvima is a multiple-receptor tyrosine kinase inhibitor. The drug works by blocking the action of abnormally activated proteins that signals cancer cells to multiply. A study of this combination showed that approximately one-third of endometrial tumors responded.

Finally, some patients with endometrial cancer may qualify for treatment with a drug targeting NTRK gene fusions, which are estimated to occur in only a small percentage of endometrial cancers. Rozlytrek (entrectinib) and Vitrakvi (larotrectinib) are approved for adults who have solid tumors with this specific genetic alteration.

FINDING NEW TARGETS

"Not every endometrial cancer that comes back or spreads will have one of the characteristics to qualify for the currently available targeted treatments. These women may want to ask their physicians about potential alternatives," Ko says.

Kim Bryant, 61, a former special education teacher from Texas, did just that when she was told in May 2019 that her endometrial cancer had spread. After receiving her diagnosis in March 2016, Bryant initially underwent surgery and radiation for the cancer. After its first recurrence a year later, she had additional surgery followed by radiation and chemotherapy.

"At that point, my local oncologist said he had done all he could and referred me to MD Anderson," Bryant says. "I was given a choice between two trials. I was enrolled in one for about a year and my cancer progressed. I have had more success with the second trial."

The second clinical trial is testing a three-drug combination of the hormone therapy Femara (letrozole); Afinitor (everolimus), a drug designed to target a protein called mTOR that promotes cell growth; and Kisqali (ribociclib), a CDK 4/6 inhibitor that is designed to interrupt the cell cycle that drives growth of cancer cells.

"CDK 4/6 inhibitors have been studied in breast cancer and are thought to potentially be synergistic when used with other hormonal drugs," Ko says.

For her first clinical trial, Bryant had been making a four-hour drive once a week from Dallas to Houston to receive treatment. On the current trial, all three drugs are oral and can be taken at home.

"All three oral treatments (are) so much easier because there are no infusions," Bryant says. "I only have to go down once every three months for bloodwork and other testing." »

» **KIM BRYANT** is currently participating in a clinical trial testing a three-drug combination for her endometrial cancer.

JARED REY HERNANDEZ

BRYANT credits targeted therapy for allowing her to stay upbeat during her cancer journey.

Bryant remains on treatment and says that, so far, the cancer is responding well.

In addition to mTOR and CDK 4/6 inhibitors, clinical trials are also testing a class of drugs that inhibit poly (ADP-ribose) polymerase — more commonly known as PARP inhibitors. This class of drugs is approved for certain breast and ovarian cancers that have an inherited mutation in the BRCA gene or have a certain genomic instability called homologous recombination deficiency (HRD), a type of DNA repair defect.

"There are a number of trials exploring these drugs alone or in combination with other targeted agents to see if there is activity in endometrial cancer," Westin says. "Probably about 20% of endometrial cancers have mutations in BRCA or other abnormalities in HRD pathway members, but there may be other abnormalities in endometrial cancer that predict benefit, so none of the trials (is) being selective."

There are also trials exploring other immunotherapy drugs that target a protein called PD-1 or PD-L1, immunotherapy drugs in combination with chemotherapy or other targeted agents, and agents targeted against other disease pathways such as the PI3K or MEK pathways, Westin says.

WHY TARGET?

Right now, these targeted therapies are considered second-line treatments — given after a first disease recurrence — because they are not as effective as primary chemotherapy for most patients, according to Chu.

"Trials are ongoing to test targeted therapies in combination with chemotherapy in the first-line setting, though," Chu says.

There have not been any completed clinical trials yet comparing the standard chemotherapy with these new targeted treatments, but they are in progress, according to Ko.

"What we are learning is that perhaps side effect profiles may be better in targeted treatment, meaning it may be worthwhile to consider an alternative targeted therapy up front in treatment rather than saving it for down the road," explains Ko.

For example, immunotherapy drugs such Keytruda do not have the traditional side effects seen with chemotherapy, such as hair loss, nausea or vomiting. Because the drug works by attempting to stimulate the immune system, many of the side effects seen with Keytruda are related to the immune system, Chu says. Similarly, side effects seen with Lenvima, which works by affecting blood vessels, can be related to a patient's blood vessels, such as high blood pressure.

Schatz says that during her treatment with Keytruda, she experienced muscle aches, pains and fatigue. Other common side effects associated with Keytruda include headache, fever, skin rash, constipation, loss of appetite and diarrhea.

"On chemotherapy, I was often sick for a full week, then a little better before preparing to go back for another treatment," Schatz says. "On the trial, I was able to cook and care for myself and establish a routine."

Bryant says that side effects during her most recent clinical trial also have been tolerable.

"I have had some decrease in appetite and some fatigue, but not enough that it keeps me from doing what I want to do," Bryant says. "It has only slowed me down some."

JARED REY HERNANDEZ

Many of the side effects related to targeted therapies can be managed easily if caught early, Westin says.

"This takes good communications between a patient and their health care team — and preparation — so that a patient knows what to look for," Westin says.

In addition to a patient's tumor having the right "target," the health care team will consider these possible side effects in their decision on whether a patient might qualify for treatment with a targeted therapy.

"We look at the best data we have available, the tumor characteristics and the overall health of each patient to decide if a targeted therapy is best," Ko says.

ADVOCACY

Schatz credits much of her progress not only to targeted therapy but also to advocating for herself and her treatment. She had one doctor who encouraged her to continue treatment, whereas another told her to stop. Since stopping treatment with Keytruda, Schatz has follow-up scans every four months, as well as other regular monitoring.

"I am also healthier," she says. "I am on a 'cancer-fighting' plant-based diet. I take it one day at a time, but I am grateful to be alive and can feel my creativity coming back."

> **"I have some decrease in appetite and some fatigue, but not enough that it keeps me from doing what I want to do."**
>
> *— KIM BRYANT*

Bryant, too, has been able to maintain an upbeat, "glass-half-full" attitude throughout her cancer journey, she says.

"I have surrounded myself with my faith, family and friends," she says.

Westin applauds patients such as Schatz and Bryant for raising their voices and sharing their stories about endometrial cancer.

"Other tumor types get more attention, but endometrial cancer is one of the only cancer types where the incidence is growing," Westin says. "A lot of women with endometrial cancer will be cured, but we have to be aware of their sisters in diagnosis who do not do as well and together raise our voices to shine more light on this problem. Hopefully that will allow us to get more funding and more companies interested in exploring new agents to treat endometrial cancer."

15 Years Later, What Have We Learned About the HPV Vaccine?

The HPV vaccine has been shown to help prevent cervical cancer, but what if you didn't get the vaccine in time to prevent the disease?

By DARLENE DOBKOWSKI, M.A.

THE HPV VACCINE GARDASIL was first approved by the Food and Drug Administration in 2006 to prevent cervical and other cancers. An updated version of the vaccine, Gardasil 9, was approved in 2014; it protects patients against the same four types of HPV as the previous version plus five additional types of the virus.

"The current vaccine protects against the HPV strains that cause 90% of cervical cancers," Dr. Anna L. Beavis, assistant professor of gynecology and obstetrics at the Kelly Gynecologic Oncology Service at Johns Hopkins Medicine in Baltimore, told *CURE*®. "We have been giving the vaccine since 2006, and, in addition to seeing how safe it is, we are already starting to see reductions in cervical precancer rates in many countries, including (regions of the United States) where vaccination rates are good."

KATE WEISSMAN underwent numerous rounds of radiation and chemotherapy throughout her cancer journey.

According to the American Cancer Society, 8 in 10 people will get HPV throughout their lifetimes, and it affects an estimated 35,000 people in the United States per year. The Centers for Disease Control and Prevention (CDC) recommends vaccination for males and females between 9 and 26 years old.

"The vaccine works best if given before any possible exposure to the virus," Beavis explains. "HPV is transmitted sexually, so giving it well before sexual activity (starts) is best. Second, the immune response to the vaccine is stronger in younger children. In fact, this means that children under the age of 15 who get the vaccine only need two doses, not three."

Although the vaccine has been available for years, some patients may have missed the chance to get the vaccine in time to potentially prevent cancer. Kate Weissman, 35, is one of those women who missed that window of opportunity. She received the vaccine when it first came out (around 2006 or 2007), but she received a diagnosis of HPV in 2013. She believes she already had HPV before she was vaccinated and adds that the problem is that co-testing for HPV was not performed as often as it should have back when she was first vaccinated.

"It was absolutely the right decision for my family at the time. And for me, unfortunately, the timing didn't work out in my favor," Weissman says.

In May 2015, Weissman was having bleeding after sex and sporadic, unexplained bleeding. She underwent tests at the guidance of her OB/GYN, which led to a colposcopy, a procedure that examines the cervix for potential cancer, in October 2015. She received a diagnosis of cervical cancer and was given a referral to Dana-Farber Cancer Institute in Boston, where she set up an appointment with an oncologist to discuss her next steps.

"I think the thing a lot of people don't realize … about cancer is that you don't get all the information at once," Weissman notes. "It's a really awful waiting game. You find out you have cancer, but there (are) six more steps that have to happen before they can get you a prognosis or go through your treatment plan with you."

Weissman adds that she underwent a series of MRIs, positron emission tomography scans and other tests to determine whether the cancer had spread and what stage it was. The disease had spread to her lymph nodes, which

PHOTOS COURTESY OF WEISSMAN

WEISSMAN and her husband, **MATT,** are currently expecting a child via a surrogate.

PHOTOS COURTESY OF WEISSMAN

led to her receiving a diagnosis of stage 2b cervical cancer. Her initial treatment included six rounds of chemotherapy and 30 rounds of radiation, which surprised her.

"I already had this perception of cervical cancer that if you do get it, you have a surgery and then you go on with your life, which is such an awful perception to have," Weissman says. "Now that I'm on the other side of it, I'm so much more educated (about) it, but it's something people don't know a lot about cervical cancer."

Her treatment ended on Dec. 23, 2015, but a post-treatment scan later indicated the cancer had spread through her lymphatic system, so she was rushed into surgery to remove her lymph nodes. She underwent treatment again to target the new cancer location, which included 25 rounds of radiation and five rounds of chemotherapy. Afterward, she underwent an 18-week course of chemotherapy to target any possible microscopic cancer that may remain, which lasted until October 2016, when cancer was no longer in her system. "It was a tough year to say the least," Weissman says.

Based on Weissman's experience with cervical cancer, she says that had the HPV vaccine come out sooner, she "absolutely" would have had it. She advocates for others to follow CDC recommendations for the HPV vaccine by speaking to high school students (under the supervision of teachers), doctors, nurses and patients. She also lobbies in Washington, D.C., and Boston, where she lives, for bills to increase access to screening, vaccination and treatment for minority communities and for those who live in rural areas.

"I once had a pediatrician say, 'You put your helmet on before you ride your bike, not after, not during,'"

> **Cervical cancer is so personal. It's an intimate cancer, and a lot of people understandably are not comfortable talking about (it).** — *KATE WEISSMAN*

Weissman says. "That's exactly what it is. These kids need to get vaccinated before any sort of (sexual) activity in their life or contact with other people is introduced because that will protect them."

There is a lot of misinformation about HPV, such as people get HPV only from sexual intercourse.

"I think one of the most important things to know is that this virus can be transmitted without necessarily having penetrative intercourse," Beavis says. "Put another way, you can get this virus from 'fooling around.' These days, most parents understand that their child will be sexually active at some point, so I also focus on the proven safety of the vaccine."

Weissman says she's not afraid to talk about cervical cancer and HPV because it is important to discuss these topics without an attached stigma.

"Cervical cancer is so personal," she says. "It's an intimate cancer, and a lot of people understandably are not comfortable talking about their cervical cancer journey. I am, so I'm going to be a voice for people who aren't comfortable, because the more we talk about it, the more awareness we'll get out there."

Weissman and her husband are having a child via a surrogate, as she is unable to bear children because of cervical cancer. She plans to have her child vaccinated for HPV at the appropriate time. "I will absolutely get my daughter vaccinated," she says. "We'll make sure that anyone in my orbit is educated on the vaccine, as well, and will encourage them to speak to their pediatrician about doing the vaccination for them."

HPV-related cervical cancer is different from other cancers, as the origin of the disease is known, and it can be prevented with a vaccine.

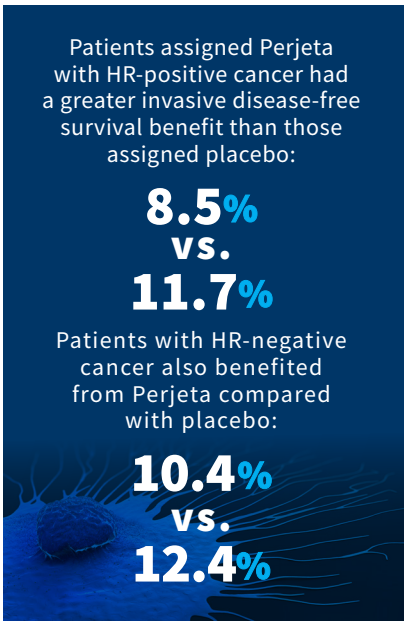
"This vaccine has been heavily studied and scrutinized," Beavis says. "It is incredibly effective and very safe. It now has (more than) 20 years of data supporting it, and the immune response to the vaccine is better than (its response) to the virus. We always talk about curing cancer, but what if we had the potential power to prevent cancer before it even developed? Parents have the potential to give this to their children by vaccinating them with the HPV vaccine."

Perjeta Plus Standard Therapy Improves Survival Outcome in HER2-Positive Breast Cancer

However, overall survival was not higher for patients treated with Perjeta plus chemotherapy and Herceptin versus those treated with placebo plus chemotherapy and Herceptin. A longer follow-up is needed to determine whether a benefit exists. By DARLENE DOBKOWSKI, M.A.

ADDING PERJETA (PERTUZUMAB) to chemotherapy and Herceptin (trastuzumab) did not significantly improve overall survival in women with human epidermal growth factor receptor 2 (HER2)-positive early-stage breast cancer, although improvements were observed in invasive disease-free survival, according to results of a study published in the *Journal of Clinical Oncology*.

Findings from the APHINITY trial demonstrated that overall survival at six years was close to 95% in patients who added Perjeta to their treatment and also for those who did not add Perjeta, which further reinforces that combination therapy directed at HER2 and chemotherapy can lead to excellent outcomes in most patients with HER2-positive, early-stage breast cancer. Despite these findings, follow-up times beyond six years are needed to fully assess the overall survival benefit of this therapy.



Researchers from this trial previously reported findings from 45 months of follow-up, which demonstrated that adding Perjeta to adjuvant Herceptin and chemotherapy significantly improved invasive disease-free survival (the time after treatment without signs of cancer) in patients with early-stage, HER2-positive breast cancer.

"Updated results from this (six-year) analysis strengthen the observation that patients with node-negative, HER2-positive early (breast cancer) show excellent (invasive disease-free survival) results up to six years from diagnosis when treated with standard adjuvant therapy without the addition of (Perjeta)," the study authors wrote.

Higher levels of HER2, a protein involved in the development of breast cancer, can lead to faster cancer growth and spread compared with other types of breast cancers. This protein is the second-most important target for therapy in breast cancer, with the first being the estrogen receptor, the study authors wrote. In breast cancer, overexpression of HER2 is found in approximately 15% to 20% of patients.

In this phase 3 trial, 4,805 patients with HER2-positive breast cancer were assigned either Herceptin and Perjeta (2,400 patients) or Herceptin and placebo (2,405 patients), both of which were administered for one year. Both groups also underwent chemotherapy.

At six years, overall survival was 95% in patients assigned Perjeta compared with 94% in those who were assigned placebo. There were 125 deaths during this time period.

The group assigned Perjeta had fewer events related to invasive disease-free survival compared with the placebo group (91% versus 88%).

Patients in the node-positive group (breast cancer affecting the lymph nodes) benefited more from Perjeta regarding invasive disease-free survival compared with those assigned placebo (88% versus 83%). Those in the node-negative group (breast cancer not affecting the lymph nodes) did not benefit from the addition of Perjeta.

When assessing invasive disease-free survival by hormone receptor (HR) status (which determines whether hormones are fueling cancer growth), patients assigned Perjeta with HR-positive cancer had a greater benefit than those assigned placebo (8.5% versus 11.7%). Patients with HR-negative cancer also benefited from Perjeta compared with placebo (10.4% versus 12.4%).

Both treatment groups had a less than 1% rate of heart-related side effects, which was consistent with the earlier report from this study. In addition, no new safety issues were observed with either treatment.

"Continued follow-up of patients is important to fully assess (overall survival) benefit at the time-driven third interim (overall survival) analysis planned for 2022," the study authors wrote.

What Is IBRANCE® (palbociclib)?

IBRANCE is a prescription medicine used in adults to treat hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer that has spread to other parts of the body (metastatic) in combination with an aromatase inhibitor as the first hormonal based therapy in postmenopausal women or in men.

Important Safety Information for Patients

IBRANCE may cause serious side effects, including:

Low white blood cell counts (neutropenia). Low white blood cell counts are very common when taking IBRANCE and may cause serious infections that can lead to death. Your doctor should check your white blood cell counts before and during treatment.

If you develop low white blood cell counts during treatment with IBRANCE, your doctor may stop your treatment, decrease your dose, or may tell you to wait to begin your treatment cycle. Tell your doctor right away if you have signs and symptoms of low white blood cell counts or infections such as fever and chills.

Lung problems (pneumonitis). IBRANCE may cause severe inflammation of the lungs during treatment that can lead to death. Tell your doctor right away if you have any new or worsening symptoms, including chest pain, cough with or without mucus, and trouble breathing or shortness of breath.

Your doctor may interrupt or stop treatment with IBRANCE completely if your symptoms are severe.

Before you take IBRANCE, tell your doctor about all of your medical conditions, including if you:

- have fever, chills, or any other signs or symptoms of infection.
- have liver or kidney problems.
- are pregnant or plan to become pregnant; IBRANCE can harm your unborn baby.
  - Females who are able to become pregnant should use effective birth control during treatment and for at least 3 weeks after the last dose of IBRANCE. Your doctor may ask you to take a pregnancy test before you start treatment with IBRANCE.
  - Males with female partners who can become pregnant should use effective birth control during treatment with IBRANCE for at least 3 months after the last dose of IBRANCE.
- are breastfeeding or plan to breastfeed. It is not known if IBRANCE passes into your breast milk. Do not breastfeed during treatment with IBRANCE and for 3 weeks after the last dose.

The most common side effects of IBRANCE include:

- Low red blood cell counts and low platelet counts. Call your doctor right away if you develop any of these symptoms during treatment:
  - dizziness
  - shortness of breath
  - weakness
  - bleeding or bruising more easily
  - nosebleeds

Other most common side effects include: infections, tiredness, nausea, sore mouth, abnormalities in liver blood tests, diarrhea, hair thinning or hair loss, vomiting, rash, and loss of appetite.

IBRANCE may cause fertility problems in males. This may affect your ability to father a child. Talk to your healthcare provider about family planning options before starting IBRANCE if this is a concern for you.

These are not all of the possible side effects of IBRANCE. For more information, ask your doctor.

Tell your doctor about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. IBRANCE and other medicines may affect each other, causing side effects.

Do not drink grapefruit juice or eat grapefruit products while taking IBRANCE as they may increase the amount of IBRANCE in your blood.

Tell your doctor if you start a new medicine. Take IBRANCE exactly as your doctor tells you.

If you take too much IBRANCE, call your doctor right away or go to the nearest hospital emergency room.

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 Important Facts About IBRANCE on the following page.

To learn more, talk to your doctor.

Can't afford your medication? Pfizer may be able to help.
Visit IBRANCE.com.

*Hormone receptor-positive includes estrogen receptor-positive (ER+) and/or progesterone receptor-positive (PR+)

IBRANCE® palbociclib | 125 mg tablets

 December 2020 PP-IBR-USA-4003-02

IBRANCE®
palbociclib | 125 mg tablets

IMPORTANT FACTS

IBRANCE® (EYE-brans)
(palbociclib)

The risk information provided here is not comprehensive. This information does not take the place of talking to your healthcare provider about your condition or treatment. To learn more about IBRANCE talk to your healthcare provider or pharmacist. To obtain the FDA-approved product labeling call 1-800-438-1985 or visit www.IBRANCE.com.

What is IBRANCE?

IBRANCE is a prescription medicine used in adults to treat hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer that has spread to other parts of the body (metastatic) in combination with:

- an aromatase inhibitor as the first hormonal based therapy in postmenopausal women or in men, or
- fulvestrant in people with disease progression following hormonal therapy.

It is not known if IBRANCE is safe and effective in children.

What is the most important safety information I should know about IBRANCE?

IBRANCE may cause serious side effects, including:

Low white blood cell counts (neutropenia). Low white blood cell counts are very common when taking IBRANCE and may cause serious infections that can lead to death. Your healthcare provider should check your white blood cell counts before and during treatment.

If you develop low white blood cell counts during treatment with IBRANCE, your healthcare provider may stop your treatment, decrease your dose, or may tell you to wait to begin your treatment cycle. Tell your healthcare provider right away if you have signs and symptoms of low white blood cell counts or infections such as fever and chills.

Lung problems (pneumonitis). IBRANCE may cause severe or life-threatening inflammation of the lungs during treatment that can lead to death. Tell your healthcare provider right away if you have any new or worsening symptoms, including:

- chest pain
- cough with or without mucus
- trouble breathing or shortness of breath

Your healthcare provider may interrupt or stop treatment with IBRANCE completely if your symptoms are severe. **See "What are the possible side effects of IBRANCE?" for more information about side effects.**

What should I tell my healthcare provider before taking IBRANCE?

Before taking IBRANCE, tell your healthcare provider about all of your medical conditions, including if you:

- have fever, chills, or any other signs or symptoms of infection.
- have liver or kidney problems.
- are pregnant, or plan to become pregnant. IBRANCE can harm your unborn baby.
  - Females who are able to become pregnant should use effective birth control during treatment and for at least 3 weeks after the last dose of IBRANCE. Your healthcare provider may ask you to take a pregnancy test before you start treatment with IBRANCE.
  - Males with female partners who can become pregnant should use effective birth control during treatment with IBRANCE for at least 3 months after the last dose of IBRANCE.
  - Talk to your healthcare provider about birth control methods that may be right for you during this time.
  - If you become pregnant or think you are pregnant, tell your healthcare provider right away.
- are breastfeeding or plan to breastfeed. It is not known if IBRANCE passes into your breast milk. Do not breastfeed during treatment with IBRANCE and for 3 weeks after the last dose.

Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. IBRANCE and other medicines may affect each other causing side effects.

How should I take IBRANCE tablets?

- Take IBRANCE exactly as your healthcare provider tells you.
- IBRANCE tablets may be taken with or without food.
- IBRANCE should be taken at about the same time each day.
- Swallow IBRANCE tablets whole. Do not chew, crush or split IBRANCE tablets before swallowing them.
- Do not take any IBRANCE tablets that are broken, cracked, or that look damaged.
- Avoid grapefruit and grapefruit products during treatment with IBRANCE. Grapefruit may increase the amount of IBRANCE in your blood.
- Do not change your dose or stop taking IBRANCE unless your healthcare provider tells you.
- If you miss a dose of IBRANCE or vomit after taking a dose of IBRANCE, do not take another dose on that day. Take your next dose at your regular time.
- If you take too much IBRANCE, call your healthcare provider right away or go to the nearest hospital emergency room.

What are the possible side effects of IBRANCE?

IBRANCE may cause serious side effects. See "What is the most important safety information I should know about IBRANCE?"

The most common side effects of IBRANCE when used with either letrozole or fulvestrant include:

- low red blood cell counts and low platelet counts. Call your healthcare provider right away if you develop any of these symptoms during treatment:
  - dizziness
  - shortness of breath
  - weakness
  - bleeding or bruising more easily
  - nosebleeds
- infections (see "What is the most important safety information I should know about IBRANCE?")
- tiredness
- nausea
- sore mouth
- abnormalities in liver blood tests
- diarrhea
- hair thinning or hair loss
- vomiting
- rash
- loss of appetite

IBRANCE may cause fertility problems in males. This may affect your ability to father a child. Talk to your healthcare provider about family planning options before starting IBRANCE if this is a concern for you.

These are not all of the possible side effects of IBRANCE.

Keep IBRANCE and all medications out of the reach of children.

Call your doctor for medical advice about side effects. 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.

To learn more, talk to your doctor.

These IMPORTANT FACTS are based on IBRANCE® (palbociclib) Patient Information LAB-1372-1.0, Rev. 11/2019.

Rubraca May Prolong Progression-Free Survival in Patients With Ovarian Cancer With BRCA Mutations, Preliminary Results Show

The phase 3 ARIEL4 trial evaluated Rubraca (rucaparib) versus chemotherapy in patients with ovarian cancer and a BRCA mutation who did not respond to two or more lines of chemotherapy. By HANNAH SLATER AND DARLENE DOBKOWSKI, M.A.

RUBRACA (RUCAPARIB) IMPROVED progression-free survival compared with chemotherapy in patients whose ovarian cancer tumors harbor BRCA mutations and who had had two or more prior lines of chemotherapy, researchers say. The findings are from the ARIEL4 study, which was recently completed but is not yet published.

Women who test positive for BRCA mutations are at higher risk of developing breast or ovarian cancer compared with those who do not have this genetic mutation.

"The ARIEL4 study (results) verified that women with relapsed, BRCA mutation-positive advanced ovarian cancer, including those who are platinum-sensitive or (platinum)-resistant, received benefit with (Rubraca) treatment when compared to chemotherapy," Dr. Amit M. Oza, head of the Division of Medical Oncology and Hematology at University of Toronto in Canada and coordinating researcher on the ARIEL4 study, said in a news release. "These results underscore the importance of (Rubraca) as a treatment option for women with BRCA-mutant advanced ovarian cancer."

The phase 3 study evaluated 600 milligrams of Rubraca twice per day versus chemotherapy in patients with a BRCA mutation and platinum-sensitive, partially platinum-sensitive or platinum-resistant relapsed ovarian, fallopian tube or primary peritoneal cancers who have received two or more prior lines of chemotherapy. Patients who are platinum sensitive are those who responded to a platinum-based chemotherapy and had the cancer recur in six or more months, whereas those who are platinum resistant had recurrent disease within six months. Overall, 349 women were enrolled in the trial across North America, South America, Europe and Israel.

The primary end point of the study was progression-free survival, or the time since treatment when the disease does not worsen. Other outcome measures include overall survival (time a patient is alive after receiving a diagnosis or the start of treatment), objective response rate (the number of patients whose tumor size was reduced for a particular period of time), duration of response (the time when a tumor responds to treatment), patient-reported outcomes, and safety and tolerability of Rubraca versus chemotherapy.

For one analysis of progression-free survival, therapy with Rubraca (220 patients) was significantly better than chemotherapy (105 patients). The median progression-free survival was 7.4 months with Rubraca compared with 5.7 months for chemotherapy alone.

Additionally, in another analysis with 349 patients, the researcher-assessed progression-free survival in the Rubraca group (233 patients) was statistically better than the chemotherapy group (116 patients). The medians were 7.4 months versus 5.7 months, respectively.

Minimal benefit with Rubraca was noted in the 7% of patients who had a BRCA reversion mutation, or when a mutation reverts back to its original state.

Results also revealed a trend toward an overall survival advantage in the chemotherapy arm; however, this was driven by the high rate (64%) of crossover to Rubraca following disease progression with chemotherapy. When comparing patients who received Rubraca at any point on the trial with those who did not, Rubraca showed a trend toward an overall survival advantage; although numerically different, it was not statistically significant.

Regarding safety, side effects were found to be consistent with the known safety profiles of Rubraca and chemotherapy. The most common serious side effects occurring in more than 5% of all patients who received Rubraca in the ARIEL4 study were anemia (low red blood cell count; 22%), neutropenia (low count of white blood cells called neutrophils; 10%), fatigue (8%), thrombocytopenia (decreased platelets; 8%) and increased alanine transaminase/aspartate transaminase (liver enzymes that may indicate injury to the liver by the drug; 8%).

"We are pleased with these topline results from the ARIEL4 trial, which confirm the clinical benefit of Rubraca versus chemotherapy, including platinum-based chemotherapy, as a treatment for women with BRCA mutation-positive advanced ovarian cancer, including patients who are platinum resistant," Patrick J. Mahaffy, president and CEO of Clovis Oncology, said in the news release. "We look forward to sharing comprehensive results at an upcoming medical meeting."

Embracing a Different Perspective After Ovarian Cancer

Fertility treatments led to a cancer diagnosis but also opened the door to adoption and a new view on life. By DARLENE DOBKOWSKI, M.A.

ELIZABETH JOHNSTON USED TO teach reading and writing to students with remedial needs at the City University of New York, but she has stayed home since July 2018, when her daughter was born. Johnston had a tumultuous year starting in February 2017, when she received a diagnosis of ovarian cancer a couple of days before her 39th birthday. She was younger than the average age when ovarian cancer is often diagnosed, which is around 50 or 60.

"In many ways, I was very lucky because I think one of the challenges with ovarian cancer is (that) it's often caught much later, since there are fewer symptoms; the symptoms that exist tend to be misdiagnosed or just assumed to be something else," Johnston says.

During fertility treatment, Johnston learned that she had ovarian cysts caused by endometriosis, but her doctor was not concerned. A year and a half later, she underwent an endometrial biopsy before her first embryo transfer to ensure her "chances were as good as possible," Johnston says, especially as there were not many embryos to transfer. The biopsy results indicated precancer in her uterus. This did concern her doctor, especially because one of her cysts had significantly grown in size.

ELIZABETH JOHNSTON with her husband, **JAKE**, and daughter, **MIRABEL**, two years after completing chemotherapy.

"It looked a little concerning, (but) the doctors still didn't think it was likely that I would have had cancer, since I was young," Johnston says. "I didn't have any risk factors. There was (no cancer) in my family."

Her reproductive endocrinologist referred her to a gynecologic oncologist for a biopsy. Johnston received a diagnosis of stage 1 ovarian cancer, although there was a surface metastasis on her colon where it touched her ovary. She says her disease staging was somewhat unclear, as she was told she technically had stage 2 cancer because of the metastasis, but her records indicated stage 1 cancer. Despite the discrepancy, her doctor ensured her there was no difference in treatment from one stage to another based on her presentation.

Her gynecologic oncologist removed the affected ovary and left her uterus and the other ovary, Johnston says. The surface metastasis was treated with six rounds of chemotherapy with CarboTaxol (a combination of paclitaxel and carboplatin), which ended in July 2017.

Johnston chose to remove her other ovary after finishing chemotherapy because she and her husband decided not to have any more egg retrievals performed as part of their fertility treatment.

"I had the opportunity to transfer the embryos that we had, which I also consider myself lucky for because … a lot of women don't (have that chance)," Johnston says. "When they face this diagnosis, (women) might get a hysterectomy and have their reproductive choices taken away from them. We, at least, still got to try to implant the few embryos we had, but none of them took."

Johnston and her gynecologic oncologist discussed starting hormone therapy, including "the side effects that were the hardest, dealing with the menopause symptoms and physical changes that happen," she explains. Before starting this treatment, her doctor performed another biopsy of Johnston's uterus, which indicated that the precancer had returned; it was just six months after she had finished chemotherapy. This led to her having a hysterectomy to remove her uterus.

After the hysterectomy, Johnston started taking low-dose estrogen in pill form and as a cream, both of which she says helped to a degree. She still had some side effects, including hot flashes and trouble sleeping, which resulted in a small increase in the dose that helped a lot, she says. Johnston also

PHOTOS COURTESY OF JOHNSTON

JOHNSTON, holding her daughter, MIRABEL, for the first time (left), and her brother, ROB (right), looked "more alike than ever" during her cancer treatment, she says.

had issues with intimacy after the procedure, which affected her both physically and psychologically. She saw a therapist to work through the issues, and she also saw a pelvic floor therapist.

"(My husband has) been very understanding about ways (my hysterectomy) has affected intimacy," Johnston says. "We have very good communication, (but) it hasn't been easy, and that's taken a lot of communication and patience."

Johnston and her husband put all their attention into adoption after her hysterectomy; it was an option they had previously considered.

"Emotionally, adoption was hard, as was IVF, in terms of the process, but at the end, once you have a kid … I don't even remember how hard it was," Johnston says.

Johnston and her husband adopted their daughter at birth in July 2018, a year after she completed treatment, which she credits to helping her feel better. The year following treatment was difficult, even with a strong support system.

"After having finished treatment, everyone's so excited that you're done and happy for you," Johnston says. "When I was in treatment, I kept waiting to complete that last round so that I would be done with chemotherapy, but then I still felt pretty terrible afterward. … It took much longer than I expected to (start feeling better). I felt like I was still dealing with this process, and the people around me had moved on, like they no longer thought of me as having cancer."

Johnston, now 42, recently had her checkups reduced from every three months to every six months thanks to good blood work and scans. Even with these successes, the thought of cancer has not escaped her mind.

"I still think about cancer, but I'm not as anxious as I think I had been in that year after treatment," Johnston says. "If it were to come back, I know that there are lots of treatments available, and I just have to keep on top of appointments so that if it does come back, we, again, catch it early."

Johnston advises women, especially those younger than 50, to listen to their body even though ovarian cancer does not have a consistent set of symptoms. She added that some of her symptoms were bloating and abdominal discomfort, which were likely associated with her 9- to 10-centimeter cyst. She also had abdominal pain two to three months before she received a diagnosis of ovarian cancer, which was reminiscent of the pain she would have with her period from endometriosis.

> **"I still think about cancer, but I'm not as anxious as I think I had been in that year after treatment."**
>
> *— ELIZABETH JOHNSTON*

Three and a half years later, the stay-at-home mom is planning a new professional direction and applying for Master of Social Work programs, which she hopes to start part time in the fall when her daughter will be in preschool.

"I feel good. I'm excited about taking a new direction professionally," Johnston says. "(My) perspective has changed. … I still want to work hard and care about my work and do something beneficial for society, but I want to have a balance in my life and prioritize that. That hadn't been something I really put enough emphasis on before. … There is a way, I guess, where you can think about life before (cancer) and after, and with time and space, I feel optimistic about the future. And my daughter's pretty awesome, so that's a great thing to have come out of this." C

PHOTOS COURTESY OF JOHNSTON

Combination Treatment Increases Quality of Life for Patients With Ovarian Cancer, Study Results Show

Women with ovarian cancer report a better quality of life when treated with a combination of Keytruda, Avastin and oral metronomic cyclophosphamide.

By COLLEEN MORETTI

A NOVEL REGIMEN CONSISTING of a combination of Keytruda (pembrolizumab), Avastin (bevacizumab) and oral metronomic cyclophosphamide shows efficacy, safety and better quality of life in patients with recurrent platinum-sensitive, platinum-resistant or refectory epithelial ovarian, fallopian tube or primary peritoneal cancer, according to data published in *JAMA Oncology*.

Treatment options for ovarian cancer are often limited in clinical benefit and negatively affect the patient's quality of life, leading to an unmet need for a tolerable therapy.

This study consisted of 40 women who had measurable recurrent ovarian cancer.

The patients received 200 milligrams of Keytruda and 15 milligrams per kilogram of Avastin every three weeks, in addition to a daily dose of 50 milligrams of oral metronomic cyclophosphamide. They received this treatment until there was disease progression, toxic effects or study withdrawal.

Of the 40 enrolled, 39 patients discontinued treatment because of progressive disease and requested treatment break and withdrawal, but all 40 were evaluated for safety and efficacy data.

Measuring objective responses (the proportion of patients who had a complete or partial response to treatment) and progression-free survival (length of time during and after cancer treatment that a patient is alive but the disease does not get worse) were the main goals of the study. Other outcomes included frequency and severity of events, duration of response, overall survival, treatment response and quality of life.

Three participants had complete responses, 16 had partial responses and 19 had stable disease in response to treatment. The objective response rate was 47.5%, clinical benefit was seen in 38 participants and durable response was seen in 10. The median progression-free survival for the entire study population was 10 months.

The patients were given quality-of-life questionnaires at the beginning of the study and then again at three and six months into treatment. During the trial, global and physical functioning scores remained high, with body image, emotional functioning and social functioning all having improved scores.

This combination of Keytruda with Avastin and oral cyclophosphamide gave positive results, as it was well tolerated by patients. The results, according to the study authors, show the novel therapy may be a future treatment option for these patients.

Cardiometabolic Risk Factors May Affect Survival in Postmenopausal Women With Cancer

This study also found that women with higher waist circumferences had a higher risk for cancer-related and all-cause death compared with those with lower waist circumferences. By DARLENE DOBKOWSKI, M.A.

CARDIOMETABOLIC RISK FACTORS, such as waist circumference, high blood pressure, high cholesterol and diabetes, may increase the risk for death in postmenopausal women diagnosed with cancer, according to findings published in *Cancer*.

This increased risk for mortality pertained to death from cancer, from cardiovascular disease and all other causes.

"Although the relevance of coexisting comorbidities, including obesity, hypertension, diabetes and high cholesterol, to cancer risk and cancer outcomes has been well established, the current analyses raise the hypothesis that in patients with cancer, interventions targeting metabolic abnormalities, which include modifiable lifestyle factors, may affect cancer outcomes," the study authors wrote.

Factors that affect cardiometabolic health include elevated triglycerides, increased waist circumference, elevated fasting glucose levels, high blood pressure and low levels of high-density lipoprotein cholesterol, also known as "good" cholesterol. Previous studies have shown that women with metabolic syndrome have an increased risk for several cancers including pancreatic, endometrial, colorectal, gastric, postmenopausal breast, ovarian and non-Hodgkin lymphoma, although data are limited on the relationship between cardiometabolic health and the risk for mortality in postmenopausal women diagnosed with cancer.

In this particular study, researchers analyzed data from 12,076 women (mean age at enrollment, 63.1 years; mean age at cancer diagnosis, 72.1 years) from the Women's Health Initiative, a study sponsored by the National Heart, Lung and Blood Institute to assess prevention strategies for breast and colorectal cancer, heart disease and osteoporosis in postmenopausal women 50 to 79 years old. This particular analysis included postmenopausal women diagnosed with local- or regional-stage colorectal, breast, kidney, endometrial, ovarian, pancreatic, liver or stomach cancer or non-Hodgkin lymphoma.

The study authors focused on several cardiometabolic abnormalities such as hypertension (systolic blood pressure greater than 130 millimetres of mercury, diastolic blood pressure greater than 85 millimetres of mercury), waist circumference (high defined as greater than or equal to 88 centimeters), high cholesterol and diabetes. The outcomes of interest were mortality from cancer, all-cause mortality, mortality from cardiovascular disease and mortality from other causes. Follow-up started at cancer diagnosis for a median of 10 years.

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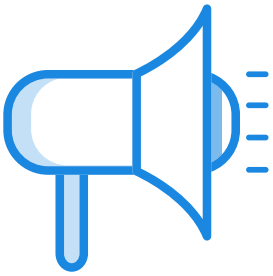
Of the participants in this study, 29% had no cardiometabolic abnormalities, 63% had one or two abnormalities and 8% had three or four abnormalities. During follow-up, 3,607 deaths occurred, of which 42.9% were related to cancer.

Compared with women with no cardiometabolic abnormalities, those with three or four abnormalities had a nearly two-fold increased risk for all-cause mortality. In addition, women with three or four cardiometabolic abnormalities had an estimated four-fold risk for death from cardiovascular disease, 1.37-fold risk for death from cancer and 2.14-fold risk for death due to other causes.

The researchers also assessed the effects of waist circumference on the risk for death in these women. Results from this analysis demonstrated that participants with a higher waist circumference had a greater risk for all-cause death and death related to cancer compared with participants with a smaller waist circumference.

"These findings suggest that interventions targeting these modifiable risk factors could potentially have a clinically meaningful impact on outcomes for cancer survivors," the study authors concluded. "The results also point out a major gap in the survivorship care of patients with cancer and the need for improved efforts by public health systems to improve survival. This hypothesis requires further prospective studies for confirmation."



Actor Scott Foley Offers Hope, Raises Awareness for Women With Ovarian Cancer

In an interview with CURE®, the "Felicity" and "Scandal" actor spoke about his experience as a caregiver to his mother and why women should not just wait for their ovarian cancer to recur. By KRISTIE L. KAHL

AS THE MEDICAL COMMUNITY and its patients wait to see how the COVID-19 pandemic continues to play out, there's something important for women with ovarian cancer to keep in mind: Do not watch and wait for a recurrence to occur.

As part of the Not On My Watch campaign, Scott Foley – best known for his roles on "Felicity," "Scandal" and now "Whiskey Cavalier" – is sharing this message to raise awareness and offer women and their families hope.

In an interview with *CURE®*, Foley discussed his role as a caregiver to his mother when he was 11 and how he hopes to raise awareness of the maintenance therapies now available for women with ovarian cancer.

Q: *CURE®*: Scott, could give us background on how you served as a caregiver for your mother during her journey with ovarian cancer?

A: Foley: My mom (received a diagnosis of) ovarian cancer when I was 11 years old. … A lot of the day-to-day pressures fell on my father, but he was at work to support a family. So, it sort of landed on my shoulders. I was the one who would help Mom with her medications and make sure she got enough rest and help her around the house, doing things and taking care of my younger brothers. Unfortunately, we lost my mom to this disease when I was 15 years old. And that was the impetus for me getting involved with Not On My Watch, talking to the group and hearing about these maintenance therapies and things that they could do. It really struck a chord in me. One of the things that stuck out to me, and still does to this day, about my mom's illness and what we went through was the feeling of helplessness. … You rely so much on your doctors, and they do what they can, but at a certain point (we had to watch and) wait. (My mom) had a round of chemotherapy, and then (we sat) back and waited to see if it worked and hoped that it did, but you just never knew. It's tough sometimes to think about. Maybe if she hadn't (become) sick back then and if she got sick now, we wouldn't have lost her, because of all these maintenance therapies that are now available. So, I feel a certain responsibility, because of what I went through, to help others who may be going through the same thing, who may be thinking, "Wow, OK, we just went through a round of radiation, we just went through a round of chemotherapy, and now we have to watch and wait, see what's going to happen." There are other options that we just didn't have (when my mother was ill).

» **SCOTT FOLEY** believes his mother's outcome would have been different if she got sick today instead of years ago.

Q: Why do you think the message of "don't watch and wait" is even more present now, especially with the COVID-19 pandemic?

A: Not just with COVID-19, but when you're dealing with something as big as ovarian cancer, anything you can do to mitigate the disease, to stop it from spreading, to delay the time between recurrences is

SABELSKAYA / STOCK.ADOBE.COM

important. I think that when you're talking about cancer, you have to prioritize. And it's hard to say that you have to prioritize your health and your wellness and the possibility of not being sick for a long time. You have to get to the hospital and you get your treatments. These maintenance therapies are there, and they're something that you have to take into your own hands. You have to talk to your doctor about it. You can talk on the phone; you don't have to go into the hospital to have these conversations; you can educate yourself about what you can do to hopefully get better.

Q: Can you talk about the Not On My Watch campaign?

A: I'm continuing my work with GSK (GlaxoSmithKline) and Not On My Watch. The reason I'm doing so is because, since my mom passed 30-some years ago, there have been advancements with these therapies, there (are) people who are eligible and who will benefit from them. I certainly see it as a responsibility of mine to get the word out.

Q: What hope do you think women with ovarian cancer have now that we have such advances in treatment options?

A: The only hope there is when it comes to cancer is life. I hope that (these advancements) will save their life, and if not save their life, improve the life that they're now living. It will delay the time between recurrences. When you're talking about someone who is very ill with this disease, you're talking about their life, and you can delay the time between recurrences. (It's worth it) if you can give someone an extra month, six months, a year, 10 years, or (save) a life. There's a whole world of people who are affected by (ovarian cancer), whether it's family members and caregivers, friends, communities; we are not alone on this Earth. We are constantly in contact and in touch. It's important. Lives are important. And that's hopefully what we're trying to do here.

Q: With the campaign, is there a key takeaway that you could offer to patients? And how can they get involved?

A: First, you can share the information about Not On My Watch on social media. The key takeaway is that we just want people to know that it's available. Up to 70% of women who are dealing with ovarian cancer right now don't even know that it's available. They don't know that these maintenance therapies can delay recurrence. And I'm not sure why. … All I hope to do here is to spread awareness. Ask your doctor. Do some research. … If you're going through this and you're watching and waiting, these maintenance therapies are available and you can benefit, you can help your life, can help those in your life. It's all about raising awareness, in my opinion.

> **When you're dealing with something as serious, as life-threatening, as ovarian cancer, giving any amount of hope is important.** — *SCOTT FOLEY*

Q: Why do you think it's also important for caregivers and patients' loved ones to understand these treatment options?

A: I think there's a certain level of frustration and a feeling of helplessness that not only the patients deal with, but also their loved ones and their caregivers. I think opening their eyes and showing them that this is available, raising that awareness, can give people hope. And when you're dealing with something as serious, as life-threatening, as ovarian cancer, giving any amount of hope is important. "Any amount of hope" can sound so strange. But it can help you. It can make you feel better. Maintenance therapies are there. But so is hope, and that's so important.

Q: Do you have advice for caregivers of patients with cancer?

A: The most important advice I could give to any caregiver is (to be confident) knowing that what you're doing makes a difference; (believe) that what you're doing is going to help a person. Just your presence, just being there, just taking the time and showing that you care, and showing that you believe in their recovery, in their treatment, is so important. You know, my mom used to do these visualization exercises at a certain point. She changed her diet. She looked into alternative medications.

She did these breathing exercises where she would visualize herself getting better; she would visualize a breath going into her body surrounding the cancer cells and exhaling them out. Anything to give that person hope is important. And it makes a huge difference in treatment. And I think as a caregiver, just being there, (it's important to) know that you are giving someone hope.

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A New Way to Fight Triple-Negative Breast Cancer Arrives

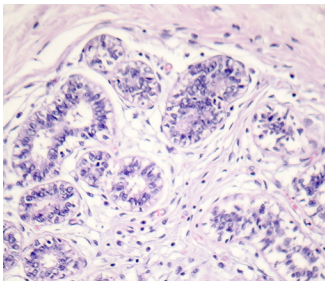
Even as chemotherapy, surgery and radiation remain treatment mainstays, immunotherapy is ready to take the stage. By KRISTIE L. KAHL

DESPITE ACCOUNTING FOR APPROXIMATELY 10% to 15% of breast cancers, triple-negative breast cancer (TNBC) has fewer treatment options compared with other types of invasive breast cancer.

However, there is good news with the advent of immunotherapy in the TNBC armamentarium.

"I think (immunotherapy is) something to look forward to in the future. Something more specific, more targeted, that will actually treat the cancer more effectively and also things that are less aggressive and less toxic," said Dr. Ogori Kalu, a surgeon at Saint Michael's Medical Center in Newark, New Jersey.

As part of its "Speaking Out" video series, *CURE®* spoke with Kalu, who is a board member of the Triple Negative Breast Cancer Foundation, about current standards of care for the disease, why the multidisciplinary approach to care is key and how immunotherapy will play a role in the future.



TNBC treatment can differ depending on the stage at which it is diagnosed.

Q: *CURE®*: How does stage affect the type of treatment a patient will receive for TNBC?

A: Kalu: For (TNBC), irrespective of the stage at diagnosis, one thing for sure is that the woman is going to receive chemotherapy or that chemotherapy will be recommended for that patient. But then, outside chemotherapy, the stage (of the disease) would determine what kind of surgery (she) would have, plus or minus radiation. So, the lower or the earlier the stage — stage 1 and maybe stage 2 — (the more likely it is) the patient could have breast-conserving therapy where they just take out the tumor, and then (the patient) would need radiation. (Compare this with) women who (receive a recommendation) to have their entire breasts removed, which is a mastectomy, plus or minus reconstruction. And then radiation might be an option, as well. So, they (all) would need chemotherapy (for early-stage disease). (There) are different options for surgery, depending on what stage (is) diagnosed. And then radiation is added, depending on what kind of surgery they have and whether they have more advanced disease.

Q: You just went over some options for early-stage TNBC treatment. What are the current standards of care for advanced disease?

A: For this disease, the standard of care is typically to start off with chemotherapy for a woman with advanced disease, which I would (say is) stage 2 onward. Usually, chemotherapy is recommended upfront. Chemotherapy allows the clinician to have an idea of how well the tumor responds to the chemotherapeutic treatment; to get a better idea of (the patient's) overall prognosis, given what is made available to them at the time for treatment; and to determine what further treatment, meaning surgery or radiation, would be needed after the initial chemotherapy.

Q: Are there different standards of care forrecurrent disease?

A: There's no difference in the standard of care, I believe, if there's just a difference in the kind of way the cancer presents itself in the patient. Once a woman has had breast cancer, initially a triple-negative disease, and has been treated, once it comes back or presents itself in a metastatic setting, then there's a host of different options. A medical oncologist knows how to treat that patient, and that all depends on how the patient responded initially to her initial medical treatment and what kind of tumor that she has, which would correspond to which medications that the oncologist will think is appropriate this second round to effectively treat the patient.

Q: With so many treatment options, why is the multidisciplinary approach in TNBC treatment important?

A: The multidisciplinary approach typically includes the medical oncologist, radiation oncologist, internist, dietitian, social worker, plastic reconstructive surgeon and a patient navigator/care coordinator. (It is important that) all these people in the woman's treatment plan (be) on the same page of what the patient needs at the time and how to coordinate (her care) in a timely fashion so that there are no gaps in treatment. Multidisciplinary approaches are also beneficial because you have different perspectives on the »

best way to treat this patient's cancer. You know, not everyone is the same. We can't have cookie-cutter treatment plans for everyone, because different things are going on in a woman's life that could either interfere with what you think is best or need to be taken into consideration for the different treatment plans that you're recommending. It's very important to have different perspectives to get the best treatment option for the patient because she would know what's best and what would work best for her.

Q: What are some of the exciting treatments that are in the pipeline?

A: The most exciting treatments out there for (TNBC) are what we call immunotherapies (for patients with triple-negative breast cancer who are positive for the PD-L1 protein), which are more targeted therapies toward triple-negative disease. This is part of what's going on in the pipeline and going through clinical trials right now, but they seem to all have a common denominator, which is what we call immunotherapy targets that would be specific for these cancer cells. And I think that's the most exciting thing that we are looking forward to seeing come into the mainstream for treatment.

Q: What do you think patients with TNBC have to look forward to when it comes to the treatment landscape?

A: I think they (will) have more options made available to them, which are also less toxic options, because we know that what we're giving now, for some women, is very hard to tolerate. I think that's something to look forward to in the future, something more specific, more targeted, that will actually treat the cancer more effectively, and also things that are less aggressive and less toxic. I'm very hopeful that we will see these treatment options become readily available in the near future.

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Jamie Foxx for Stand Up To Cancer. Photo By G L Askew II

STAND UP TO CANCER

EXACT SCIENCES

We are helping to move mountains for myeloma patients

Moving Mountains for Multiple Myeloma, (MM4MM), is an award-winning collaboration between CURE Media Group and the Multiple Myeloma Research Foundation (MMRF) which raises funds and awareness for myeloma research.

Since its inception in 2016, Moving Mountains for Multiple Myeloma teams have climbed Mt. Kilimanjaro, hiked the Grand Canyon, summited Mount Fuji, trekked the Inca Trail to Machu Picchu, reached Everest Base Camp and conquered Iceland's many landscapes. Our team members have raised over $2.9 million, 100% of which goes directly to the MMRF, which spearheads and funds critical myeloma research. These amazing journeys are captured via blogs, social media posts, and video.

Due to COVID-19 the 2020 program has shifted - all 2020 teams will continue fundraising and training this year and will hike in early 2021.

Patients, caregivers, myeloma loved ones, and others impacted directly by multiple myeloma will take on the Alaskan Kenai Peninsula, summit Mount Washington, explore the terrain of Greenland, and more! They will raise funds for multiple myeloma research and demonstrate that the advancements being made in recent years, led by the MMRF, are helping patients live longer with a higher quality of life than ever before.

To learn more and join a MM4MM team visit:
MovingMountainsForMultipleMyeloma.com

To learn more about the MMRF, visit **TheMMRF.org**

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Machu Picchu Trek
May 1-11, 2021

New 2021 hikes & dates coming soon!
Email **teammanager@themmrf.org** to get on our waitlist!

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