FOR PATIENTS, SURVIVORS & THEIR CAREGIVERS

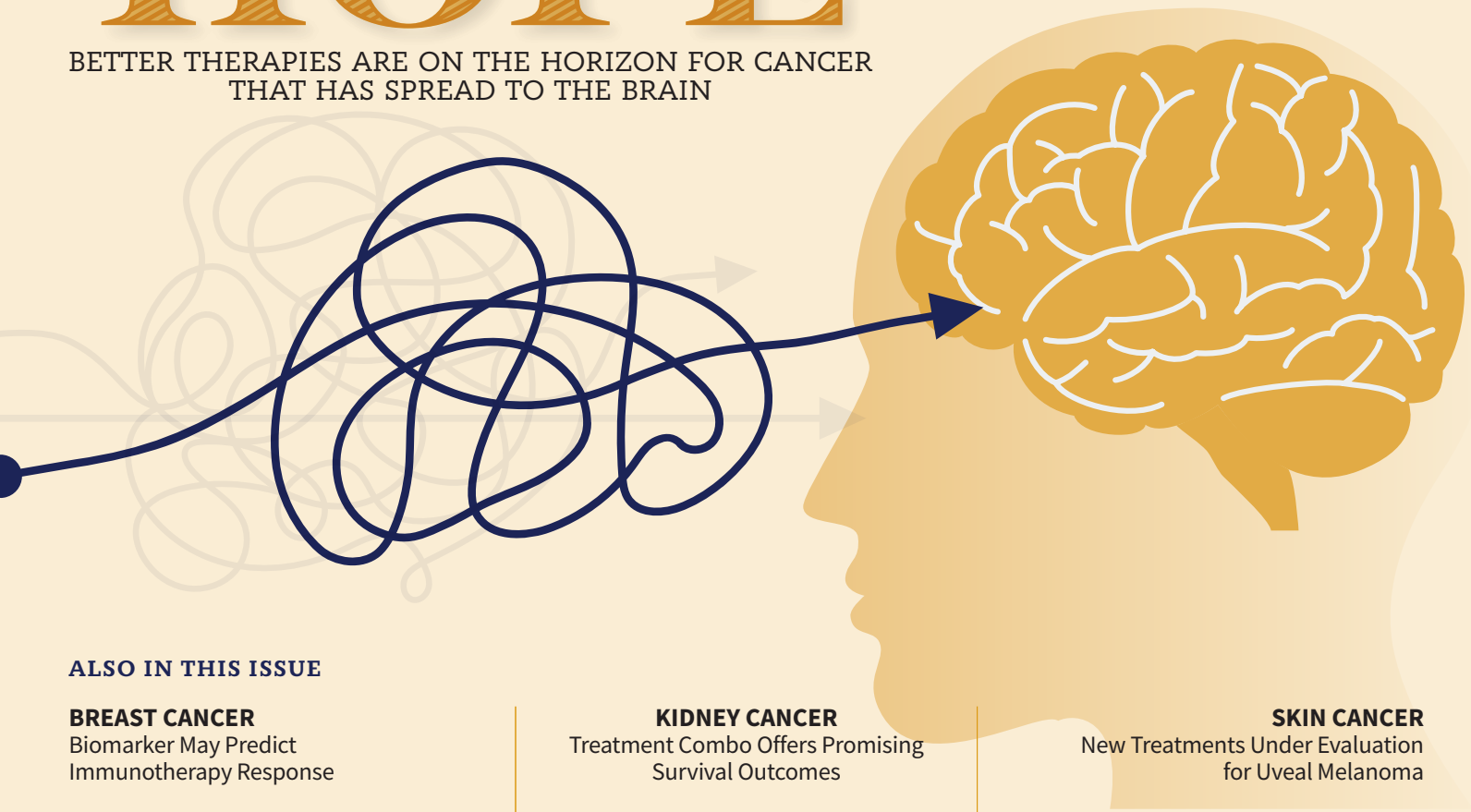
cure®

Cancer Updates, Research & Education®

FALL 2021

LIVING LONGER WITH TREMENDOUS HOPE

BETTER THERAPIES ARE ON THE HORIZON FOR CANCER THAT HAS SPREAD TO THE BRAIN



ALSO IN THIS ISSUE

curetoday.com

KEYTRUDA IS A BREAKTHROUGH IMMUNOTHERAPY.

FOR TODAY

KEYTRUDA is a potential first treatment for **3 out of 4 patients** with advanced non–small cell lung cancer (NSCLC).

KEYTRUDA is also used to treat **more patients** with advanced lung cancer than any other immunotherapy.

FOR THE FUTURE

Ongoing clinical trials are exploring if KEYTRUDA can help treat more patients.

KEYTRUDA may be your first treatment for advanced NSCLC, either in combination with chemotherapy or used alone as a chemotherapy-free option.
Ask your doctor if KEYTRUDA is right for you.

KEYTRUDA is a prescription medicine used to treat a kind of lung cancer called non–small cell lung cancer (NSCLC).

- **KEYTRUDA + CHEMOTHERAPY, NONSQUAMOUS**
  It may be used with the chemotherapy medicines pemetrexed and a platinum as your first treatment when your lung cancer has spread (advanced NSCLC) **and** is a type called "nonsquamous" **and** your tumor does not have an abnormal "EGFR" or "ALK" gene.
- **KEYTRUDA + CHEMOTHERAPY, SQUAMOUS**
  It may be used with the chemotherapy medicines carboplatin and either paclitaxel or paclitaxel protein-bound as your first treatment when your lung cancer has spread (advanced NSCLC), **and** is a type called "squamous."
- **KEYTRUDA USED ALONE, PD-L1 POSITIVE**
  It may be used alone as your first treatment when your lung cancer has not spread outside your chest (stage III) and you cannot have surgery or chemotherapy with radiation, **or** your NSCLC has spread to other areas of your body (advanced NSCLC), **and** your tumor tests positive for "PD-L1" **and** does not have an abnormal "EGFR" or "ALK" gene.
- **KEYTRUDA AFTER CHEMOTHERAPY, PD-L1 POSITIVE**
  It may also be used alone for advanced NSCLC if you have tried chemotherapy that contains platinum and it did not work or is no longer working **and**, your tumor tests positive for "PD-L1" **and** if your tumor has an abnormal "EGFR" or "ALK" gene, you have also received an "EGFR" or "ALK" inhibitor medicine that did not work or is no longer working.

PD-L1 = programmed death ligand 1;
EGFR = epidermal growth factor receptor;
ALK = anaplastic lymphoma kinase.

IMPORTANT SAFETY INFORMATION

KEYTRUDA is a medicine that may treat certain cancers by working with your immune system. KEYTRUDA can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen any time during treatment or even after your treatment has ended.

Call or see your health care provider right away if you develop any signs or symptoms of the following problems or if they get worse. These are not all of the signs and symptoms of immune system problems that can happen with KEYTRUDA:

- **Lung problems:** cough, shortness of breath, or chest pain.
- **Intestinal problems:** diarrhea (loose stools) or more frequent bowel movements than usual; stools that are black, tarry, sticky, or have blood or mucus; or severe stomach-area (abdomen) pain or tenderness.
- **Liver problems:** yellowing of your skin or the whites of your eyes; severe nausea or vomiting; pain on the right side of your stomach area (abdomen); dark urine (tea colored); or bleeding or bruising more easily than normal.
- **Hormone gland problems:** headaches that will not go away or unusual headaches; eye sensitivity to light; eye problems; rapid heartbeat; increased sweating; extreme tiredness; weight gain or weight loss; feeling more hungry or thirsty than usual; urinating more often than usual; hair loss; feeling cold; constipation; your voice gets deeper; dizziness or fainting; changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness.
- **Kidney problems:** decrease in the amount of your urine; blood in your urine; swelling of your ankles; loss of appetite.
- **Skin problems:** rash; itching; skin blistering or peeling; painful sores or ulcers in your mouth or in your nose, throat, or genital area; fever or flu-like symptoms; swollen lymph nodes.
- **Problems can also happen in other organs and tissues.** Signs and symptoms of these problems may include: chest pain; irregular heartbeat; shortness of breath; swelling of ankles; confusion;

Important Safety Information is continued on the next page.

keytruda.com/lung

IMPORTANT SAFETY INFORMATION *(continued)*

sleepiness; memory problems; changes in mood or behavior; stiff neck; balance problems; tingling or numbness of the arms or legs; double vision; blurry vision; sensitivity to light; eye pain; changes in eyesight; persistent or severe muscle pain or weakness; muscle cramps; low red blood cells; bruising.

- **Infusion reactions that can sometimes be severe or life-threatening.** Signs and symptoms of infusion reactions may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, feeling like passing out, fever, and back pain.
- **Rejection of a transplanted organ.** Your health care provider should tell you what signs and symptoms you should report and they will monitor you, depending on the type of organ transplant that you have had.
- **Complications, including graft-versus-host disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic).** These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with KEYTRUDA. Your health care provider will monitor you for these complications.

Getting medical treatment right away may help keep these problems from becoming more serious. Your health care provider will check you for these problems during treatment with KEYTRUDA. They may treat you with corticosteroid or hormone replacement medicines. They may also need to delay or completely stop treatment with KEYTRUDA if you have severe side effects.

Before you receive KEYTRUDA, tell your health care provider if you have immune system problems such as Crohn's disease, ulcerative colitis, or lupus; have had an organ transplant or have had or plan to have a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic); have had radiation treatment in your chest area; have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome.

If you are pregnant or plan to become pregnant, tell your health care provider. KEYTRUDA can harm your unborn baby. If you are able to become pregnant, you will be given a pregnancy test before you start treatment.

Use effective birth control during treatment and for at least 4 months after your final dose of KEYTRUDA. Tell them right away if you think you may be pregnant or you become pregnant during treatment with KEYTRUDA.

Tell your health care provider if you are breastfeeding or plan to breastfeed. It is not known if KEYTRUDA passes into your breast milk. Do not breastfeed during treatment with KEYTRUDA and for 4 months after your final dose of KEYTRUDA.

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

Common side effects of KEYTRUDA when used alone include feeling tired; pain, including pain in muscles, bones or joints and stomach-area (abdominal) pain; decreased appetite; itching; diarrhea; nausea; rash; fever; cough; shortness of breath; and constipation.

Common side effects of KEYTRUDA when given with certain chemotherapy medicines include feeling tired or weak; nausea; constipation; diarrhea; decreased appetite; rash; vomiting; cough; trouble breathing; fever; hair loss; inflammation of the nerves that may cause pain, weakness, and paralysis in the arms and legs; swelling of the lining of the mouth, nose, eyes, throat, intestines, or vagina; mouth sores; headache; weight loss; stomach-area (abdominal) pain; joint and muscle pain; and trouble sleeping.

These are not all the possible side effects of KEYTRUDA. Talk to your health care provider for medical advice about side effects.

Please read the adjacent Important Information About KEYTRUDA and discuss it with your oncologist.

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.

Having trouble paying for your Merck medicine?

Merck may be able to help. www.merckhelps.com

IT'S TRU. KEYTRUDA® (pembrolizumab) Injection 100 mg

MERCK

Important Information About KEYTRUDA® (pembrolizumab) injection 100 mg. Please speak with your healthcare professional regarding KEYTRUDA (pronounced key-true-duh). Only your healthcare professional knows the specifics of your condition and how KEYTRUDA may work with your overall treatment plan. If you have any questions about KEYTRUDA, speak with your healthcare professional. **℞ONLY**

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

KEYTRUDA is a medicine that may treat certain cancers by working with your immune system. KEYTRUDA can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:

Lung problems

- cough
- shortness of breath
- chest pain

Intestinal problems

- diarrhea (loose stools) or more frequent bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdomen) pain or tenderness

Liver problems

- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting
- pain on the right side of your stomach area (abdomen)
- dark urine (tea colored)
- bleeding or bruising more easily than normal

Hormone gland problems

- headaches that will not go away or unusual headaches
- eye sensitivity to light
- eye problems
- rapid heartbeat
- increased sweating
- extreme tiredness
- weight gain or weight loss
- feeling more hungry or thirsty than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive,

Kidney problems

- decrease in your amount of urine
- swelling of your ankles
- blood in your urine
- loss of appetite

Skin problems

- rash
- itching
- skin blistering or peeling
- painful sores or ulcers in your mouth or in your nose, throat, or genital area
- fever or flu-like symptoms
- swollen lymph nodes

Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with KEYTRUDA. Call or see your healthcare provider right away for any new or worsening signs or symptoms, which may include:

- chest pain, irregular heartbeat, shortness of breath, swelling of ankles
- confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- persistent or severe muscle pain or weakness, muscle cramps
- low red blood cells, bruising

Infusion reactions that can sometimes be severe or life-threatening. Signs and symptoms of infusion reactions may include:

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- feeling like passing out
- fever
- back pain

Rejection of a transplanted organ. Your healthcare provider should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.

Complications, including graft-versus-host-disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications can be serious and can lead to death. These

complications may happen if you underwent transplantation either before or after being treated with KEYTRUDA. Your healthcare provider will monitor you for these complications.

Getting medical treatment right away may help keep these problems from becoming more serious. Your healthcare provider will check you for these problems during treatment with KEYTRUDA. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with KEYTRUDA if you have severe side effects.

Before receiving KEYTRUDA, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have received an organ transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have received radiation treatment to your chest area
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. KEYTRUDA can harm your unborn baby.

  Females who are able to become pregnant:

  - Your healthcare provider will give you a pregnancy test before you start treatment with KEYTRUDA.
  - You should use an effective method of birth control during and for at least 4 months after the final dose of KEYTRUDA. Talk to your healthcare provider about birth control methods that you can use during this time.
  - Tell your healthcare provider right away if you think you may be pregnant or if you become pregnant during treatment with KEYTRUDA.
- are breastfeeding or plan to breastfeed. It is not known if KEYTRUDA passes into your breast milk. Do not breastfeed during treatment with KEYTRUDA and for 4 months after your final dose of KEYTRUDA.

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 KEYTRUDA?

- Your healthcare provider will give you KEYTRUDA into your vein through an intravenous (IV) line over 30 minutes.
- In adults, KEYTRUDA is usually given every 3 weeks or 6 weeks depending on the dose of KEYTRUDA that you are receiving.
- In children, KEYTRUDA is usually given every 3 weeks.
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will do blood tests to check you for side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of KEYTRUDA?
KEYTRUDA can cause serious side effects. See "What is the most important information I should know about KEYTRUDA?"

Common side effects of KEYTRUDA when used alone include: feeling tired, pain, including pain in muscles, bones or joints and stomach-area (abdominal) pain, decreased appetite, itching, diarrhea, nausea, rash, fever, cough, shortness of breath, and constipation.

Side effects of KEYTRUDA when used alone that are more common in children than in adults include: fever, vomiting, upper respiratory tract infection, headache, and low levels of white blood cells and red blood cells (anemia).

Common side effects of KEYTRUDA when given with certain chemotherapy medicines include: feeling tired or weak, nausea, constipation, diarrhea, decreased appetite, rash, vomiting, cough, trouble breathing, fever, hair loss, inflammation of the nerves that may cause pain, weakness, and paralysis in the arms and legs, swelling of the lining of the mouth, nose, eyes, throat, intestines, or vagina, mouth sores, headache, weight loss, stomach-area (abdominal) pain, joint and muscle pain, and trouble sleeping.

Common side effects of KEYTRUDA when given with axitinib include: diarrhea, feeling tired or weak, high blood pressure, liver problems, low levels of thyroid hormone, decreased appetite, blisters or rash on the palms of your hands and soles of your feet, nausea, mouth sores or swelling of the lining of the mouth, nose, eyes, throat, intestines, or vagina, hoarseness, rash, cough, and constipation.

These are not all the possible side effects of KEYTRUDA.

Call your healthcare provider 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 KEYTRUDA

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 KEYTRUDA that is written for health professionals.

Based on Medication Guide usmg-mk3475-iv-2107r043 as revised July 2021.

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cure® Contents

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NEWS & INSIGHTS

» **PENNY** dealt with relationship issues while undergoing treatment for ductal carcinoma in situ.

» **CAROL BRICKELL** switched treatments several times as her cancer stopped responding to certain therapies.

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COVER ART: GANG / STOCK.ADOBE.COM; BRICKELL BY JARED REY HERNANDEZ; PENNY BY JANERIS MARTE

GINA HOLLENBECK and her husband, **GREG,** never gave up hope as she underwent treatment for lung cancer that spread to her brain.

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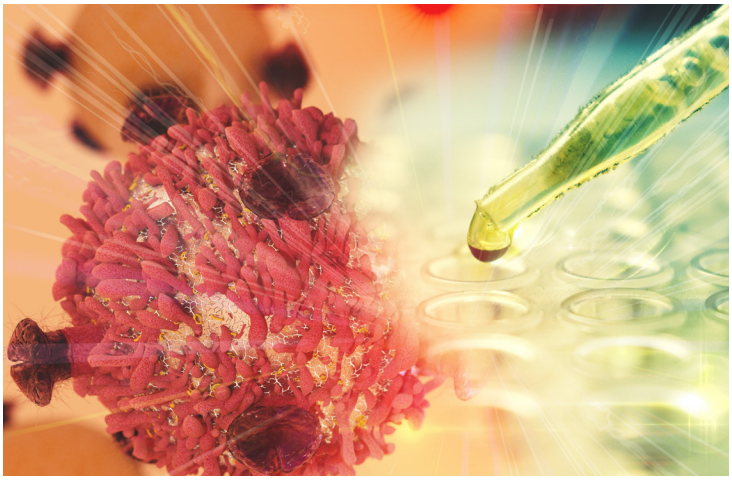
SHANNON LENOIR

chairman's letter

FALL ISSUE • 2021



Hope in Your Back Pocket

WHAT HAPPENS WHEN A PATIENT'S disease stops responding to particular cancer treatments? As disheartening as it may feel, it's no reason to lose hope. Today, different treatments are available along the cancer journey to provide options for patients.

Cancers can become resistant to treatment because patients are living longer and on treatment for years. In addition, cancer can evolve over time, changing how it responds to a particular treatment.

When a patient's disease stops responding, doctors can usually, depending on the specific type of cancer, offer patients several options for a next treatment that will accommodate the patient's needs and goals. Patients can also consider enrolling in clinical trials or obtaining a second opinion. No matter what option a patient selects, having a choice gives patients the opportunity to steer their cancer journey in the direction they want to go.

In this issue of *CURE*®, we speak to two patients with cancer whose disease stopped responding to treatment. One patient with advanced non-small cell lung cancer was responding well to chemotherapy and immunotherapy, but a year later, scans indicated swollen lymph nodes. She took the news in stride because she knew she had a targeted therapy option "in her back pocket," so to speak, that she could use next (it was originally explained and offered as a potential treatment after she received her biomarker test results). Another patient with advanced colorectal cancer that had spread to his lungs decided to get a second opinion about his next best treatment option after he had tried various treatments that were ineffective for the spots on his lungs, which continued to multiply. This patient believes the second opinion saved his life. We also speak with several experts who emphasize the importance of education and knowing your options when cancer stops responding to treatment.

In addition, a feature article examines not only the effects of cancer on a patient's body but also the patient's relationship with their partner. We speak with one couple whose relationship strengthened after the start of her Hodgkin lymphoma journey. We also learned another patient's story

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chairman's letter

involving a relationship that could not withstand the stress of her breast cancer journey. She was able to overcome body image issues and develop more confidence.

You'll also meet two women who were pregnant when they received a diagnosis of cancer. Advances in care have made it more possible for women to be treated for cancer while pregnant, although it's still a very difficult journey. Learn more about these women's different outcomes as well as an ongoing, long-term, observational research study that has been collecting information about the diagnosis and treatment of cancer in pregnant women since 1997 — and continues to inform oncologists about what's possible.

Also in this issue: the benefits of combination therapy for advanced renal cell carcinoma; a nurse who climbed a mountain in Alaska with a group of patients, family members and advocates for multiple myeloma; and how quitting smoking after receiving a lung cancer diagnosis may still add years to your life.

As always, thank you for reading.

MIKE HENNESSY SR.
Chairman and Founder
MJH LIFE SCIENCES™

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Expanding Options for Brain Metastases

AT THE BEGINNING OF my career as an oncologist in the late 1980s, brain metastases were often considered an "end of the road" diagnosis. Yes, there was the rare metastases resection or whole brain radiation regimen that had a durable effect, but for the most part, the drugs used for the rest of the body just did not seem effective in the brain. In this Fall issue of *CURE*®, we explore transformational strategies for brain metastases — a pattern of spread we are seeing more for many tumor types as patients are living longer with metastatic cancer and we more readily use an array of brain imaging technologies when needed.

It has been known that the brain is a protected space, with a highly functional layer called the meninges that controls the passage of nutrients, among other things, and is also designed to keep toxins that might be ingested away from the delicate brain tissue. This protective layer also restricts most drugs used for cancer therapy so that only a small fraction of the concentration is seen in the brain versus the bloodstream.

In the past decade or two, we have learned much more about how drugs enter the brain and the cerebrospinal fluid, which bathes the brain and the spinal cord to which it is connected. In addition, there have been critical advancements in other key components of brain cancer treatment, which we collectively refer to as local treatment, including radiation (especially stereotactic using a focused beam), laser-based therapy and sophisticated neurosurgical techniques that minimize the complications of brain surgery so that many patients are up and walking within a day or two of surgery.

> "These encouraging trends are expected to continue as more clinical trials and innovations are dedicated to brain metastases."

As medical treatments of breast cancer have transitioned to targeted therapies and immunotherapies and as chemotherapy has become more effective, some treatments are able to shrink brain metastases as well as tumors in other parts of the body. Many clinical trials of newer agents now permit the enrollment of patients with brain metastases to expand the number of patients who could potentially benefit and to test whether brain metastases can respond.

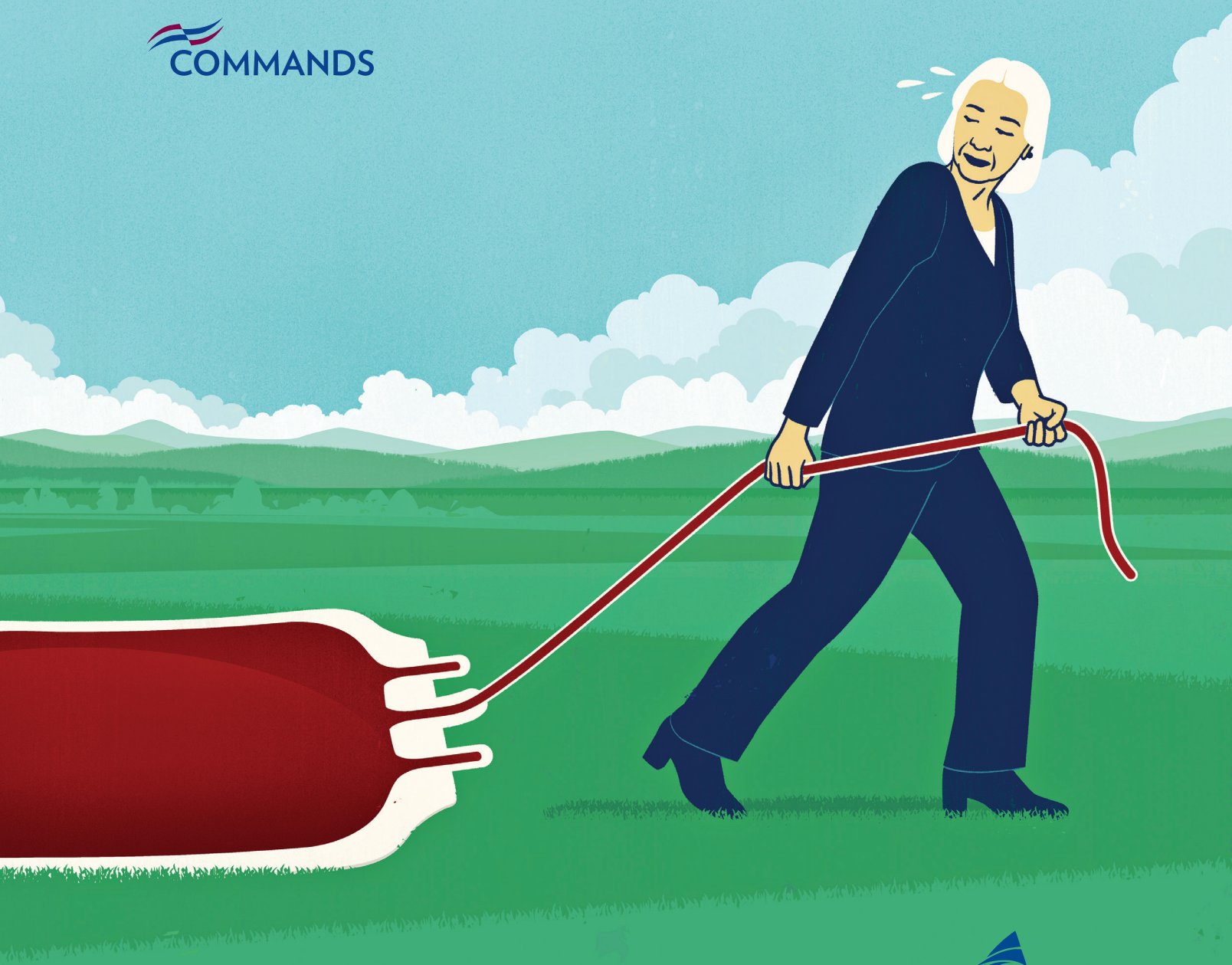
Some of the targeted drugs that are referred to as "small molecules" have been shown to more readily penetrate the blood-brain barrier (a network of tissue and blood vessels that keeps harmful substances from accessing the brain), making them effective for tumors that have metastasized to any organ including the brain. One recent clinical trial testing the HER2 kinase inhibitor Tukysa (tucatinib) for breast cancer showed responses in brain metastases and demonstrated that patients receiving this drug lived longer than with standard treatment. This drug is even showing effectiveness in a particularly aggressive pattern of brain metastasis known as leptomeningeal disease.

Immunotherapy used for metastatic melanoma had been found to be so effective for brain metastases that radiation is often skipped as the initial part of treatment. These encouraging trends are expected to continue as more clinical trials and innovations are dedicated to brain metastases.

ARE BLOOD TRANSFUSIONS HOLDING YOU BACK?

If you've been diagnosed with myelodysplastic syndromes (MDS) with anemia, the phase 3 COMMANDS Trial is a clinical research study investigating a potential treatment option that may help reduce the number of blood cell transfusions you need. To learn more, talk to your doctor and visit **COMMANDSClinicalStudy.com**.

COMMANDS



Celgene

ACE-536-MDS-002_COMMANDS_V1_26FEB2019_US_ENG

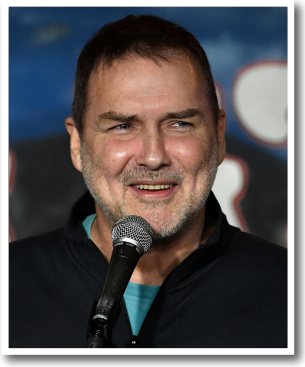
FIRSTLINE

compiled *by* JAMIE CESANEK and DARLENE DOBKOWSKI, M.A.

Norm Macdonald, Comedian and 'Saturday Night Live' Star, Dies From Cancer

COMEDIAN NORM MACDONALD died at age 61 after having cancer for nine years, which he kept private.

Macdonald was known for his work on "Saturday Night Live" as a comedian, actor and writer from 1993 to 1998. He is especially remembered as the anchor on the show's "Weekend Update" segment, which he hosted for three seasons.



NORM MACDONALD

Before "Saturday Night Live," he wrote for the sitcom "Roseanne" and then starred in the film "Dirty Work" and his own sitcom, "The Norm Show." He was well known for his impressions of Burt Reynolds, David Letterman, Larry King and Quentin Tarantino.

Tributes from colleagues in the entertainment community who worked with Macdonald poured out on social media.

"My dear friend Norm Macdonald passed after a brave 10-year (sic) battle. He was one of our most precious gems. An honest and courageous comedy genius. I love him," wrote comedian and actor Jim Carrey on Twitter.

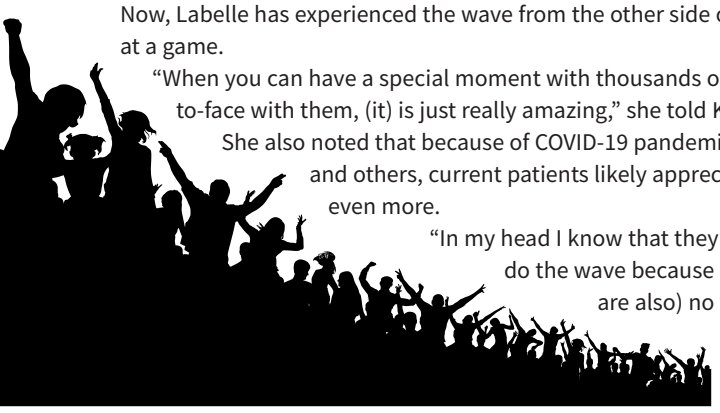
"No one could make you break like Norm Macdonald. Hilarious and unique. F--- cancer," tweeted comedian and former "The Daily Show" host Jon Stewart. "We loved Norm Macdonald," wrote comedian and actor Steve Martin on Twitter. "One of a kind."

Patient With Cancer Experiences 'The Wave' From Both Sides of the Window

MORGAN LABELLE, a B-cell acute lymphoblastic leukemia survivor, received a diagnosis at age 17 and received treatment at the University of Iowa Stead Family Children's Hospital in Iowa City.

During her time there, she witnessed a special tradition that occurred each time the university had a home football game: Fans do "the wave" to pay tribute to the young patients at the hospital who are watching from their windows.

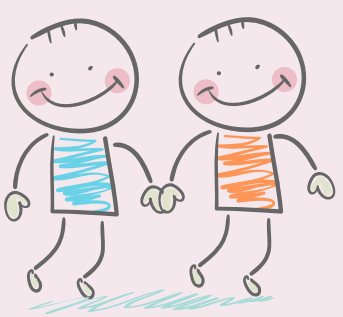
Now, Labelle has experienced the wave from the other side of the window, in person at a game.



"When you can have a special moment with thousands of people but not be face-to-face with them, (it) is just really amazing," she told KCRG of Iowa City, Iowa.

She also noted that because of COVID-19 pandemic restrictions on visitors and others, current patients likely appreciate the tradition even more.

"In my head I know that they're so happy to get to do the wave because during (COVID-19, there are also) no volunteers, no one that can hang out with them like those volunteers," Labelle said.



Preschoolers Reunite After Treatment, When They Became Best Friends

MACK PORTER AND PAYSON ALTICE, both 3 years old, met at Phoenix Children's Hospital while undergoing treatment for cancer — Porter for anaplastic large cell lymphoma and Altice for B-cell acute lymphoblastic leukemia. After Porter finished his treatments, he was adamant about wanting to go back to the "doctor house" to see his best friend.

"Every morning, his first question was 'When can I play with Payson?'" said his mom, Dani Porter, to "TODAY Parents."

The two tiny friends were reunited last month, and their encounter was documented in a video on Twitter in which Porter hands Altice a bouquet of flowers (that he chose himself) before they hug and dance in Altice's kitchen. Both children, who will begin preschool this year, are now in remission.

According to Porter's mom, the two initially met when he saw Altice walking around the hospital with balloons.

"I just knew Mack would like her," Dani Porter said. So she asked Altice's mother, Traci Barrett, if they wanted to join them for a walk (the playroom at the hospital was closed due to the COVID-19 pandemic).

Porter and Altice live 30 minutes away from each other in Arizona and have since gone swimming together.

"It's just a really special relationship," Porter's mom said.

FANS: NOSYREVY / STOCK.ADOBE.COM; WMACDONALD: MICHAEL S. SCHWARTZ / WIREIMAGE / GETTY IMAGES; CHILDREN: AEROKING / STOCK.ADOBE.COM

Sen. Amy Klobuchar Shares Her Recent Breast Cancer Journey

U.S. SENATOR AMY KLOBUCHAR, 61, of Minnesota, discussed her experience with cancer on "Good Morning America," revealing that she received a diagnosis of breast cancer eight months ago after her doctors at Mayo Clinic discovered calcifications during a routine mammogram. A biopsy then revealed she had stage 1A breast cancer.

SEN. AMY KLOBUCHAR

Klobuchar has since been declared cancer-free, following a lumpectomy and radiation.

"Of course, this has been scary at times, since 'cancer' is the word all of us fear, but at this point, my doctors believe that my chances of developing cancer again are no greater than the average person," she wrote in a statement.

The senator also urged people to continue getting screened and not put off routine examinations. "So that's my first practical advice. Get those screenings. Go in, get a mammogram. Get whatever health checkup that you should normally be getting ... and the second is, just be grateful for the people around you."

blink-182's Mark Hoppus Announces He Is Cancer-Free

MARK HOPPUS, blink-182 bassist and vocalist, announced in late September that he has been declared cancer-free. He had previously shared news of his stage 4a diffuse large B-cell lymphoma diagnosis this past summer, later disclosing it was the same type of cancer that his mother had survived.

MARK HOPPUS

"Just saw my oncologist and I'm cancer free!!" he wrote via Instagram.

The performer thanked friends and family for their support, kindness and love. The news came just two weeks after he shared that he had completed his last round of chemotherapy, which he had spoken openly about.

"Let me tell you something that is real, and it absolutely sucks," he said, according to Outsider. "A side effect of the chemotherapy is you get something called 'chemo brain.' And for me, I forget things that I should have just on call. Like people's names, song titles, like anything. I just forget stuff. People will be talking to me, and five minutes later I'll ask them a question, and they'll be like, 'I just told you that five minutes ago.' So, kind of sucks."

However, now cancer-free and finished with chemotherapy, Hoppus explained that he'll just need scans every six months to make sure all is well.

"It'll take me until the end of the year to get back to normal," he wrote. "But today is an amazing day, and I feel so blessed."

Cancer Survivor Walks the Runway, Inspires Others

ERICA CAMPBELL WAS DIAGNOSED with stage 4 Hodgkin lymphoma at age 27, and as a result, underwent months of chemotherapy, surgeries, biopsies and blood transfusions. In September 2013, she had her last chemotherapy treatment, after which she became interested in plus-size modeling.

She has since become a face and a voice for the cancer community.

In 2014, she did her first runway show for cancer awareness, which sparked a love of modeling that prompted her to become further involved. She has walked the runway for DC Fashion Week, New York Fashion Week and various other events, and she has also graced the cover of *Luxe* magazine.

She continues to use her influence to help others.

"It's been a blessing to use my modeling platform to help women and young girls who are facing adversities in their life — and it doesn't have to be cancer," Campbell told WTOP News out of Washington, D.C. "To let them know that you too can overcome this. You're resilient."

She went on to write a book about her experiences titled "I Survived: From Cancer to the Runway," and she works with various cancer advocacy groups to help others who are on this difficult journey.

U.S. Marine Surprises Little Sister for Her Last Cancer Treatment

A U.S. MARINE FROM HALDER, Wisconsin, Dawson Lang, surprised his younger sister, Madisyn, by coming home from boot camp so that he could be with her for her last cancer treatment. Their reunion took place at her softball game, where they hugged on the field as members of the community cheered them on.

Lang had to leave for boot camp while Madisyn was in treatment for leukemia, a diagnosis she received in 2019, and they had not seen each other for six months.

"It was very hard being away from her," Lang told Wausau, Wisconsin's WSAW-TV, "so finally being able to see her and give her a hug was very nice."

KLOBUCHAR: UNITED STATES SENATE; HOPPUS: TOMMASO BODDI/WIREIMAGE/GETTY IMAGES

The Winners of *CURE*®'s Inaugural Poetry Contest

POETRY IS A FORM OF ART that many patients and survivors use to help cope with their cancer diagnosis, including the highs and lows to follow. This year, *CURE*® held its first poetry contest, allowing patients, survivors and caregivers to submit their original poems that relate to their journey with cancer. We received 205 entries, and a committee of judges picked four to be featured in this publication. Below are this year's winners.

An Ode to Dr. Press

By RICHARD STRICKLAND

He'd burst into the room,
With energy he'd zoom—
A full-sized man of power,
Career fully in flower.

A top doc in the nation,
A cause for celebration.
If he can't make you well,
There's nothing left to tell.

Let me give him a plug:
He gave the magic drug.
He broke the evil spell
That was my deathly knell.

He always was on time,
His manner was sublime.
He always was my friend
Right to the very end.

Nobody worked so hard
Blood cancer to discard.
He worked like twenty men.
He reached his peak and then—

Befell the dreaded blight,
And he was forced to fight
Into the cancer ward.
As lived, died by the sword.

A tumor in his brain—
It must have caused such pain!
His doctors tried to treat,
But all led to defeat.

As I was up about,
He was emptied out.
It's easy to opine
He gave his life for mine—

And those of many more
Who had slow death in store.
Our lives had greater length
As he was sapped of strength.

We met before he passed,
So very near the last
Time he could take a swim—
That man was barely him.

He wandered in the lane,
Not sure he knew my name.
But he was kicking on
Till energy was gone.

If life on Earth were fair.
Instead of losing hair,
He'd carry on apace,
And I'd die in his place.

He made me fully free,
He made the cancer flee.
How can I him repay?
I write this ode today.

Dr. Oliver Press (University of Washington [UW], UW Medicine, Fred Hutchinson Cancer Research Center, Seattle Cancer Care Alliance) was a social friend, a fellow lap swimmer whom I got to know at the local public pool. When I was diagnosed with chronic lymphocytic leukemia and it came time to be treated with chemotherapy, "Ollie" was assigned as my oncologist. I have been in full remission for seven years. Dr. Press died from a form of brain cancer in September 2017. I saw him for the last time at the pool in June 2017. I live with the irony that the man who arrested my cancer died of cancer himself.

— RICHARD STRICKLAND

Straighten Your Crown

By AMY SMART

Straighten your crown my dear.
Hold your head up high.
This is no reason to break down and cry.

Straighten your crown my dear.
It will grow back in time.
Making me feel this type of vanity is some sort of crime.

Straighten your crown my dear.
You have tougher battles ahead.
But they don't have to wake up with handfuls in their bed.

Straighten your crown my dear.
You look beautiful just as you are.
But they don't see the inside, the everlasting scar.

Straighten your crown my dear.
Soon you'll look just as you did before.
But they don't have to watch my crown fall to the floor.

They say straighten my crown to be supportive and kind.
And for them I'll pretend that everything is fine.
But that crown on my head is a symbol, a sign.

They don't understand that it's more than just hair.
My soul is tired, but I won't break down.
I'll just silently cry and simply straighten my crown.

In March 2021 I was diagnosed with triple-negative breast cancer at 39 years old. One of the biggest struggles for me has been losing my hair. And although people mean well, I hate being told "it's just hair." I want to help people understand that losing our hair is a big struggle for a lot of cancer patients — that it's not just hair but a sign of the journey we are on, a path we have no control over.

— AMY SMART

The Couch

By DANA STEWART

It is where I sit every week and talk about you.
It's cozy and quiet and yes, quite comfy.
I do the talking and all it holds me up.
It listens.
Back and forth,
Back and forth,
My legs shift as I get uncomfortable.
Words can't describe
That uncomfortable in my mind.
It is you,
Always you.
Lean to the left,
Lean to the right.
My physical presence is in its hands.
You try and speak
STOP!

It's not your turn.
You have done enough.
We are not in this for you.
It is because of you.
You constantly interrupt.
As if we want to hear what you have to say.
Of course you sit here too.
You always tag along,
Making yourself known.
Fidgeting hands
Together
Apart.
My hands do a dance
As they sense you.
It's why I am here.

I have suffered from PTSD (post-traumatic stress disorder) and anxiety for many years, thanks to my breast cancer diagnosis 11 years ago when I was 32 years old. Therapy has been my saving grace, and that weekly seat on the couch in a therapy session is what has helped me work through my fears, anxiety and emotions that cancer dumps on me daily. "The Couch" is my story of therapy, the cancer that keeps trying to creep into those sessions and the couch that holds me up.

— DANA STEWART

Texting You

By DESIREE LEROY

Message alert
the scan showed four spots on my lungs
i have a biopsy tomorrow
he said short of a miracle
it is cancer
i just want to start the meds and be clear
i have a lot of fight in me
i replied, you do

Message alert
it's weird
it blows air into the hospital gown
to keep me warm
i turned it off cause I was getting sweaty, lol
i deflated myself
you sent a picture, your head adorned in a hospital beret,
your face scared but a familiar silly

Message alert
i'm nervous
but ready to know
once they have all the facts
they can attack
i love you

Message alert
i haven't gotten the results back yet
but I promise to let you know ASAP
any pointers when you choreograph a dance?
i kind of scratched out a routine on the plane
i need to cut the song
i also need to work on my toe fall
you sent a picture of the mountains

Message alert
i got the biopsy results back
cancer
i have to keep fighting
also, can I teach my work friends the hip hop routine
you taught me?
i gotta try and break it down
work it, girl

Message alert
i have a scan in a few weeks
to find out if the treatment
is working
until then
just keepin going

Message alert
hey
can you update the gofundme?
it needs to say
stage 4
metastatic breast cancer
it has now spread
to my lungs and brain

--

we met after your brain surgery
we sipped on chamomile tea
melting into your living room
laughing all afternoon
you asked about donating a box of shampoo to
a local shelter

our last dinner
you shared travel plans
filling every month of the year
you could barely eat
but you still said mmm after every bite
tikka masala riches
i was scared
but your flight schedule held us both

our texts, sacred
i will never delete your contact
our exchanges of life, love, fear, and onward
your dance of messages, forever mine

herceptin autocorrected to perspective
and
ibrance autocorrected to vibrance
so I'm taking those with me

strength remains strength
and i refuse to type the word forget

My dear friend, Amanda, was diagnosed with metastatic triple-negative breast cancer at 31, and she is now glowing amongst the stars. I submitted my poem in honor of her vibrance and to share our strengths and fears during the tougher moments. Sometimes she would text me while in the middle of a treatment, and other times, she would text with just two feet out of the doctor's office. At times, I knew how to support her and was truly unafraid, and many times, my heart felt too heavy for positivity. That hard year was captured through our messages, and I want to share her words and my peace, in support of those who have been diagnosed and for those who love someone who has been diagnosed with cancer. If I can help one person feel less alone in their confusion, grief, healing and beyond, then I'm here for it. Legacies of love live on.

— DESIREE LEROY

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GRYT HEALTH

Treating Two Patients, Not One

Doctors are learning that cancer can be treated during pregnancy with relative safety in the second and third trimester. *By* DARLENE DOBKOWSKI, M.A.

PROGRESS HAS BEEN MADE over the past few decades for women who are diagnosed with cancer while pregnant, leading to improved outcomes for both mother and baby. Cancer during pregnancy, however, is still a very difficult journey to navigate.

Much of the progress in this area has been made with the help of long-term observational research studies like the Cancer and Pregnancy Registry, which has been collecting information about the diagnosis and treatment of cancer in pregnant women since 1997.

"Now, after so many years of collecting information on many patients and their children, publishing and lecturing about such follow-up, the recommendation for (pregnancy) termination is less, which is good," said Dr. Elyce H. Cardonick, director of the Cancer and Pregnancy Registry and a maternal-fetal medicine specialist at Cooper University Health Care in Camden, New Jersey, in an interview with *CURE*®. "Oncologists are realizing that cancer can be treated during pregnancy with relative safety in (the) second and third trimester."

PUTTING THE BALL IN ONE'S COURT

Stacey Jamerson, a 36-year-old first-grade teacher from Mansfield, Massachusetts, received a diagnosis of stage 3

EMILIAU / STOCK.ADOBE.COM

alveolar rhabdomyosarcoma — an extremely rare, aggressive cancer more commonly diagnosed in childhood or adolescence — while she was pregnant with her fifth child.

After receiving a cancer diagnosis, pregnant women are given three options: terminate the pregnancy, deliver the baby preterm (before completing 37 weeks of pregnancy) so cancer treatment can begin (increasing the risk for the fetus), or allow the pregnancy to go full term and then provide treatment afterward (increasing the risk for mom).

A few weeks after diagnosis, Jamerson met with her doctor at Dana-Farber Cancer Institute in Boston and, to her surprise, set up a treatment plan and underwent chemotherapy.

"I was about 17 weeks pregnant, I think, when I met with my doctor the first time," Jamerson said. "I Googled a little bit, but I didn't Google a lot, so I just assumed you couldn't have chemotherapy while you're pregnant. It just didn't seem to me like it was even a possibility. So I went into that first appointment assuming that it was going to be kind of a 'We're going to schedule the termination, and then we'll go from there.' But immediately, my doctor at Dana-Farber … set up an appointment that same day with a high-risk (obstetrician) who … was familiar with chemotherapy in pregnancy."

Jamerson added that the specialized obstetrician discussed the different chemotherapy options available and worked with her oncologist to recommend a treatment that would be safe for both the mother and fetus while keeping Jamerson's best interests in mind.

"Immediately (the obstetrician) put it in my court," Jamerson noted. "They said some women don't want to even consider being pregnant while going through chemo, and (they'd) support that. And some women need that bright spot of knowing that they have this baby that they're working for, and if that's what you choose, (they'd) support that as well. … But all along, it was under the understanding that they had no idea how it would turn out."

After Jamerson made her decision, her health care team constantly monitored her, not only because she was undergoing cancer treatment during pregnancy, but also because her pregnancy was already considered high risk; she previously gave birth preterm to two sets of twins. The monitoring included nonstress tests and ultrasounds, among other precautions.

ADJUSTING FOR BABY

Sara Diemer, a 37-year-old adjunct professor of art, youth director at her church and mother of two children (a 3-year-old daughter and 9-year-old stepdaughter) from Washington, Illinois, received a diagnosis of stage 4 inflammatory breast cancer while pregnant with her second biological child. She was also referred to a maternal-fetal specialist to help her through the treatment decision-making process.

"Being pregnant at the time was a big part of the conversation," Diemer said. "But what controlled what we were going to do next was the fact that it was inflammatory breast cancer, which is an incredibly aggressive form of breast cancer. »

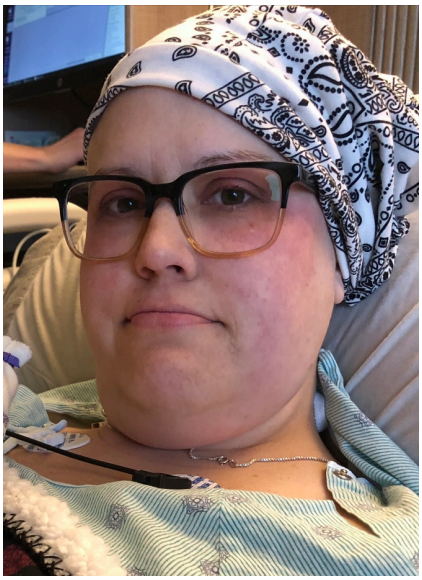
« **SARA DIEMER,** a mother of two children, with her husband, **ERIC.** Her family has been by her side during her cancer journey.

PHOTOS COURTESY OF DIEMER

We couldn't even do necessarily all the normal staging with the best hopes of protecting our baby at the time, so we kind of piecemealed things together with X-rays (and) wearing the heavy lead vests over my stomach area. We did different ultrasounds on specific organs in my body because I couldn't go do an MRI."

Those tests determined that Diemer had stage 4 cancer that had spread to many areas in her liver. A week later, she started chemotherapy, a treatment option that both her oncologist and her maternal-fetal specialist were on board with. After the second treatment, she had some spotting, and she immediately called her maternal-fetal medicine doctor, who asked that she come into the office right away. At that time, everything with Diemer and her baby looked good.

"There are a million reasons that (spotting) could be going on," Diemer said. "(The doctors) were so good with sitting down (and) talking to me about everything. But at that point, we were still really, really hopeful that even though I was getting fairly beat up, the baby was OK."



SARA DIEMER underwent more aggressive cancer treatment after the loss of her daughter.

After Diemer's third round of chemotherapy, she went home and noticed she was spotting again. She ended up going to the emergency department because it was late on a Friday night and she couldn't get hold of her doctors.

"I was at 19 weeks at this point," Diemer said. "If you were at 20 weeks, you're automatically sent to (labor and delivery), and I was one day away from flipping to 20 weeks. I was like, 'Just send me to (labor and delivery), just let me go up there.'"

She ended up sitting in the emergency department's waiting area for hours, which she said was excruciating. Once Diemer was taken to a room, her first examination determined that everything still looked fine, but that changed during the ultrasound. Diemer didn't think at the time to ask her husband to join her for the ultrasound, but now she wishes she had. "I regret it to this day," she said.

During her ultrasound, Diemer noticed that her daughter was in a strange position.

"The tech was really looking around. I said, 'You can't hear a heartbeat, can you?' She said, 'I can't tell you anything.' … I'm piecing it together myself fairly well at this time," Diemer said. "(The tech) leaves the room to go get the doctor, and I have my phone. I texted my husband: 'I don't think there's a heartbeat.'"

Once the doctor came in, he also tried to find a heartbeat. Diemer said she thinks it was difficult for him to deliver the news to her. A few minutes later, he said he couldn't find the baby's heartbeat.

"I was kind of in shock," Diemer said. "I was kind of upset. I was kind of a lot of things at that point."

Her husband then joined her in the room, during which the doctor gave the news to both of them. Once an obstetrician met with the couple, Diemer said she needed to confirm herself via a sonogram that, as the doctor told her, there was no heartbeat.

"We had named her. Her name was Leah," Diemer said. "(When we looked at the sonogram), she was bent over backward. And I'm like, 'I know that's not a position that a baby's in when they're in the womb.' And then there was just clearly no heartbeat. We listened for quite a while. And as absolutely crappy as that was, there's that confirmation I needed so we could make that next step."

AFTERMATH OF TREATMENT

Surgery can be performed at any gestational age, especially nonabdominal surgery, with relative safety for both mom and fetus. Radiation therapy is avoided, if possible, except for brain cancer. Although the effects of chemotherapy have not been studied in a large trial, researchers have observed its effects through case reports. These have shown that commonly used types of chemotherapy, like those used for breast cancer, leukemia and Hodgkin lymphoma, are often tolerated well by babies, whereas newer agents in development are relatively understudied in pregnancy.

"The placenta does its job of metabolizing the agents for the fetus," Cardonick said. "If you wait a good three weeks after most chemotherapy agents until you deliver the fetus, then a couple things happen. The placenta has time to metabolize those drugs before the baby's born, so we don't have to rely on the baby's liver to do it. And that's why you want to avoid a preterm birth — because the baby's preterm liver is not as good at metabolizing any drugs that are left in their system. Secondly, it allows for (the baby's) blood count and mom's blood count to come up."

Cardonick added that researchers have compared the development of babies exposed to chemotherapy with those who have not been exposed, and there is no significant difference between the two groups; however, the difference is more pronounced when babies exposed to chemotherapy are born preterm.

Although doctors know more now about the potential effects of different treatments on a fetus, the prognosis is also based on how sick the mom is.

"If there's widespread disease, think about how they have to maintain their own health and then support a pregnancy," Cardonick said. "I don't think that happens, honestly, in stage 1 and early cancers. … There are reports of losses of babies more so in acute leukemia because the women can tend to be so sick, and it's a bloodborne cancer as opposed to a solid cancer limited to the breast."

Jamerson said she underwent treatments for about a year and is now cancer free. She said her pregnancy went smoothly during cancer treatment and through delivery. Her daughter is now 4 years old.

"She is amazing," Jamerson said. "Medically, she's been fine. She's still followed by the cardiologists, who check her blood every now and then, but nothing has ever come up. She received speech therapy early on (for what) we thought was delayed speech, and she ended up graduating from that. This past December, she was diagnosed with (a mild case of) cerebral palsy. … After looking at the MRI, (doctors) determined that it was probably (caused by) a stroke in utero, which their best guess was maybe (from) one of the chemos."

Jamerson noted that her doctors suspected the stroke was associated with doxorubicin, although they could not prove that. "It was one of the risks we knew could happen, and it was one we were willing to take," she added.

Diemer continued cancer treatment after she got her white blood cell count back up, during which the plan switched from chemotherapy to more targeted treatment.

"(Our doctor) came in and said, 'We have been focused on you, and we have been focused on baby. It's been a dual focus,'" Diemer said. "And he's like, 'I hate how this wound up, but when you leave here, your focus is on you and you alone. It's time to switch gears. I'm not saying it's easy, but you have to focus on you because now this is about your life.' … And I think it was perfect advice."

Diemer said she still experiences some side effects from her cancer treatment, like neuropathy, adding that her nurse navigator made an interesting analogy about the journey.

"It's a chess game," Diemer said. "When cancer does something right, then you do something. (My nurse navigator) said, 'We got plenty of moves left.' There's no checkmate going on right now. It's just what's the next smart move."

> It is horrifically hard and very difficult, but it's not the end. … (But) you have to feel like you can do it in order to do it.
>
> — STACEY JAMERSON

LOOKING FORWARD

Cardonick noted that oncologists are treating cancers sooner, which may allow a pregnant woman to have a better prognosis. In addition, pregnancy may prompt a woman to see a doctor about signs or symptoms that she might have otherwise ignored.

"The odd thing about it — and I would choose it to be different, a thousand times over — is that if I hadn't been pregnant, I don't think I would have really had the impetus to go have a doctor check my breast out the way I did," Diemer said. "Still, it would have been weird, and they would have (said), 'Sara, you should probably go have someone look at that.' But I'm not sure that I would have felt the same urgency. In so many ways, I think her little life helped save mine. And there's a part of me that's just so grateful that I'm still here for my two other kids and my husband."

Cardonick advised pregnant women with cancer to ask their oncologist how they would be treated if they weren't pregnant.

"The way pregnant women do well is if they're treated similarly to nonpregnant women as much as possible," Cardonick said. "To give someone a lower dose or leave out one of the agents of a regimen just because someone's pregnant is not going to serve the pregnant patient well."

Cardonick noted that patients should still remind oncologists that they're treating both mom and fetus.

"A patient told me that she felt comfortable when her oncologist said, 'I realize I'm treating two patients, not one,'" she said, adding that it made her patient "feel much better, much more secure in the treatment she was getting, knowing that they were looking out for the fetus too."

Jamerson offered some helpful advice to pregnant women who receive a diagnosis of cancer.

"It's not the end," she said. "I went into it thinking that cancer and a baby were totally incompatible. … It is horrifically hard and very difficult, but it's not the end. … (But) you have to feel like you can do it in order to do it.

"We were given the statistics of a 30% to 50% chance of living with the change in (treatment) protocol. I remember thinking, 'Those odds aren't that great, but why can't I be one of those 30% or one of those 50%?' You have to go into it positive (and) ask the questions you need." C

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- **Lung problems:** new or worsening cough; shortness of breath; chest pain
- **Intestinal problems:** diarrhea (loose stools) or more frequent bowel movements than usual; stools that are black, tarry, sticky, or have blood or mucus; severe stomach-area (abdominal) pain or tenderness
- **Liver problems:** yellowing of your skin or the whites of your eyes; severe nausea or vomiting; pain on the right side of your stomach area (abdomen); dark urine (tea colored); bleeding or bruising more easily than normal
- **Hormone gland problems:** headaches that will not go away or unusual headaches; eye sensitivity to light; eye problems; rapid heartbeat; increased sweating; extreme tiredness; weight gain or weight loss; feeling more hungry or thirsty than usual; urinating more often than usual; hair loss; feeling cold; constipation; your voice gets deeper; dizziness or fainting; changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness
- **Kidney problems:** decrease in the amount of urine; blood in your urine; swelling in your ankles; loss of appetite
- **Skin problems:** rash; itching; skin blistering or peeling; painful sores or ulcers in mouth or nose, throat, or genital area
- **Eye problems:** blurry vision, double vision, or other vision problems; eye pain or redness

Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with OPDIVO and YERVOY. Call or see your healthcare provider right away for any new or worsening signs or symptoms, which may include:

- Chest pain; irregular heartbeat; shortness of breath; swelling of ankles
- Confusion; sleepiness; memory problems; changes in mood or behavior; stiff neck; balance problems; tingling or numbness of the arms or legs
- Double vision; blurry vision; sensitivity to light; eye pain; changes in eye sight
- Persistent or severe muscle pain or weakness; muscle cramps
- Low red blood cells; bruising

Getting medical help right away may help keep these problems from becoming more serious. Your healthcare team will check you for these problems during treatment and may treat you with corticosteroid or hormone replacement medicines. Your healthcare team may also need to delay or completely stop your treatment if you have severe side effects.

What should I tell my healthcare provider before receiving OPDIVO and YERVOY? Before you receive OPDIVO and YERVOY, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have received an organ transplant

- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have received radiation treatment to your chest area in the past and have received other medicines that are like OPDIVO
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. OPDIVO and YERVOY can harm your unborn baby
- are breastfeeding or plan to breastfeed. It is not known if OPDIVO or YERVOY passes into your breast milk. Do not breastfeed during treatment with OPDIVO or YERVOY and for 5 months after the last dose of OPDIVO or YERVOY

Females who are able to become pregnant: Your healthcare provider should do a pregnancy test before you start receiving OPDIVO or YERVOY.

- You should use an effective method of birth control during your treatment and for at least 5 months after your last dose of OPDIVO or YERVOY. Talk to your healthcare provider about birth control methods that you can use during this time.
- Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment with OPDIVO or YERVOY. You or your healthcare provider should contact Bristol Myers Squibb at 1-844-593-7869 as soon as you become aware of the pregnancy.

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

Know the medicines you take. Keep a list of them to show your healthcare providers and pharmacist when you get a new medicine.

What are the possible side effects of OPDIVO and YERVOY?

OPDIVO and YERVOY can cause serious side effects, including:

- **See "What is the most important information I should know about OPDIVO + YERVOY?"**
- **Severe infusion reactions.** Tell your healthcare team or nurse right away if you get these symptoms during an infusion of OPDIVO or YERVOY: chills or shaking; itching or rash; flushing; shortness of breath or wheezing; dizziness; feel like passing out; fever; back or neck pain
- **Complications, including graft-versus-host disease (GVHD), of bone marrow (stem cell) transplant that uses donor stem cells (allogeneic).** These complications can be severe and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with OPDIVO or YERVOY. Your healthcare provider will monitor you for these complications.

The most common side effects of OPDIVO when used in combination with YERVOY include: feeling tired; diarrhea; rash; itching; nausea; pain in muscles, bones, and joints; fever; cough; decreased appetite; vomiting; stomach-area (abdominal) pain; shortness of breath; upper respiratory tract infection; headache; low thyroid hormone levels (hypothyroidism); decreased weight; and dizziness.

These are not all the possible side effects of OPDIVO and YERVOY. Call your doctor for medical advice about side effects.

You are encouraged to report side effects of prescription drugs to the FDA. Call 1-800-FDA-1088.

OPDIVO (10 mg/mL) and YERVOY (5 mg/mL) are injections for intravenous (IV) use.

This is a brief summary of the most important information about OPDIVO and YERVOY. For more information, talk with your healthcare providers, call 1-855-673-4861, or go to www.OPDIVO.com.

Bristol Myers Squibb™

LEARN MORE ONLINE
SCAN the QR code for a collection of content on breast cancer.

Researchers Identify Biomarker to Predict Immunotherapy Response

Clinical tests for MHC-II expression potentially offer a reliable way to discern who needs this treatment and who doesn't. By JAMIE CESANEK

THE BIOMARKER MHC-II, which was previously shown to be a predictor of immunotherapy responses in patients with melanoma, could also prove useful for patients with breast cancer. In a recent study published in *Clinical Cancer Research*, MHC-II showed potential as a predictor of response for two types of breast cancer: early-stage, triple-negative breast cancer (TNBC) and high-risk, estrogen-receptor (ER)-positive breast cancer.

"With these newer therapies, because of the potential for side effects and the high costs associated with the drugs, (the goal) is to really try to personalize medicine and care for patients," said Justin Balko, who holds a doctorate in pharmacy, in an interview with *CURE*®.

« Identifying which patients can benefit from certain drugs can open many doors in breast cancer research.

SCIEPRO / STOCK.ADOBE.COM

Balko, an assistant professor of medicine and pathology, microbiology and immunology at Vanderbilt University Medical Center in Nashville, conceived and designed the study.

"When we started years ago in melanoma, we were (asking), 'What are some markers that might help us decide whether or not a patient (is) likely to get a benefit from these immunotherapy drugs?' And we've learned a lot over the years. What we've essentially found (is) ... this one marker, (which) we can very easily test (for) in cancer cells by ... a pathology test or immunohistochemistry, (gives) us a pretty good idea on the likelihood of whether ... that patient would respond."

This research that began in melanoma is now being applied to breast cancer in anticipation of future use of the immunotherapy drugs awaiting approval from the Food and Drug Administration. If researchers can identify which patients will respond to immunotherapies, breast cancer research as a whole will benefit because future clinical trials can be tailored specifically to patients who will benefit from certain drugs.

"The most important takeaway, I think, is that these are preliminary results — we haven't validated them or (had) what we call a prospective, randomized phase 3 trial," said Balko. "But they are very encouraging because what we found is that from big trials, only about 15% of patients that are treated with these drugs actually need the drug and/or benefit from the drugs."

For this study, researchers analyzed three groups with breast

cancer: patients with nonimmunotherapy-treated breast cancer, patients with TNBC treated with Imfinzi (durvalumab) and standard chemotherapy, and patients with HER2-negative breast cancer treated with standard chemotherapy alone or with Keytruda (pembrolizumab).

They observed that MHC-II was expressed in a subgroup of TNBC and ER-positive breast cancers.

The results are promising — and much needed in the field of breast cancer research because medical-care costs continue to rise. "(Immunotherapies are) very powerful drugs, and they've helped many, many patients," Balko said.

"But the problem is that because they're immune mediated, a small percentage of patients can have what's called immune-related adverse events.

"And those, while they're generally rare, can be significant. A big part of our laboratory's research is trying to understand why these immune-related adverse events occur. They can (affect) any organ system — patients can (end up with) Type 1 diabetes and require insulin for the rest of their lives after being treated with these drugs. Again, this is very rare, but they're significant toxicities that the patient might have to live with for the rest of their life."

Clinical tests for MHC-II expression could identify patients with breast cancer who don't need immunotherapy to prevent possible treatment complications and additional costs. The researchers also noted that MHC-II has the potential to be a pan-cancer biomarker for anti-PD-1 or anti-PD-L1 immunotherapies because its clinical relevance has been demonstrated with melanoma, Hodgkin lymphoma and breast cancer.

In terms of next steps, Balko noted the need for "a very large phase 3 trial" to validate their findings in breast cancer.

Survival May Be Possible Even With Small Amounts of Disease After Treatment

Detectable amounts of minimal residual disease after treatment does not mean that all hope is lost for survival without disease progression. *By* DARLENE DOBKOWSKI, M.A.

PATIENTS WITH CHRONIC lymphocytic leukemia (CLL) who have a very small number of cancer cells left after Imbruvica (ibrutinib)-based therapy may still have prolonged survival without cancer progression.

Minimal residual disease (MRD), according to the National Cancer Institute, describes a small number of cancer cells that remain during or after treatment and is assessed using highly sensitive lab methods that can find one cancer cell among a million normal cells. MRD testing, which is mostly used for blood cancers, can be used to plan treatment, assess how a treatment is working, determine whether cancer has returned or make a prognosis.

"We now know … that even if (MRD) is detectable, it does not appear to be as concerning for patient clinical outcomes to therapy as if it would be in the setting of receiving (chemoimmunotherapy)," Dr. Neil E. Kay, a consultant and professor of medicine at Mayo Clinic in Rochester, Minnesota, told *CURE*®. "In addition, we can now use the levels of (MRD) to assist us in predicting which patients will have better outcomes."

Studying MRD in CLL is not an entirely new focus in research.

"The detection of residual but measurable CLL disease, designated traditionally as detection of minimal residual disease, has been the subject of studies in CLL for many years," Kay said. "This is because we want to know if there (are) any remaining CLL cells after a certain time on therapy where we cannot detect CLL by routine measures such as physical exam and imaging. This can be done in that situation by monitoring for MRD in patients' blood."

Kay added that there are some existing beliefs about minimal residual disease.

"It is thought … that if CLL patients are negative for (minimal) residual disease (called undetectable MRD) by sensitive laboratory techniques like flow cytometry, they will do better than if there is obvious residual disease by usual clinical assessment," he said.

In the trial published in *Blood* by Kay and his team, patients treated indefinitely with Imbruvica and six cycles of Rituxan (rituximab) had a longer progression-free survival (the time during and after treatment when a patient lives with cancer without worsening) compared with those treated with six cycles of chemo-immunotherapy, particularly if they had undetectable MRD periodically up to 36 months.

They also found that patients treated with Imbruvica and Rituxan who had detectable MRD did not have significantly worse progression-free survival versus those with undetectable MRD. In addition, patients with lower levels of MRD had longer progression-free survival versus those with higher levels of MRD.

"The use of sequential testing of MRD for patients treated with (Imbruvica and Rituxan) was of value in predicting clinical outcomes in two ways," Kay said. "For patients with detectable MRD, they did not have a worse progression rate than those with undetectable MRD. Also, we found that patients with a very low but still detectable MRD level had a longer progression-free status than those that were at higher MRD levels. These are new findings for the value of MRD … in previously untreated CLL patients."

Although this trial provided some insight into MRD, more answers are needed, Kay said.

"The additional questions that remain are the following: Are there better ways to measure MRD?" he asked. "What is the best timing for testing MRD in treated patients? Can you use MRD levels to decide on stopping a specific therapy, or can you use MRD levels to determine if a patient's clinical response is fading and will now need additional treatments?"

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CLL=chronic lymphocytic leukemia; SLL=small lymphocytic lymphoma.

Select Safety Information

CALQUENCE is a prescription oral treatment for adults with chronic lymphocytic leukemia or small lymphocytic lymphoma. May cause serious side effects including: serious infections, bleeding problems, decrease in blood cell count, new cancers, and heart rhythm problems. Some may lead to death. Tell your doctor if you experience infections such as flu-like symptoms; unexpected bleeding such as blood in your stool or urine; or heart rhythm problems such as fast or irregular heartbeat. Use sun protection when outside.

If you cannot afford your medication, AstraZeneca may be able to help. Visit AstraZeneca-us.com to find out how.

Please see Brief Summary of Prescribing Information on adjacent pages.

CALQUENCE® (acalabrutinib) 100 mg capsules

PATIENT INFORMATION
CALQUENCE® (KAL-kwens) (acalabrutinib) capsules

CALQUENCE®
(acalabrutinib) 100 mg capsules

What is CALQUENCE?

CALQUENCE is a prescription medicine used to treat adults with:

- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

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

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

- have had recent surgery or plan to have surgery. Your healthcare provider may stop CALQUENCE for any planned medical, surgical, or dental procedure.
- have bleeding problems.
- have or had heart rhythm problems.
- have an infection.
- have or had liver problems, including hepatitis B virus (HBV) infection.
- are pregnant or plan to become pregnant. CALQUENCE may harm your unborn baby and problems during childbirth (dystocia).
  - If you are able to become pregnant, your healthcare provider may do a pregnancy test before you start treatment with CALQUENCE
  - Females who are able to become pregnant should use effective birth control (contraception) during treatment with CALQUENCE and for at least 1 week after the last dose of CALQUENCE.
- are breastfeeding or plan to breastfeed. It is not known if CALQUENCE passes into your breast milk. Do not breastfeed during treatment with CALQUENCE and for at least 2 weeks after your final dose of CALQUENCE.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking CALQUENCE with certain other medications may affect how CALQUENCE works and can cause side effects. Especially tell your healthcare provider if you take a blood thinner medicine.

How should I take CALQUENCE?

- Take CALQUENCE exactly as your healthcare provider tells you to take it.
- Do not change your dose or stop taking CALQUENCE unless your healthcare provider tells you to.
- Your healthcare provider may tell you to decrease your dose, temporarily stop, or completely stop taking CALQUENCE if you develop certain side effects.
- Take CALQUENCE 2 times a day (about 12 hours apart).

(continued)

- Take CALQUENCE with or without food.
- Swallow CALQUENCE capsules whole with a glass of water. Do not open, break, or chew capsules.
- If you need to take an antacid medicine, take it either 2 hours before or 2 hours after you take CALQUENCE.
- If you need to take certain other medicines called acid reducers (H-2 receptor blockers), take CALQUENCE 2 hours before the acid reducer medicine.
- If you miss a dose of CALQUENCE, take it as soon as you remember. If it is more than 3 hours past your usual dosing time, skip the missed dose and take your next dose of CALQUENCE at your regularly scheduled time. Do not take an extra dose to make up for a missed dose.

What are the possible side effects of CALQUENCE?

CALQUENCE may cause serious side effects, including:

- **Serious infections** can happen during treatment with CALQUENCE and may lead to death. Your healthcare provider may prescribe certain medicines if you have an increased risk of getting infections. Tell your healthcare provider right away if you have any signs or symptoms of an infection, including fever, chills, or flu-like symptoms.
- **Bleeding problems (hemorrhage)** can happen during treatment with CALQUENCE and can be serious and may lead to death. Your risk of bleeding may increase if you are also taking a blood thinner medicine. Tell your healthcare provider if you have any signs or symptoms of bleeding, including:
  - blood in your stools or black stools (looks like tar)
  - pink or brown urine
  - unexpected bleeding, or bleeding that is severe or you cannot control
  - vomit blood or vomit that looks like coffee grounds
  - cough up blood or blood clots
  - dizziness
  - weakness
  - confusion
  - changes in your speech
  - headache that lasts a long time
  - bruising or red or purple skin marks
- **Decrease in blood cell counts.** Decreased blood counts (white blood cells, platelets, and red blood cells) are common with CALQUENCE, but can also be severe. Your healthcare provider should do blood tests to check your blood counts regularly during treatment with CALQUENCE.

(continued)

- **Second primary cancers.** New cancers have happened in people during treatment with CALQUENCE, including cancers of the skin or other organs. Your healthcare provider will check you for skin cancers during treatment with CALQUENCE. Use sun protection when you are outside in sunlight.
- **Heart rhythm problems (atrial fibrillation and atrial flutter)** have happened in people treated with CALQUENCE. Tell your healthcare provider if you have any of the following signs or symptoms:
  - fast or irregular heartbeat
  - dizziness
  - feeling faint
  - chest discomfort
  - shortness of breath

The most common side effects of CALQUENCE include:

- headache
- diarrhea
- muscle and joint pain
- upper respiratory tract infection
- bruising

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

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store CALQUENCE?

- Store CALQUENCE at room temperature between 68°F to 77°F (20°C to 25°C).

Keep CALQUENCE and all medicines out of the reach of children.

General information about the safe and effective use of CALQUENCE.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use CALQUENCE for a condition for which it was not prescribed. Do not give CALQUENCE to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for more information about CALQUENCE that is written for health professionals.

What are the ingredients in CALQUENCE?

Active ingredient: acalabrutinib

Inactive ingredients: silicified microcrystalline cellulose, pregelatinized starch, magnesium stearate, and sodium starch glycolate.

Capsule shell contains: gelatin, titanium dioxide, yellow iron oxide, FD&C Blue 2, and black ink.

AstraZeneca

For more information, go to www.CALQUENCE.com or call 1-800-236-9933.
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US-34063 11/19

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 11/2019 US-34063 11/19

Never Too Late: Smoking Cessation Provides 'Huge' Benefit After Diagnosis

Patients who quit could live almost two years longer — and without disease recurrence — than those who continue to smoke. *By* DARLENE DOBKOWSKI, M.A.

ANDREY POPOV / STOCK.ADOBE.COM

QUITTING SMOKING AFTER receiving a diagnosis of early-stage non-small cell lung cancer may still add years to a patient's life.

In a study published in the *Annals of Internal Medicine*, researchers reported improved overall survival (time from diagnosis when a patient is still alive) and progression-free survival (time during and after cancer treatment that a patient lives with the disease without worsening) over an average follow-up of seven years.

"We found that patients who (smoked and developed) lung cancer could significantly benefit from quitting smoking even after they are diagnosed with cancer," lead study author Dr. Mahdi Sheikh, a scientist at the World Health Organization's International Agency for Research on Cancer in Lyon, France, said in an interview with *CURE*®. "These patients, on average, could live almost two years longer and without (recurrence of disease) than patients who did not quit smoking. I would say (a two-year) improvement in the survival time is a huge effect."

Cigarette smoking is a major risk factor for non-small cell lung cancer, a subtype that makes up approximately 80% to 85% of all lung cancer cases, according to the American Cancer Society. In fact, Sheikh noted that at least 80% of patients with non-small cell lung cancer have a history of smoking cigarettes and that many are current smokers when they receive the diagnosis.

"When we look at the statistics of patients with lung cancer, we see that almost 50% of patients (smoke) at the time of (receiving a) cancer diagnosis," Sheikh said. "If we can convince this 50% to quit smoking, the ultimate effects on the global burden of lung cancer could be massive."

To assess the significance of smoking cessation on survival and mortality, researchers analyzed data from 517 current smokers with early-stage non-small cell lung cancer (stages 1A to 3A). Data from these patients were collected before they received any cancer treatment. For this study, current smokers were defined as those who smoked at least one cigarette per day for more than one year at the time of diagnosis. Patients were followed up with each year for an average of seven years to determine tumor progression, vital status, therapeutic procedures received, and recurrence or metastasis after diagnosis.

Of the patients in the study, 42.5% quit smoking after receiving a diagnosis of non-small cell lung cancer and 57.4% continued smoking. During follow-up, 63.2% of patients died from any cause, with 52.8% of them reported to have died from cancer. Tumor progression, which included local recurrence or metastasis, was recorded in 33.7% of patients. »

Patients who quit smoking had a longer overall survival time than those who continued smoking (6.6 years versus 4.8 years), an improved five-year overall survival rate (60.6% versus 48.6%) and an improved progression-free survival rate (54.4% versus 43.8%).

Researchers also performed an analysis for which they adjusted the data for risk factors and other variables. Smoking cessation continued to be associated with a lower risk for cancer-specific mortality, all-cause mortality and disease progression.

The beneficial effects of smoking cessation were comparable in patients who were mild-to-moderate and heavy smokers and in those with earlier- and later-stage cancer.

Sheikh noted that these survival benefits may help squash the misconception that it's too late for smokers to quit after receiving a lung cancer diagnosis.

"Unfortunately, patients at the time of cancer diagnosis may feel fatalistic," he said. "They might feel it is too late now, (so) there is no point of quitting smoking. However, this study shows that even after being diagnosed with cancer, it is still very useful to stop smoking. The main message we want to tell (patients is) that it is never (too) late. Even if you get cancer, you can benefit a lot from quitting smoking, so (patients) shouldn't lose hope."

Sheikh added that "we encourage (patients) to quit smoking after diagnosis — the earlier, the better," and that patients should always be "encouraged and supported by their physicians and the health care system to quit smoking."

In fact, quitting smoking is "as necessary as the treatments," he said. "The effect that we saw is comparable to the emerging and new therapeutics for lung cancer that are being investigated, which could cost thousands of dollars and might not be accessible for many patients. But (quitting smoking) is potentially feasible for all patients and is free."

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Keytruda-Lenvima Combo Offers Promising Survival Outcomes

This frontline duo is an effective treatment, with life-prolonging benefits and side effects that can be managed when patients are monitored closely. *By* DARLENE DOBKOWSKI, M.A.

THE FOOD AND DRUG ADMINISTRATION (FDA) approved Keytruda (pembrolizumab) plus Lenvima (lenvatinib) in August for the frontline treatment of adults with advanced renal cell carcinoma, adding it to the list of three other recommended first-line options: Yervoy (ipilimumab) plus Opdivo (nivolumab), Cabometyx (cabozantinib) plus Opdivo, and Keytruda plus Inlyta (axitinib).

"(Keytruda plus Lenvima) is another option," Dr. Toni K. Choueiri, director of the Lank Center for Genitourinary Oncology at Dana-Farber Cancer Institute in Boston, told *CURE*®. "It did have the longest (progression-free survival) and highest response rate and complete response rates ... compared to other combinations, though not through a direct head-to-head comparison."

"Those are the four choices now," said Dr. Andrew J. Armstrong, a professor of medicine, surgery, pharmacology and cancer biology at Duke University School of Medicine in Durham, North Carolina, in an interview with *CURE*®. "We never thought we'd have four choices."

Choueiri said this recent FDA approval "is an example, yet again, of combination therapies in advanced (renal cell carcinoma) being the rule, not the exception."

Armstrong added that in the early 2000s, the only available therapies for adults with advanced renal cell carcinoma did not prolong patients' lives. Anti-angiogenic drugs, which block the growth of blood vessels that support tumor growth, became more standard of care about 15 years ago and were shown to prolong life and delay the time until disease progression. Immune checkpoint inhibitors, which rev up the immune system to attack cancer, have revolutionized the treatment of advanced renal cell carcinoma over the past five years.

"The exciting thing about these immune therapies is now you can see patients go into remission and then eventually even stop therapy and maintain that remission," Armstrong said. "Our hope is that some of these remissions may result in a cure. Long-term, durable remissions, even off therapy, (have been) seen for many different cancers like melanoma, (and) we're hoping (this) will turn out to be the case with long-term follow-up in kidney cancer."

Keytruda plus Lenvima adds another option for the frontline treatment of patients with advanced renal cell carcinoma.

AXEL KOCK / STOCK.ADOBE.COM

The recent FDA approval of Keytruda plus Lenvima was based on findings from the CLEAR clinical trial, which demonstrated a 61% reduced risk of disease progression or death in patients treated with the combination therapy.

The regimen showed a progression-free survival of 23.9 months compared with 9.3 months in patients treated with Sutent (sunitinib).

Although the benefits of Keytruda plus Lenvima are evident, the combination treatment also comes with some risks, more so than single therapies. Keytruda, an immunotherapy, may cause shortness of breath, cough, rash, diarrhea, cold intolerance and fatigue.

"Doctors and patients need to be particularly attuned to these things because they're readily reversible with steroids like prednisone," Armstrong noted. "These immune checkpoint inhibitors, that's their power — they can rev up the immune system to induce remissions — but (they) also can cause these immune-related side effects."

In addition, Lenvima, an oral targeted therapy, comes with its own side effects, especially at the 20-milligram dose given to patients in the CLEAR trial. These side effects led to dose reductions, interruptions or discontinuations for several patients.

"We've learned from this cocktail that the combination is very effective, but the side effects of Lenvima, particularly at the doses that they used in this CLEAR trial, are particularly concerning," Armstrong said. "Even though (there are) significant benefits in terms of survival and delaying progression, I think we have to manage patients very carefully with dose reductions and drug holds because of some of the side effects from (Lenvima), which can cause high blood pressure, fatigue, loss of appetite, diarrhea or stomach upset."

Armstrong added that this highlights the importance of following patients carefully for potential side effects and being flexible with dosing to find the right dose — to provide personalized care.

"It is a great time for the field of (renal cell carcinoma)," Choueiri said. "What an honor and privilege to see these advances impacting the lives of patients."

IMPORTANT FACTS ABOUT BLENREP

The risk information provided here is not comprehensive. To learn more, talk to your healthcare provider or pharmacist. Visit BLENREP.com or call 1-888-825-5249 to get FDA-approved product labeling, including Medication Guide.

What is BLENREP?

BLENREP is a prescription medicine used to treat adults with multiple myeloma who have received at least 4 prior medicines to treat multiple myeloma, **and** their cancer has come back or did not respond to prior treatment. It is not known if BLENREP is safe and effective in children.

BLENREP is approved based on patient response rate. Studies are ongoing to confirm the clinical benefit of BLENREP for this use.

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

Before you receive BLENREP, you must read and agree to all of the instructions in the BLENREP REMS. Before prescribing BLENREP, your healthcare provider will explain the BLENREP REMS to you and have you sign the Patient Enrollment Form.

BLENREP can cause serious side effects, including:

Eye problems. Eye problems are common with BLENREP. BLENREP can cause changes to the surface of your eye that can lead to dry eyes, blurred vision, worsening vision, severe vision loss, and corneal ulcer. Tell your healthcare provider if you have any vision changes or eye problems during treatment with BLENREP.

- Your healthcare provider will send you to an eye specialist to check your eyes before you start treatment with BLENREP, prior to each dose of BLENREP, and for worsening symptoms of eye problems.
- Even if your vision seems fine, it is important that you get your eyes checked during treatment with BLENREP because some changes can happen without symptoms and may only be seen on an eye exam.
- You should use preservative-free lubricant eye drops at least 4 times per day during treatment with BLENREP as instructed by your healthcare provider.
- You should use caution when driving or operating machinery as BLENREP may affect your vision.
- Avoid wearing contact lenses during treatment with BLENREP unless directed by your eye specialist.

Decrease in platelets (thrombocytopenia) is common with BLENREP, and can also be serious. Platelets are a type of blood cell that help your blood to clot. Your healthcare provider will check your blood cell counts before you start treatment with BLENREP and during treatment. Tell your healthcare provider if you have bleeding or bruising during treatment with BLENREP.

Infusion reactions are common with BLENREP, and can also be serious. Tell your healthcare provider or nurse right away if you get any of the following signs or symptoms of an infusion reaction while receiving BLENREP:

- chills or shaking
- redness of your face (flushing)
- itching or rash
- shortness of breath, cough, or wheezing
- swelling of your lips, tongue, throat, or face
- dizziness
- feel like passing out
- tiredness
- fever
- feel like your heart is racing (palpitations)

If you don't have prescription coverage or need help paying for your medicines, call us at 1-844-4GSK-ONC (1-844-447-5662).

IN RELAPSED OR REFRACTORY MULTIPLE MYELOMA...

RESOLVE BROUGHT YOU THIS FAR

TALK TO YOUR DOCTOR TO SEE WHERE

BLENREP MAY TAKE YOU

BLENREP is an antibody-drug conjugate (ADC) that targets the B-cell maturation antigen (BCMA) protein.

BLENREP is the first and only medication of its kind to help you fight relapsed or refractory multiple myeloma. It is also a single agent, which means that it doesn't need to be combined with other treatments.

What is BLENREP?

BLENREP is a prescription medicine used to treat adults with multiple myeloma who have received at least 4 prior medicines to treat multiple myeloma, **and** their cancer has come back or did not respond to prior treatment. It is not known if BLENREP is safe and effective in children.

BLENREP is approved based on patient response rate. Studies are ongoing to confirm the clinical benefit of BLENREP for this use.

BLENREP is available only through a restricted program called the BLENREP REMS (Risk Evaluation and Mitigation Strategy).

The most common side effects of BLENREP include vision or eye changes such as findings on eye exam (keratopathy), decreased vision or blurred vision, nausea, low blood cell counts, fever, infusion-related reactions, tiredness, and changes in kidney or liver function blood tests.

How will I receive BLENREP?

- BLENREP will be given to you by your healthcare provider by intravenous infusion into your vein over approximately 30 minutes and is usually given every 3 weeks.
- Your healthcare provider will decide how many treatments you need and may decrease your dose, temporarily stop or completely stop treatment with BLENREP if you have serious side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

Before receiving BLENREP, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of vision or eye problems.
- have bleeding problems or a history of bleeding problems.
- are pregnant or plan to become pregnant. BLENREP can harm your unborn baby. **Females who are able to become pregnant:** Your healthcare provider may do a pregnancy test before you start treatment with BLENREP. You should use effective birth control during treatment with BLENREP and for 4 months after the last dose. Talk to your healthcare provider about birth control methods you can use during this time. Tell your healthcare provider if you become pregnant or think you may be pregnant during treatment with BLENREP. **Males with female partners who are able to become pregnant** should use effective birth control during treatment with BLENREP and for 6 months after the last dose.
- are breastfeeding or plan to breastfeed. It is not known if BLENREP passes into your breast milk. Do not breastfeed during treatment with BLENREP and for 3 months after the last dose.
- BLENREP may affect fertility in males and females. Talk to your healthcare provider if this is a concern for you.

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

These are not all the possible side effects of BLENREP.

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.

Find out more by visiting **BLENREP.com**

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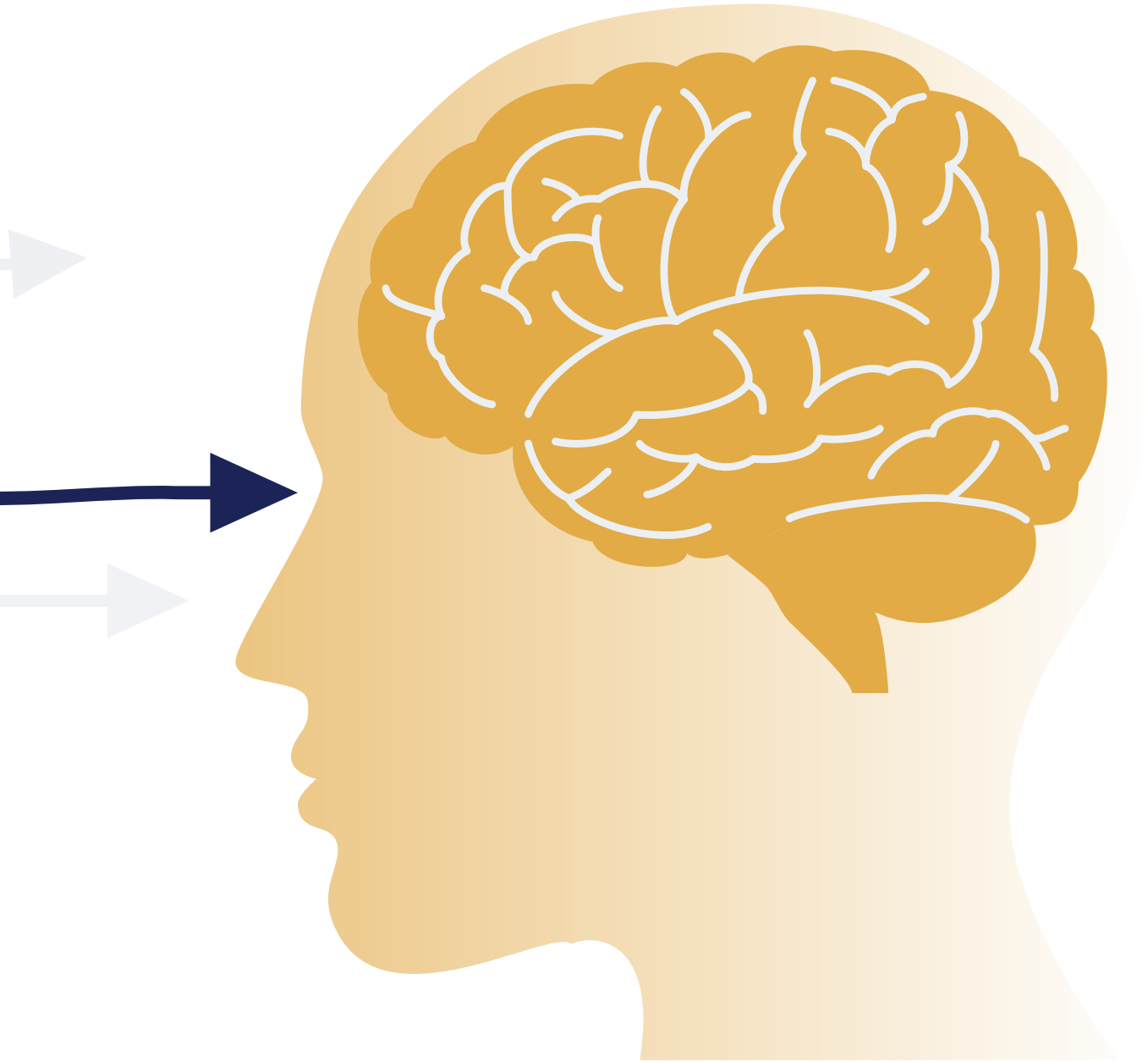
LIVING LONGER WITH TREMENDOUS HOPE

Better therapies are on the horizon for cancer that has spread to the brain, including a clinical trial matching patients with treatments based on unique genetic changes in brain metastases.

By JEANNETTE MONINGER

PCH.VECTOR / STOCK.ADOBE.COM ADAPTED BY GWEN SALAS



What seemed like an innocent but persistent cough prompted Boston resident Lisa M.* to call her doctor in December 2014. "I thought I might have the flu and was hoping for something to make me feel better," she says. Instead, Lisa, who had received a diagnosis of melanoma two years earlier at age 50, was sent for chest X-rays.

"When the technician asked me to raise my arm above my head, I couldn't do it. I didn't understand the directions," she recalls. This wasn't the first time Lisa was confused — she had been experiencing unusual symptoms for a while. "I kept hitting the same curb with my car," she says. "Egg yolks ended up on the countertop because I'd somehow miss the bowl." But it wasn't until the X-ray incident that Lisa realized something could be seriously wrong.

The X-rays revealed spots on her lungs — a sign that the cancer had probably spread or metastasized. Follow-up MRIs and CT scans also found a golf ball-sized tumor and multiple smaller tumors in her brain.

Lisa had brain metastases. »

*Last name omitted by request.

NEW TREATMENTS TO ADDRESS A GROWING PROBLEM

Brain metastases are 10 times more common than primary brain cancer. Certain types of cancers — melanoma, breast, lung, kidney, colorectal and blood cancers like leukemia and lymphoma — are most likely to spread to the brain.

According to the American Association of Neurological Surgeons, approximately 200,000 Americans will learn they have brain metastases this year, and experts say that number is on the rise. "With treatment advancements, people with all types of cancers are living longer. The additional years give cancer a chance to come back and spread, and the brain is a common site for metastases," explains Dr. Chetan Bettegowda, Jennison and Novak Families Professor of Neurosurgery at Johns Hopkins Medicine in Baltimore. Improvements in diagnostic screenings also are a factor. "With high-resolution MRIs, we can now find smaller tumors in the brain that older imaging scans missed," he says. "We're finding brain metastases before symptoms occur."

> We can now find smaller tumors in the brain that older imaging scans missed. We're finding brain metastases before symptoms occur.
>
> —DR. CHETAN BETTEGOWDA

Lisa had a craniotomy surgical procedure to remove the largest brain tumor. Pathology tests on the tumor confirmed that the melanoma had spread. As recently as 15 years ago, brain tumor treatment options were limited to surgery, radiation therapy (either whole-brain or stereotactic radiosurgery) or a combination of the two. Although treatments like chemotherapy have proved highly successful at treating cancers that affect the liver, lungs, breasts and blood, they're less effective against brain tumors.

"The blood-brain barrier, which protects our brain from toxins, can also limit the amount of drug that gets into the brain," explains Dr. Priscilla Brastianos, director of the Central Nervous System Metastasis Program at Mass General Cancer Center in Boston. "But researchers have been working to develop drugs that can cross this brain barrier and target brain tumors."

Because Lisa had a lot of smaller tumors scattered throughout her brain, her doctor recommended forgoing whole-brain radiation therapy (which can cause irreversible memory loss and other problems) for a relatively new brain tumor treatment: immunotherapy.

"Cancer cells can fool your immune system, making it impossible for your system to go after the diseased cells," says Dr. Michael Vogelbaum, chief of neurosurgery and program leader of the department of neuro-oncology at Moffitt Cancer Center in Tampa, Florida. "Immunotherapy reactivates the immune system and engages its intended function to eradicate cancerous cells."

The most promising immunotherapy drugs for brain tumors are immune checkpoint inhibitors. But the drugs work best when given before the onset of brain metastases symptoms, which include headaches, vision and speech problems, nausea and vomiting, and seizures. As many as 8 in 10 patients see initial improvements with immunotherapy drugs, says Vogelbaum. Unfortunately, that success is often short-lived. "Within six months of the start of treatment, immunotherapy may stop working," he says. "New tumors appear or existing tumors grow."

The first immunotherapy drug Lisa tried, Yervoy (ipilimumab), caused the tumors to get bigger instead of smaller, so her doctors switched to targeted therapy. This type of treatment targets the Achilles' heel of cancer cells, says Bettegowda. "Molecular changes in a cell's genetic makeup or DNA cause cancer cells to grow and divide. Targeted therapies go after the cells that have this specific change or vulnerability," he says. "The drugs have been very successful treating melanoma caused by BRAF gene mutations and lung cancers caused by (ALK) gene mutations. The good news is that the drugs can also target brain metastases that these primary cancers cause in some patients."

Lisa initially had success with a combination of two therapies that target the BRAF mutation: Tafinlar (dabrafenib) and Mekinist (trametinib). But after four months, the drugs started to cause liver injury. Fortunately for Lisa, the Food and Drug Administration approved a new immunotherapy drug for melanoma, Keytruda (pembrolizumab), the same year she was diagnosed with brain metastases. The drug is an anti-PD-1 checkpoint inhibitor, and it works by preventing cancer cells from activating the PD-1 pathway where T cells — healthy white blood cells that fight cancer — are suppressed. Without being able to block the pathway, the cancer cells are vulnerable to the T cells primed by the

GINA HOLLENBECK and her husband, **GREG,** host events to raise awareness for patients with the ALK gene mutation.

SHANNON LENOIR

targeted therapy drug. Lisa calls Keytruda a "wonder drug." For her, it stopped new brain tumors from forming and shrunk the existing ones.

IMPROVING SURVIVAL RATES FOR PEOPLE WITH BRAIN METASTASES

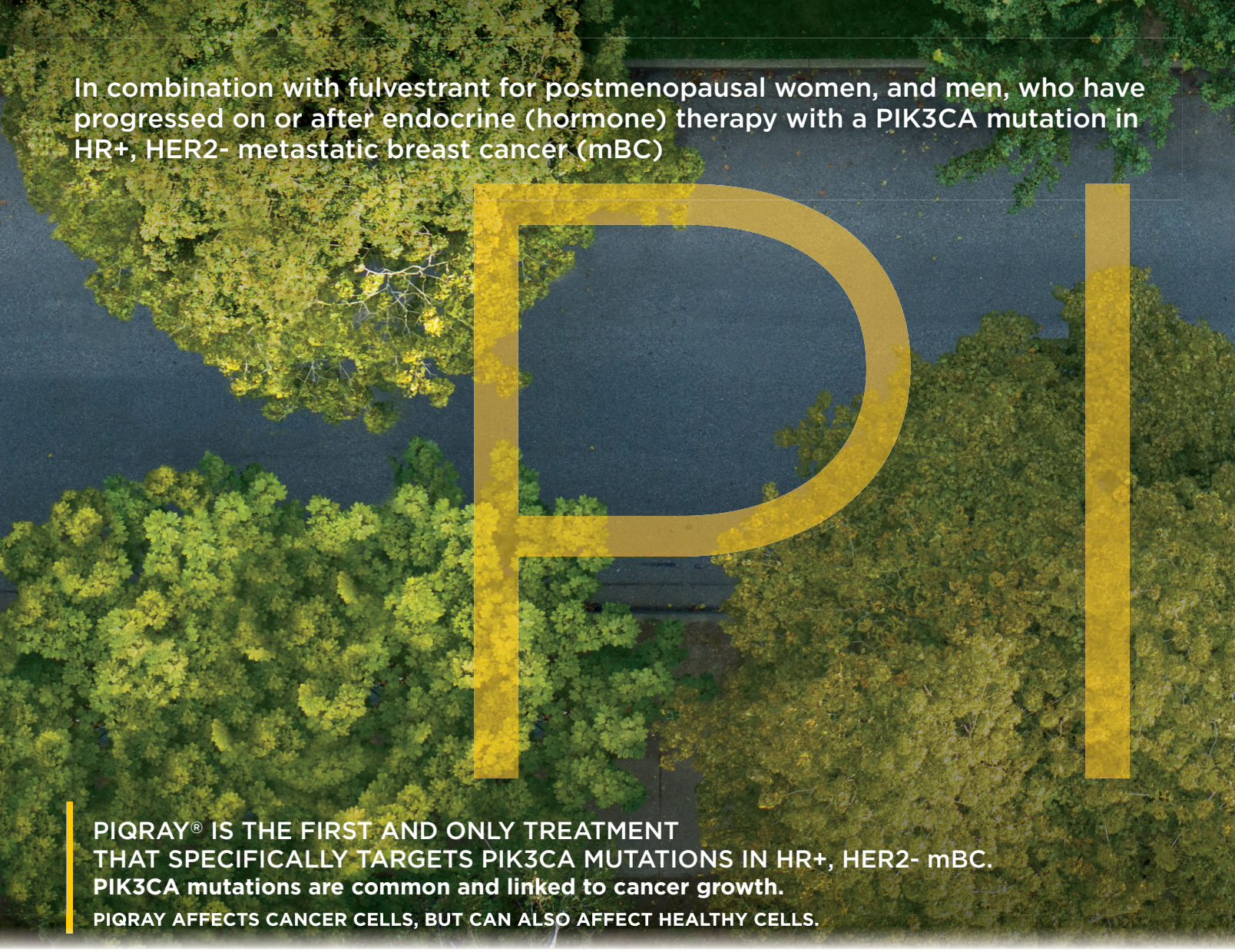
Brain tumor experts say there's a lot of reason for people like Lisa to have hope. "A brain metastases diagnosis used to be terminal, with survival measured in months," says Dr. Bettegowda. "Today, our ability to treat brain metastases has improved to the point where this cancer is often not the cause of someone's eventual decline and death. A person may be more likely to die from the primary cancer or from cancer that spreads to other organs, causing organ failure."

Memphis resident Gina Hollenbeck knows a thing or two about hope. Hollenbeck was 38 years old and training for a triathlon in 2015 when she was found to have stage 4 non-small cell lung cancer that had already spread to her brain. "One doctor told me to get my affairs in order because I had less than 10 months to live," she recalls. Six years later, Hollenbeck is doing well thanks to numerous treatments that started with a targeted therapy drug called Zykadia (ceritinib) that is directed at the ALK gene mutation found to be a key driver of the cancer. She took the daily pill while undergoing surgery to remove a brain tumor and getting follow-up targeted radiation therapy. When Zykadia stopped working, she had several years of success with other targeted therapies, including Alecensa (alectinib) and Lorbrena (lorlatinib).

The need to frequently switch medications is a problem with targeted therapies. Over time, cancer cells can mutate again, rendering the targeted therapy ineffective. Sometimes, the cells find a new pathway to hide from the T cells. For these reasons, doctors may prescribe two therapies that target different parts of the diseased cells or combine a targeted therapy with another drug.

Earlier this year, the Lorbrena pills Hollenbeck took every day for almost three years stopped working. "One tiny spot on my brain grew to 10 spots on my brain," she says. The cancer has also affected her pancreas, lymph nodes and pericardium, the sac that covers the heart. In May, Hollenbeck enrolled in a clinical trial that combines Lorbrena with an experimental drug (currently called ARRY-558). Researchers hope the new drug will block a protein called SHP2, making the cancer cells more vulnerable to the targeted therapy.

continued on page 41



INDICATION

PIQRAY® (alpelisib) tablets is a prescription medicine used in combination with the medicine fulvestrant to treat women who have gone through menopause, and men:

- who have hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer or breast cancer that has spread to other parts of the body (metastatic), with an abnormal phosphatidylinositol-3-kinase catalytic subunit alpha (PIK3CA) gene, **and**
- whose disease has progressed on or after endocrine therapy

Your health care provider will test your cancer for an abnormal "PIK3CA" gene to make sure that PIQRAY is right for you.

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

IMPORTANT SAFETY INFORMATION

Do not take PIQRAY if you have had a severe allergic reaction to PIQRAY or are allergic to any of the ingredients in PIQRAY.

PIQRAY may cause serious side effects, including:

- **Severe allergic reactions:** Tell your health care provider or get medical help right away if you have trouble breathing, flushing, rash, fever, or fast heart rate during treatment with PIQRAY
- **Severe skin reactions:** Tell your health care provider or get medical help right away if you get severe rash or rash that keeps getting worse, reddened skin, flu-like symptoms, blistering of the lips, eyes or mouth, blisters on the skin or skin peeling, with or without fever
- **High blood sugar levels (hyperglycemia):** Hyperglycemia is common with PIQRAY and its complications can be severe. Your health care provider will monitor your blood sugar levels before you start and during treatment with PIQRAY. Your health care provider may monitor your blood sugar levels more often if you have a history of type 2 diabetes. Tell your health care provider right away if you develop symptoms of hyperglycemia and its complications, including excessive thirst, dry mouth, urinating more often than usual or having a higher amount of urine than normal, increased appetite with weight loss, confusion, nausea, vomiting, fruity odor on breath, difficulty breathing, or dry or flushed skin
- **Lung problems (pneumonitis):** Tell your health care provider right away if you develop new or worsening symptoms of lung problems, including shortness of breath or trouble breathing, cough, or chest pain
- **Diarrhea:** Diarrhea is common with PIQRAY and can be severe. Severe diarrhea can lead to the loss of too much body water (dehydration) and kidney problems. If you develop diarrhea during treatment with PIQRAY, tell your health care provider right away. Your health care provider may tell you to drink more fluids or take medicines to treat diarrhea

Your health care provider may tell you to decrease your dose, temporarily stop your treatment, or completely stop your treatment with PIQRAY if you get certain serious side effects.

Before you take PIQRAY, tell your health care provider about all of your medical conditions, including if you:

- have a history of diabetes
- have a history of skin rash, redness of skin, blistering of the lips, eyes or mouth, or skin peeling
- are pregnant or plan to become pregnant. PIQRAY can harm your unborn baby

  Females who are able to become pregnant:
  - Your health care provider will check to see if you are pregnant before you start treatment with PIQRAY
  - You should use effective birth control during treatment with PIQRAY and for 1 week after the last dose. Talk to your health care 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 health care provider right away

  Males with female partners who are able to become pregnant should use condoms and effective birth control during treatment with PIQRAY and for 1 week after the last dose. If your female partner becomes pregnant, tell your health care provider right away.
- are breastfeeding or plan to breastfeed. It is not known if PIQRAY passes into your breast milk. Do not breastfeed during treatment with PIQRAY and for 1 week after the last dose

You should also read the Full Prescribing Information of fulvestrant for important pregnancy, contraception, infertility, and lactation information

Tell your health care provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. PIQRAY and other medicines may affect each other causing side effects. Know the medicines you take. Keep a list of them to show your health care provider or pharmacist when you get a new medicine.

The most common side effects of PIQRAY when used with fulvestrant include:

- rash
- nausea
- tiredness and weakness
- decreased appetite
- mouth sores
- vomiting
- weight loss
- hair loss
- changes in certain blood tests

PIQRAY may affect fertility in males and in females who are able to become pregnant. Talk to your health care provider if this is a concern for you.

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

Please see Summary of Important Information on the following page.

SUMMARY OF IMPORTANT INFORMATION

WHAT IS PIQRAY USED FOR?

PIQRAY® (alpelisib) tablets is a prescription medicine used in combination with the medicine fulvestrant to treat women who have gone through menopause, and men:

- who have hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer or breast cancer that has spread to other parts of the body (metastatic), with an abnormal phosphatidylinositol-3-kinase catalytic subunit alpha (PIK3CA) gene, **and**
- whose disease has progressed on or after endocrine therapy

Your health care provider will test your cancer for an abnormal "PIK3CA" gene to make sure that PIQRAY is right for you.

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

WHO SHOULD NOT TAKE PIQRAY?

Do not take PIQRAY if you have had a severe allergic reaction to PIQRAY or are allergic to any of the ingredients in PIQRAY.

WHAT SHOULD I TELL MY HEALTH CARE PROVIDER BEFORE TAKING PIQRAY?

Before you take PIQRAY, tell your health care provider about all of your medical conditions, including if you:

- have a history of diabetes
- have a history of skin rash, redness of skin, blistering of the lips, eyes or mouth, or skin peeling
- are pregnant or plan to become pregnant. PIQRAY can harm your unborn baby

  Females who are able to become pregnant:
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  - You should use effective birth control during treatment with PIQRAY and for 1 week after the last dose. Talk to your health care 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 health care provider right away

  Males with female partners who are able to become pregnant should use condoms and effective birth control during treatment with PIQRAY and for 1 week after the last dose. If your female partner becomes pregnant, tell your health care provider right away.

  You should also read the fulvestrant Prescribing Information for important pregnancy, contraception, and infertility information.
- are breastfeeding or plan to breastfeed. It is not known if PIQRAY passes into your breast milk. Do not breastfeed during treatment with PIQRAY and for 1 week after the last dose.

WHAT OTHER MEDICATIONS MIGHT INTERACT WITH PIQRAY?

Tell your health care provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. PIQRAY and other medicines may affect each other causing side effects. Know the medicines you take. Keep a list of them to show your health care provider or pharmacist when you get a new medicine.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF PIQRAY?

PIQRAY may cause serious side effects, including:

- **Severe allergic reactions:** Tell your health care provider or get medical help right away if you have trouble breathing, flushing, rash, fever, or fast heart rate during treatment with PIQRAY
- **Severe skin reactions:** Tell your health care provider or get medical help right away if you get severe rash or rash that keeps getting worse, reddened skin, flu-like symptoms, blistering of the lips, eyes or mouth, blisters on the skin or skin peeling, with or without fever
- **High blood sugar levels (hyperglycemia):** Hyperglycemia is common with PIQRAY and its complications can be severe. Patients with a history of type 2 diabetes may require closer monitoring by their health care professional. Your health care provider will check your blood sugar levels before you start and during treatment with PIQRAY. Tell your health care provider right away if you develop symptoms of hyperglycemia and its complications, including excessive thirst, dry mouth, urinating more often than usual or having a higher amount of urine than normal, increased appetite with weight loss, confusion, nausea, vomiting, fruity odor on breath, difficulty breathing, or dry or flushed skin
- **Lung problems (pneumonitis):** Tell your health care provider right away if you develop new or worsening symptoms of lung problems, including shortness of breath or trouble breathing, cough, or chest pain
- **Diarrhea:** Diarrhea is common with PIQRAY and can be severe. Severe diarrhea can lead to the loss of too much body water (dehydration) and kidney problems. If you develop diarrhea during treatment with PIQRAY, tell your health care provider right away. Your health care provider may tell you to drink more fluids or take medicines to treat diarrhea

Your health care provider may tell you to decrease your dose, temporarily stop your treatment, or completely stop your treatment with PIQRAY if you get certain serious side effects.

The most common side effects of PIQRAY when used with fulvestrant include:

- rash
- nausea
- tiredness and weakness
- decreased appetite
- mouth sores
- vomiting
- weight loss
- hair loss
- changes in certain blood tests

PIQRAY may affect fertility in males and in females who are able to become pregnant. Talk to your health care provider if this is a concern for you.

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

WHAT LABORATORY MONITORING TESTS DO I NEED WHEN TAKING PIQRAY?

Your health care provider will check your blood sugar levels before you start and during treatment with PIQRAY. Your health care provider may monitor your blood sugar levels more often if you have a history of type 2 diabetes.

GENERAL INFORMATION ABOUT THE SAFE AND EFFECTIVE USE OF PIQRAY

Medicines are sometimes prescribed for purposes other than those listed. Do not use PIQRAY for a condition for which it was not prescribed. Do not give PIQRAY to other people, even if they have the same symptoms you have. It may harm them. You can ask your health care provider or pharmacist for more information about PIQRAY that is written for health professionals.

For more information about PIQRAY, talk with your doctor or pharmacist or call 1-833-4-PIQRAY (1-833-474-7729). The FDA-approved product labeling or prescribing information can be found at PIQRAY.com.

NOVARTIS

PIQRAY® (alpelisib) tablets

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Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

continued from page 37

In three months, all of Hollenbeck's tumors shrunk to half their original size. "I'm grateful for every day that I'm here," says Hollenbeck, who has outlived the doctor's prediction by five years and counting.

"It's an exciting time in oncology. We now understand so much more about the molecular underpinnings of tumors," says Brastianos, who founded the Brastianos Lab at Mass General Cancer Center to further research into the genetic drivers of brain tumors. "We've discovered that brain metastases can have additional genetic mutations not found in the original primary cancer. We also found common molecular alterations across brain metastases."

Because of these findings, more than 300 hospitals nationwide are enrolling patients in a National Cancer Institute-sponsored clinical trial to match patients with treatments based on unique genetic changes identified in their brain metastases. The opportunity to participate in clinical trials is a fairly new and positive step for people with brain metastases. Historically, this type of metastatic cancer automatically made them ineligible to participate, a stance that greatly limited treatment options. "We still have a long way to go when it comes to finding better therapies for patients with cancer that has spread to the brain," says Brastianos. "But there is tremendous hope."

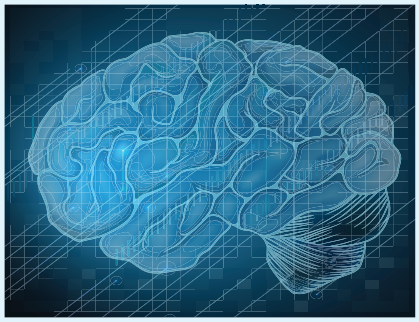
A tattoo on **GINA HOLLENBECK'S** wrist is a reminder to see the positive in the journey.

Leptomeningeal Disease: A Rare Metastasis

THE BRAIN ISN'T THE ONLY part of the central nervous system where primary cancers spread. Studies have shown that for up to 5% of people, cancer moves to the cerebrospinal fluid that surrounds the brain and spinal cord or to the brain and spinal cord lining (called the leptomeninges). The condition, known as leptomeningeal disease or leptomeningeal carcinomatosis, most commonly affects those with melanoma, lung cancer or breast cancer. Because the cancer cells float freely in the cerebrospinal fluid, the disease quickly spreads throughout the central nervous system, leading to an approximate three-month survival rate after diagnosis.

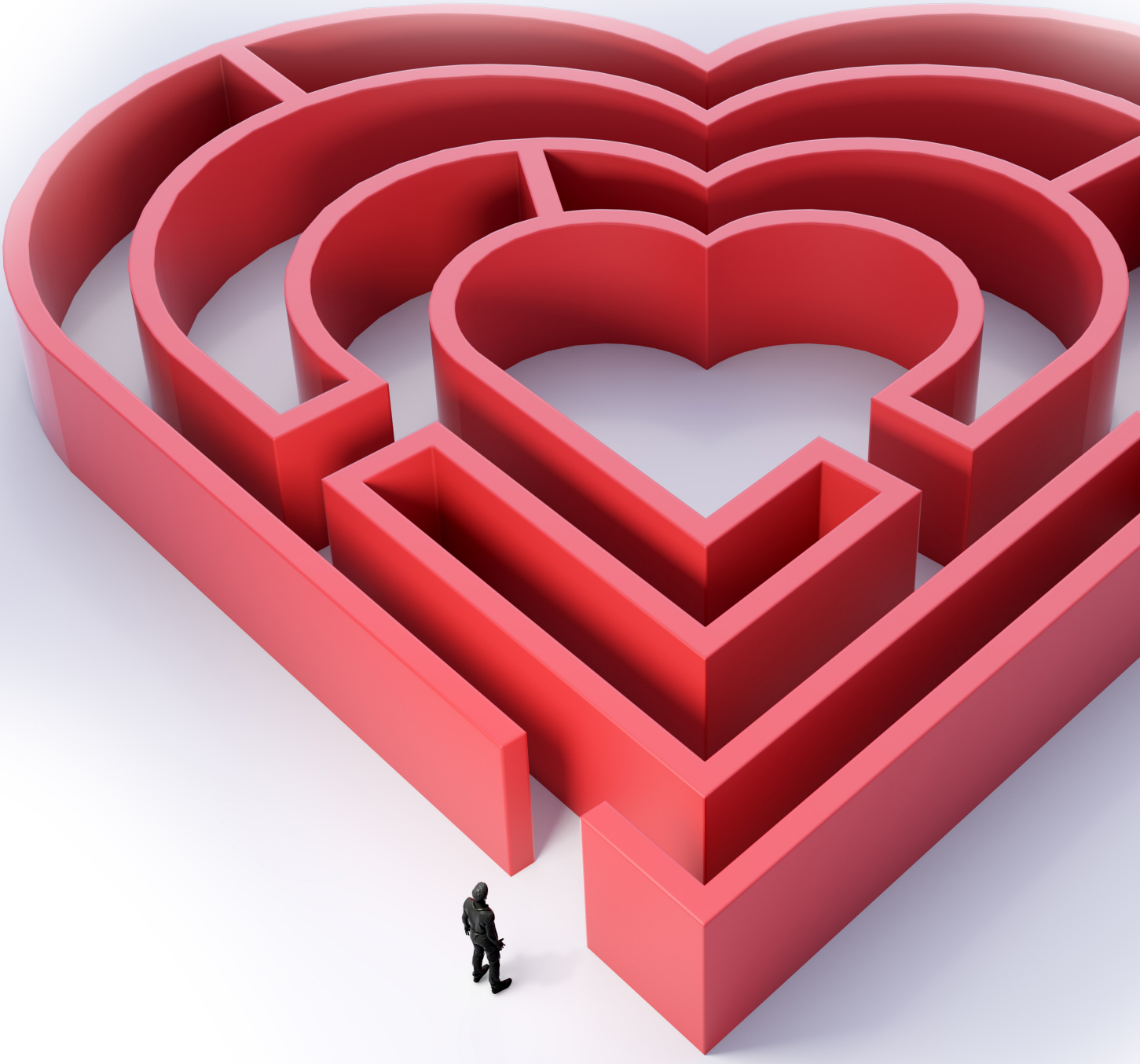
"People have tumor cells in the brain, as well as the fluid and tissue that coat the brain and brainstem," says Dr. Chetan Bettegowda, a Jennison and Novak Families Professor of Neurosurgery at Johns Hopkins Medicine in Baltimore. Symptoms are similar to brain metastases but may also include facial or other muscle weakness or pain, difficulty swallowing, double vision and difficulty thinking clearly.

The number of people developing leptomeningeal disease is increasing for the same reason that diagnoses of brain metastases are on the rise: People are living longer, giving cancer more time to spread. Doctors use MRIs and spinal taps (lumbar punctures), to make a diagnosis. Treatments have been limited to radiation therapy to shrink tumors and intrathecal chemotherapy delivered directly into the spinal fluid through a small, quarter-sized port called an Ommaya reservoir implanted underneath the skin on the scalp. Less commonly, chemotherapy is injected into the fluid via a spinal tap procedure. These treatments, however, are considered palliative — they ease symptoms but won't stop the disease.



Clinical trials are underway to identify molecular changes to primary cancer cells that may signal a higher risk of leptomeningeal disease. This new knowledge could lead to the use of targeted therapies to treat metastatic cancer and prevent it. Ongoing trials are also showing encouraging results of immunotherapy and certain targeted therapies.

SHANNON LENOIR; BRAIN: BLUERINGMEDIA / STOCK.ADOBE.COM



MOPIC / STOCK.ADOBE.COM

Love LOST: The Effects *of* Cancer on Marriage and Relationships

Although being in a close relationship during the cancer journey can dramatically improve outcomes, the stress of treatment and the diagnosis itself can take a toll on couples, sometimes in a negative way.

By DON VAUGHAN

A diagnosis of cancer can affect every aspect of a patient's life — including their relationship with their spouse or partner.

In most cases, couples draw closer during the cancer journey and come through the experience with their relationship intact. This is important because studies show that being in a close relationship can dramatically improve patient outcomes. A study published in the *Journal of Clinical Oncology*, for example, noted that married patients tended to have cancer diagnosed at an earlier stage, when it can be more successfully treated; receive more appropriate treatment; and live longer than patients who are not married.

However, not all relationships are strong enough to survive a cancer diagnosis, and the details of the cancer course can affect this as well. According to a study published in the journal *Cancer*, a woman with cancer or other serious illness is six times more likely to be separated or divorced soon after receiving her diagnosis than a male patient. "Female gender was found to be the strongest predictor in separation or divorce in each cohort," the study authors noted. A 2015 study published in the *Journal of Health and Social Behavior* offered a similar conclusion regarding the impact on female patients. »

PENNY experienced challenges in her relationship after being diagnosed with ductal carcinoma in situ.

JANERIS MARTE

Penny* of Pompano Beach, Florida, saw her marriage flounder and ultimately collapse after she received a diagnosis of ductal carcinoma in situ in her left breast. Penny underwent a lumpectomy then received chemotherapy and radiation. Her husband, however, became resentful and emotionally absent, leaving Penny to deal with the trauma of treatment and challenges of recovery on her own. "Our marriage was failing, so I knew no support would be forthcoming," she says.

IMPACT OF DIAGNOSIS

Cancer can damage a marriage or relationship in a number of ways, counselors say.

"A cancer diagnosis often has a ripple effect on how patients see themselves, on their life and on their relationships," says Cheyenne Corbett, director of cancer support and survivorship at Duke Cancer Institute in Durham, North Carolina. "When you think of it in the context of marriage, it brings additional pressure, distress and changes to how a couple typically operate in terms of their relationship."

*Name changed by request.

In many cases, communication — which may have been difficult before the diagnosis — suffers further, Corbett notes. A cancer diagnosis also can have a practical impact, negatively affecting job security, finances, basic family dynamics and more. "It can be very difficult to navigate," Corbett says.

Receiving a diagnosis of cancer also can have a devastating emotional impact on the caregiving spouse or partner. Mark Cantrell, a writer based in Wake Forest, North Carolina, recalls coming home, dropping to his knees and weeping "until there were no tears left," upon learning that his wife, Maryanne, had been diagnosed with Hodgkin lymphoma in her chest.

Mark unhesitatingly assumed the role of caregiver, doing all he could to help Maryanne. But not all partners are up for the job, which can be physically and mentally grueling. Unable or unwilling to face the challenges, they simply walk away from the relationship.

"In many cases, underlying issues that were preexisting for the couple really come to the surface as a result of the stress of a cancer diagnosis," notes Jessica Worthington, a licensed

marriage and family therapist in Austin, Texas. "It can be really hard for many people."

STRESS AND TREATMENT

A variety of stressors may erupt as a couple works through cancer and recovery, notes Worthington. One of the biggest stressors tends to be money — especially if finances were an issue prior to the cancer diagnosis. "It may have been something they could manage before, but now it becomes a much bigger issue and much harder to deal with," Worthington says.

Another significant stressor may be resentment on the part of the caregiver. Although they may not directly express their feelings to the patient, those emotions can fester and manifest in more subtle ways. Penny's husband, for example, expressed his resentment by refusing to take her to chemotherapy and radiation appointments, forcing her to ask her parents instead.

"I was receiving an anti-nausea drug called Zofran (ondansetron) as part of my infusion, and it made me so dizzy, I couldn't drive," Penny recalls. "(My husband) said he didn't want to take time off from work. He was also creeped out about medical things, so he didn't want to be in a medical office. His family was very anti-doctor."

At one point, he told Penny that he didn't want to be with her anymore but that he would stay until her treatment was done. "I don't think I said anything when he said that. I took that as 'I can count on you for nothing,'" Penny says.

But Penny admits to her role in his resentment and the final breakup of their marriage, noting that she had an affair because she was miserable in the relationship. "You can point fingers at both of us," Penny says. "I don't want this to sound like he was the only bad guy, because I earned some of this."

PENNY was able to overcome body dysmorphia after she started to date again.

REGAINING INTIMACY

Intimacy is commonly affected by cancer treatment and recovery. The inability to engage in sex due to vaginal dryness, lack of libido or other issues can put incredible pressure on a relationship. But there are alternatives.

"It takes a conscious effort to figure out what's right for each couple because intimacy doesn't have to be intercourse," says Mary Dev, a licensed clinical social worker and counselor at The University of Texas MD Anderson Cancer Center in Houston. "It can be talking about something that is near and dear to you and having that deep connection. It's building trust to have a safe space to have that intimacy."

"I would challenge couples to expand their idea of what sex and intimacy can be," advises Worthington. "Anything that is pleasurable and helps you feel connected counts as sex, even if it's just cuddling or a full body massage. Get creative."

"We didn't have relations for a very long time, and that hurt our emotional bond," notes Maryanne Cantrell. "But being in love with each other is exactly what saw us through this. The act of touching, cuddling, giving voice to feelings of gratitude and appreciation for the other; reassurance in stressful moments — this was the glue for us."

In addition, the effects of cancer treatment may influence a patient's body image, especially if surgery has left scars and other physical changes. Penny developed body dysmorphia because of her lumpectomy and the negative attitude of her husband, and she was fearful she would be rejected by future partners. However, that proved not to be the case.

"The first man I was with didn't seem to care about it at all, so that was nice," Penny says. "The second man I was with was a nudist, and he asked me to accompany him to a nude beach in north Miami. I thought, 'I know this is baptism by fire, but there is nothing that will help you get over this better than a nude beach, so you need to go.' I went, and it was magnificent. No one cared. No one looked at me. It was very healthy for me to do that."

HOW STRESS AFFECTS TREATMENT OUTCOMES

Understandably, stress on the patient can become overwhelming when their spouse or partner leaves the »

MARK CANTRELL and his wife, **MARYANNE,** grew closer together as she was treated for Hodgkin lymphoma.

SEASON MOORE

relationship, and that can have a dramatic impact on treatment outcomes. "When divorce or separation occurred, quality of care and quality of life were adversely affected," wrote researchers in the *Cancer* report on partner abandonment.

Financial difficulties, for example, may become even more dire, especially if the separation or divorce affects the patient's access to health insurance. "If the caregiver has the insurance, that may have to be negotiated when a couple goes to divorce," says Dev. "If it's not negotiated, it can leave the patient struggling to figure out how they will pay for their care."

Separation or divorce also can adversely affect the patient's access to care by leaving them without reliable transportation or child care and forcing them to rely on other family members or friends for comfort and support.

Cancer negatively affects many relationships, but the majority of couples find their way through it. In some cases, says Corbett, the experience even strengthens their bond.

"There are a lot of negative impacts, but you also hear about couples who become closer to one another during that time," Corbett notes. "Often with a cancer diagnosis and treatment, people talk about the more existential side of it. While they would not have chosen to go through this cancer experience, there are things they gain from it and learn about themselves and their relationships."

This was true for the Cantrells, who had a complicated on/off relationship for many years before marrying. They had been wed just a year and a half when Maryanne learned that she had cancer.

"Maryanne handled the diagnosis much better than I did," Mark says. "She's always been a pragmatist and started gathering information on chemotherapy and radiation treatments as she was recovering from surgery. As a writer, I used to do research on the internet, so I was able to help with that process. I'd never been much of a cook, but now that I was a caregiver, I learned to make a few dishes, started doing laundry for both of us and did all the housecleaning. Basically, I became a housewife for a few months and developed a new respect for homemakers."

Maryanne was grateful. "Mark supported me in so many ways. He bathed me, fed me, helped me dress. And he also weathered my mood swings, crying jags and inability to help with strenuous chores. He drove me to every appointment."

KEEPING RELATIONSHIPS HEALTHY

There are ways for couples in crisis to keep their relationships strong during cancer treatment and recovery. Foremost, counselors say, is to maintain open lines of communication. "I always tell people with cancer that it's not just one conversation, it's several," Dev advises. "Keep trying to talk because the minute you stop, that's when walls get built up, and it's hard to tear them down."

If a person is having trouble communicating, reach out to others on the care team who may be able to help, including the oncologist and social worker. And don't hesitate to see a therapist. "They are a neutral party who will be unbiased," Dev explains. "Counseling provides a safe space to talk."

Partner caregivers are especially encouraged to seek outside support to help them deal with the stress of the job, as well as their own emotional turmoil. This may be in the form of a mental health professional such as a therapist or a local support group. "A support group allows you to talk with others who have a loved one facing cancer about how they are navigating all of the changes in their life and their relationship," says Corbett. "That can be a great resource."

Worthington agrees, noting, "Caregivers really need a good support system. They are supporting the person with cancer, so they need tons of support themselves. They need so much because they give so much."

According to the American Society of Clinical Oncology, counseling can help patients and caregivers:

- Feel less overwhelmed and more in control.
- Manage anxiety and depression better.
- Communicate more clearly with each other and their care team.
- Talk with family and friends and adjust to changes.
- Manage fears and worries about the future.

SEASON MOORE

ADVICE FROM LIFE EXPERIENCE

Maryanne Cantrell and Penny are now many years beyond their cancer experiences and doing well. It was a grueling, life-altering journey for both. Although their marriage ended, Penny and her ex-husband have worked through the hurt and have a healthy friendship today.

Reflecting on her journey, Maryanne shared the most important lesson she learned along the way.

"I highly recommend both spouses build a mental and emotional toolbox, something to keep you emotionally resilient," she advises. "For example, as a patient, I will not always be the same person emotionally and physically. I have to give myself permission to not be OK and also to realize it is temporary. As a caregiver, I must acknowledge that my needs will be put aside to help my spouse win the cancer battle. It is OK to express frustration, but also realize it is temporary.

"As a couple, we will arm ourselves with knowledge. We will ask questions of each other and our medical support staff. And as a couple, we will help each other find ways to affirm our bond throughout the ordeal. Be gentle with yourself and your spouse because the outcome is important to both."

There Are 2 Sides to Every MPN Story

When you're living with a myeloproliferative neoplasm (MPN), a rare, chronic blood cancer, you may say that you're *fine*—even when physical and emotional symptoms are affecting your quality of life. But when you don't discuss how your MPN makes you feel, you miss the opportunity to get the care and support you may need from friends, family and *especially* your MPN Healthcare team.

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Louise, real MPN patient

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ITCHING AFTER
HOT SHOWERS

NIGHT SWEATS
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EATING LESS
BECAUSE I'M
FEELING
FULL

FINE | FINE IS NOT ENOUGH

When Treatment Stops Working: *Is It the End of the Line?*

Absolutely not. Most patients with advanced disease will be on continuous therapy, and that means trying different options along the way.

By SONYA COLLINS

In 2018, when Carol Brickell learned at the age of 60 that she had advanced non-small cell lung cancer, she was already sick. She'd had a stubborn cough for a couple months and felt weak and tired. Her oncologist in Dallas started her on a combination of chemotherapy and immunotherapy right away. The goal was for her to start feeling better while they awaited the results of biomarker tests that would tell them whether she was a candidate for targeted therapy.

According to the tests, her tumors were ROS1 positive, which made Brickell eligible for a promising targeted therapy called Xalkori (crizotinib). But her disease was already responding well to her current treatment.

"I was feeling almost normal, so my oncologist and I decided to ride it out and keep doing chemotherapy,'" says Brickell, a certified professional career coach. »

« CAROL BRICKELL was diagnosed with advanced non-small cell lung cancer at age 60.

CAROL BRICKELL found comfort in knowing she had other options when her cancer no longer responded to chemoimmunotherapy.

A year later, Brickell started having pain in her abdomen, and a scan showed swollen lymph nodes in the area. But she wasn't very upset about the news. "I knew I had (Xalkori) in my back pocket," she said.

Today, patients with different types of advanced cancers have several options to keep in their back pockets, so to speak, in case their first treatment stops working. When cancer becomes resistant to a particular therapy, that doesn't mean it's the end of the line.

"If the cancer is getting worse or if the therapy is too toxic for the patient, then it's time to move on to a different treatment — so we look in our proverbial toolbox to see what will be the next-best tool," says Dr. Erica Mayer, a senior physician in breast oncology at Dana-Farber Cancer Institute in Boston.

HOW CANCERS BECOME RESISTANT TO TREATMENT

Because of the many available therapies, people can live with different types of cancer, such as breast, lung and gastrointestinal, for many years by staying on treatment.

When a particular medicine stops working, "it's just an expected part of the process and time to switch to something else," says Dr. Arturo Loaiza-Bonilla, the National GI Program director and medical director of clinical research at Cancer Treatment Centers of America.

But why do treatments stop working?

"We believe that advanced cancer is always changing, mutating and trying to evade whatever treatment strategy we have directed toward it, no matter how effective that strategy might be," Mayer says. Of most mutations or other changes that may develop in a cancer cell, only a small fraction might cause drug resistance by random chance, but it is those cells that will continue to grow in the presence of the drug and ultimately repopulate the tumor, which is now treatment resistant.

The form of treatment resistance depends on the type of treatment.

With chemotherapy, for example, one of the main ways cells become resistant is that proteins called drug transporters — their job is to protect healthy cells — start to flush chemotherapy agents out of cancer cells in a misguided attempt to protect the harmful cells from the toxic drugs. Then the chemotherapy can't do its job.

Targeted therapy, on the other hand, attacks the specific gene in the tumor, called a driver mutation, that is causing the growth and spread of the cancer. It shuts down that gene so that it can no longer drive the advancement of the cancer. That works for a while, Loaiza-Bonilla says, "but eventually a co-pilot gene can take over and drive the cancer."

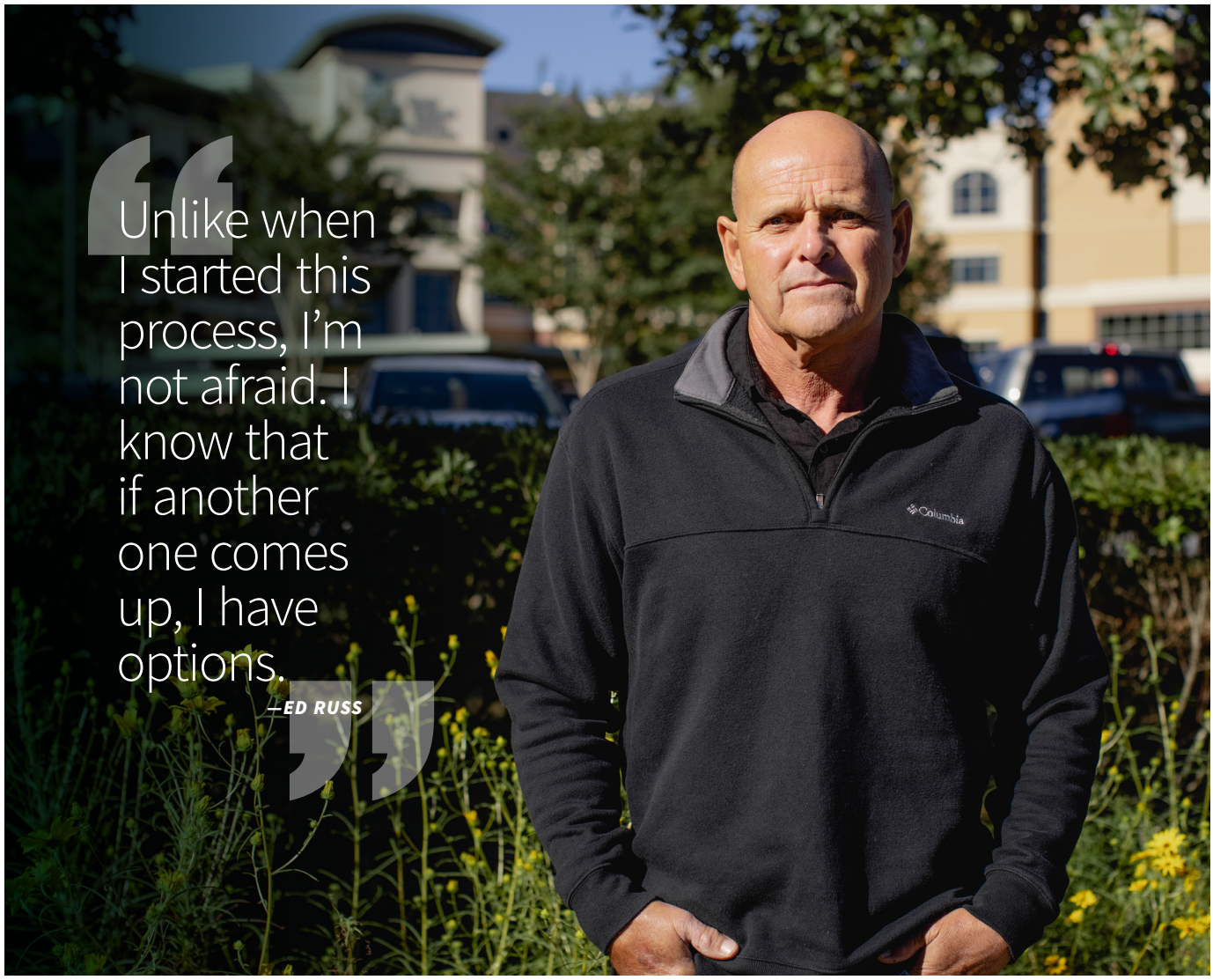
When that happens, patients need to switch to or add a medication that targets that new driver.

Resistance to immunotherapy can happen in several ways. That's because immunotherapy refers to many different drugs that work in distinct ways. But most people on immunotherapy take what's called checkpoint inhibitors, such as Keytruda (pembrolizumab), Yervoy (ipilimumab), Opdivo (nivolumab) and Tecentriq (atezolizumab). These drugs prompt the immune system to recognize cancer cells and block the body's built-in checkpoints.

"But then the cancer cells just change the way they look, and the T regulatory cells say, 'Don't attack these guys. They're my friends,'" Loaiza-Bonilla explains.

Cancer cells may change to resist treatment in other ways too, including ways that researchers are still working to discover. Researchers also look for ways to thwart resistance.

JARED REY HERNANDEZ



ED RUSS found out that he had advanced colorectal cancer that spread to his lungs in 2016.

KAYE SNYDER

"A tremendous amount of work that goes on in cancer biology labs is studying best ways to try to overcome and prevent further resistance," Mayer says.

WHEN IT'S TIME TO CHANGE TREATMENTS

When a treatment stops working, the cancer resumes growing or begins cropping up in other places in the body as metastases. Doctors may find this through routine scans or tests that are typically done at scheduled intervals, or the patient may describe new symptoms, as Brickell did, that prompt the doctor to run tests.

In addition to Brickell's abdominal pain, a lymph node in her neck started to grow. If scans showed it was the cancer coming back, she knew she had an effective option awaiting her in Xalkori.

"When you're living with cancer, it's like, 'Well, there's another one,'" she said of the enlarged lymph node in her neck. "And you just have to report it."

She took Xalkori for 15 months, during which the spots on her lungs disappeared and the lymph nodes returned to normal size. "I had no evidence of disease," she says.

For Ed Russ it was different. The 64-year-old retired police detective from Homestead, Florida, was diagnosed in 2016 with advanced colorectal cancer that had spread to his lungs, but the lung metastases caused no symptoms at all.

"Honestly, I wouldn't have even known it was there," he said. But every time the doctors ordered a new round of scans after trying a different treatment, the images showed that the rectal tumor hadn't budged and that more spots had appeared on his lungs. »

For both Brickell and Russ, it was time to try something new, which can be nerve-racking.

"Patients with advanced disease, with some exceptions, are going to be on continuous treatment," notes Dr. Patricia Ganz, director of cancer prevention and control research at Jonsson Comprehensive Cancer Center at UCLA Medical Center in Los Angeles. "When the disease is well controlled, they know the routine, they know what the side effects are, so if they have to face a change, it's distressing,"

It also raises this question: Is this the end of the line?

"No," says Loaiza-Bonilla. Patients with advanced cancers should be prepared for treatment changes from the start.

"I tell patients, 'Sometimes advanced cancers are not curable, but they're treatable, and that means that we have to try different options as we go along,'" he says. "When it is time to try a new treatment, patients just know that this is an expected part of the process."

HOW TO CHOOSE THE NEXT MOVE

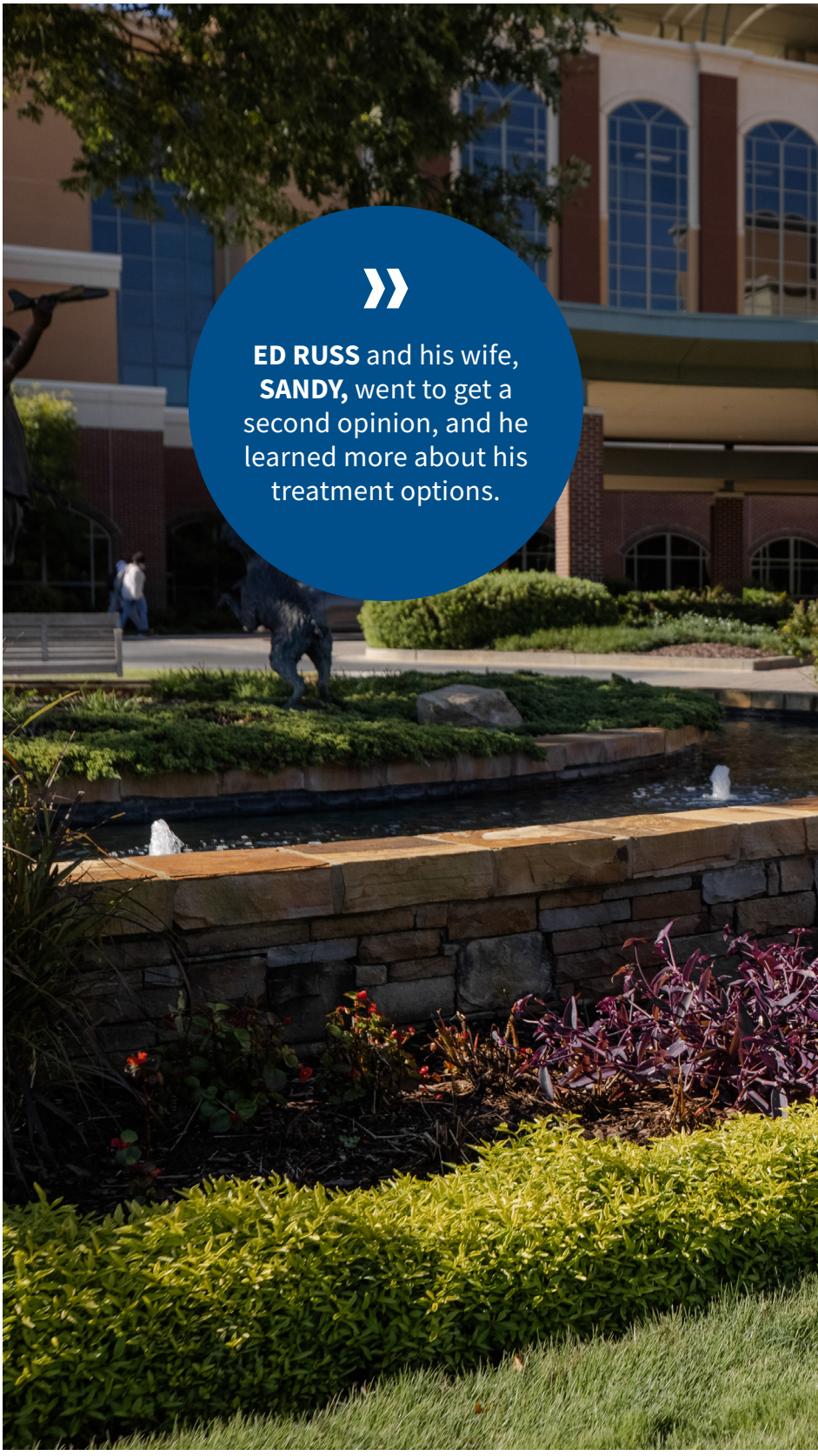
Oftentimes, doctors offer several options as a next treatment.

"Sometimes, there's no single so-called best next step because we can't predict the future. A treatment could work beautifully for patient A and then not work for patient B. There's so much unknown," says Dr. Xiuning Le, a thoracic oncologist at The University of Texas MD Anderson Cancer Center in Houston.

When a doctor offers multiple options, Le recommends that patients consider a few factors as they work with their doctor to decide.

"Gather as many options as possible, and then have your care team provide you with the benefit and toxicity data for each," she says. "For example, treatment A could have a 30% response rate but cause kidney damage 50% of the time, while treatment B could have a 15% response rate but little risk of harming you in any way."

If the benefits and efficacy of the different treatment options are similar, patients may choose based on possible side effects and other personal preferences. For example, logistics can figure in. Patients should consider whether a treatment, such as a clinical trial or an IV infusion, requires frequent travel to a faraway cancer center or multiple trips to an infusion center. In this case, a daily pill taken at home, for example, may be preferable.



» **ED RUSS** and his wife, **SANDY,** went to get a second opinion, and he learned more about his treatment options.

KAYE SNYDER

WHEN TREATMENT OPTIONS INCLUDE A CLINICAL TRIAL

Sometimes a clinical trial is among the available treatment options. Although participation may require travel and more frequent doctor visits, many physicians consider these studies to be an extra level of care. But patients often have misconceptions about them.

"We thought clinical trials were the last resort, when you're on your deathbed," says Sandy Russ, Ed's wife and his caregiver while he underwent treatment. "We were also afraid that in a clinical trial, somebody gets the drug and somebody gets the placebo. Who wants to take that chance?"

But the Russes learned that both are common misconceptions.

"Nowadays, there are lots of trials at all stages of care, even very early in the course of metastatic disease. So clinical trials are always an option," Ganz says.

What's more, cancer clinical trials are no longer placebo controlled unless standard-of-care treatment is given with the placebo. "No one gets a sugar pill or saline," Loaiza-Bonilla says. "You either get the standard treatment or the standard of care plus the experimental drug." But placebo is still needed in trials where the physicians and patients are providing information about response and side effects that might be biased by their knowing if the experimental drug is being given.

People might choose a clinical trial because the drug looks more promising than the other options, because they don't have other options or because they want the extra care and heightened surveillance that come along with it.

Brickell chose a clinical trial after her disease stopped responding to Xalkori. She had the choice between Lorbrena (lorlatinib), a Food and Drug Administration (FDA)-approved targeted drug for ALK-positive non-small cell lung cancer, and a clinical trial of repotrectinib, a drug that targets genetic changes in ROS1, ALK and TRK, at UT Southwestern Medical Center in Dallas.

"The main reason I chose to go with the clinical trial was if I did the FDA-approved (Lorbrena) first and it didn't work, that would be too many treatments and I would no longer qualify for that clinical trial," Brickell said. "So I thought, 'Let's try the clinical trial first.'" »

Brickell learned quickly that the drug wasn't helping her. She stopped the trial, and her primary oncologist put her on chemotherapy with docetaxel, to which the cancer is responding very well.

When patients have several options, sometimes they can (like Brickell planned to) choose one now and the other later. Some oncologists like to plan well in advance and start discussing clinical trial options that are most suitable when the patient is still doing well on their current treatment in case the patient progresses in the future. They might even send tissue for testing ahead of time, as more trials now require specific protein or genetic characteristics to qualify, and this avoids the time crunch if a patient needs new therapy quickly.

Just as with standard treatment, patients should make sure they understand the risks of the clinical trial treatment.

"Medications in phase 2 or 3 trials have usually gone through a number of trials, so the safety and dosing have been established," Le says. "Early-phase trials have detailed protocols in place to protect patients from harm. Overall, I encourage patients to consider enrolling in clinical trials."

> Overall, I encourage patients to consider enrolling in clinical trials.
>
> —DR. XIUNING LE

WHEN TO GET A SECOND OPINION

When a treatment stops working and it's time to move on, it may also be a good time to get a second opinion.

When the clinical trial didn't work for Brickell, she and her oncologist reached out to another oncologist, who is an expert in ROS1 gene changes, for a second opinion. He looked at the results of Brickell's most recent biopsy and saw that a second gene change, called a RET fusion, was copiloting and helping the ROS1 gene drive the cancer. Based on this new information, the oncologist recommended that Brickell stay on chemotherapy. If the chemotherapy stopped working, Brickell would go back to a ROS1-targeted therapy and add a RET inhibitor such as Retevmo (selpercatinib) or Gavreto (pralsetinib).

"Getting a second opinion is always very helpful, both to confirm the recommendation of the primary oncologist and to also potentially be offered other options," Ganz says.

Russ says a second opinion saved his life.

He had started his treatment at a local hospital in Florida near where he lives, and he had taken each of his doctor's recommendations. First, he got radiation and the oral chemotherapy capecitabine. The radiation shrunk the rectal tumor by a whopping 80%. But the chemo didn't affect the spots in his lungs. Next, Russ received the combination chemotherapy regimen known as FOLFOX (folinic acid, fluorouracil and oxaliplatin) via infusion for 24 weeks. The lung metastases, however, continued to grow and spread, and the rectal tumor was unchanged after the original dramatic response to radiation. Next, by then a year after receiving his diagnosis, Russ had surgery to remove the rectal tumor. It was a successful surgery, but the recovery was extremely difficult.

"I was at my lowest point after the surgery," Russ recalls.

And he still needed to have yet another round of chemotherapy — this time, with FOLFIRI (folinic acid, fluorouracil and irinotecan) — to try, yet again, to get the cancer that continued to grow and spread in his lungs. His care team at the local hospital said his only other option was surgery to remove nearly half of the left lobe of his lung. They warned him that it would be a very difficult surgery. When Russ' wife researched and presented other options to her husband's doctors, they dismissed each one.

Things were bleak by that point. "Ed was in such bad shape. He was just existing," says his wife, Sandy. "He wasn't living. My biggest fear was that he would die, and I would find out that there was something else available that he could have tried."

The Russes went to Cancer Treatment Centers of America for a second opinion. There, doctors confirmed that surgery was a good possible option for Russ but that if he didn't want to undergo another procedure, there were alternatives.

A biopsy revealed that his lung tumors were HER2 positive, a common characteristic of breast tumors, making him eligible for targeted therapy. But because he would receive the targeted drug via IV infusion, like chemotherapy, he worried it would wipe him out in the same way. So he opted for surgery.

The surgeon removed the entire lower left lobe of his lung and all the cancer with it. When the cancer returned, Russ knew he had options. He started an experimental regimen of Herceptin (trastuzumab) and Perjeta (pertuzumab), FDA-approved drugs for HER2-positive breast cancers.

At Russ' nine-week scan, the lesions on his lungs were notably smaller. At 18 weeks, they were gone.

In December 2020, Russ was able to stop the drugs. He had one small recurrence in his lungs, which was removed with surgery. His last two scans were clean, so Russ is currently cancer-free.

"Unlike when I started this process, I'm not afraid," Russ said. "I know that if another one comes up, I have options."

CANCER

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MMRF and ***CURE***® led a team of 12 individuals on a hike through Alaska's Kenai Peninsula.

A '*Jolt*' of Inspiration

Myeloma survivors, their loved ones and clinicians trekked up the Alaska-Kenai Peninsula to raise money and funds for the disease, offering one nurse the inspiration she needed after more than a year of the COVID-19 pandemic.

By BRIELLE BENYON

AS THE COVID-19 PANDEMIC continues to put added stress on health care workers across the nation, one New York City-based nurse practitioner reconnected with her passion for treating patients in an unlikely place: hiking in Alaska alongside myeloma survivors, their loved ones and other clinicians.

"(COVID-19) had hit New York City hard. We all got redeployed to the front lines, and I think it was a really hard spring 2020 — a lot of health care professionals retired shortly after that," said Donna Catamero, associate director of myeloma translation research at Mount Sinai Health System, in an interview with *CURE*®. "I felt like I never got my mojo back. … I really needed a jolt to get me inspired again."

That "jolt" was found this past August when Catamero participated in the Moving Mountains for Multiple Myeloma program, a joint initiative between the Multiple Myeloma Research Foundation (MMRF) and *CURE*® to raise funds and awareness for myeloma. This year's fundraising effort took a team of 12 individuals on a journey hiking through Alaska's Kenai Peninsula. Previous treks included Kilimanjaro, Everest Base Camp (in Nepal), Machu Picchu, the Grand Canyon and Mount Fuji.

Catamero was joined by a dozen other people who also share the drive to improve outcomes for individuals with myeloma — including five patients currently living with myeloma — for the five-day trek that spanned 37 miles. She recently discussed the climb in an interview with *CURE*®.

» DONNA CATAMERO

Q: How did you hear about the MMRF program, and what was your first reaction?

A: It was a few years ago. I worked with the MMRF on research studies. I run the clinical trials program in our network sites. We're focusing on bringing novel therapies to underserved areas. … They were having a trek in Machu Picchu. (I) and some of my colleagues were really excited about (it), so we joined in.

I did my first hike … and I thought it was really inspiring to hike alongside patients and their caregivers.

And this next opportunity came … to (hike) in Alaska, and I said, "I think (it) would be good for me to do (this) on my own." It was such a great experience, even more so than Machu Picchu, because I really got to know the patients and their caregivers. And it really was inspiring. It gave me a little boost to rejuvenate my career, meaning it gave me more inspiration and the boost I needed post-COVID-19 slump.

Q: How did the fellow climbers — especially the myeloma survivors — encourage you throughout the climb?

A: I'm helping them, they're helping me. And seeing what they go through on a day-to-day basis and seeing them being able to do these (difficult) climbs … really was inspiring. It gave me a different perspective, and I was able to walk in their shoes because (at work), I go into an exam room, I talk to patients about their cancer, their treatments, their side effects, how to manage it, but (I) don't see the day-to-day life of a patient. This gave me the opportunity to really experience everything outside of the clinic with them. So, you know, we laughed, we joked, we cried together. It was really inspiring.

Q: What do you hope for these patients — and the myeloma field as a whole — in coming years?

A: I started (my career) in clinical research. When I started, the overall survival of a myeloma patient, regardless of their risk factors, was about three years. So patients did not do well. And this was in the mid-'90s. And now patients are living 10, 15, even 20 years out from their diagnosis. And, you know, this is all within my lifetime.

I still have a lot of life to live. So I hope that if we can't see a cure, I feel like myeloma will be — and it is to some (extent) — a chronic disease that can be managed well while patients are maintaining a really good quality of life.

PHOTOS COURTESY OF MMRF

INDICATIONS

KISQALI® (ribociclib) is a prescription medicine used in combination with:

- an aromatase inhibitor to treat pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer that has spread to other parts of the body (metastatic), as the first endocrine-based therapy; or
- fulvestrant to treat postmenopausal women with HR-positive, HER2-negative metastatic breast cancer as the first endocrine-based therapy or with disease progression following endocrine therapy

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

IMPORTANT SAFETY INFORMATION

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

KISQALI may cause serious side effects, including:

Lung problems. KISQALI may cause severe or life-threatening inflammation of the lungs during treatment that may lead to death. Tell your health care provider right away if you have any new or worsening symptoms, including:

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

Severe skin reactions. Tell your health care provider or get medical help right away if you get severe rash or rash that keeps getting worse; reddened skin; flu-like symptoms; skin pain/burning; blistering of the lips, eyes, or mouth; or blisters on the skin or skin peeling, with or without fever.

Heart rhythm problems (QT prolongation). KISQALI can cause a heart problem known as QT prolongation. This condition can cause an abnormal heartbeat and may lead to death. Your health care provider should check your heart and do blood tests before and during treatment with KISQALI. Tell your health care provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or if you feel dizzy or faint.

Liver problems (hepatobiliary toxicity). KISQALI can cause serious liver problems. Your health care provider should do blood tests to check your liver before and during treatment with KISQALI. Tell your health care provider right away if you get any of the following signs and symptoms of liver problems:

- yellowing of your skin or the whites of your eyes (jaundice)
- dark or brown (tea-colored) urine
- feeling very tired
- loss of appetite
- pain on the right side of your stomach area (abdomen)
- bleeding or bruising more easily than normal

Low white blood cell counts (neutropenia). Low white blood cell counts are very common when taking KISQALI and may result in infections that may be severe. Your health care provider should check your white blood cell counts before and during treatment with KISQALI. Tell your health care provider right away if you have signs and symptoms of low white blood cell counts or infections such as fever and chills.

Your health care provider may tell you to decrease your dose, temporarily stop, or completely stop taking KISQALI if you develop certain serious side effects during treatment with KISQALI.

KISQALI is helping women like Dee live longer than ever before

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In clinical trials, KISQALI in combination with hormone therapy extended the length of time women were alive from the start of treatment—also called overall survival (OS). It also extended progression-free survival (PFS)—the primary outcome measure of the trials—which is the length of time a treatment puts cancer growth on pause.

At a 54-month observational check in during a clinical trial for premenopausal women, which was not predetermined or controlled for a false positive, results showed the median OS was 58.7 months for KISQALI + a nonsteroidal aromatase inhibitor (NSAI) + goserelin vs 47.7 months for an NSAI + goserelin.

In the same clinical trial at a 35-month check in, KISQALI + an NSAI + goserelin delayed disease progression for a median of 27.5 months vs 13.8 months for an NSAI + goserelin.

KISQALI is not approved for use with tamoxifen.

What should I tell my health care provider before taking KISQALI?

Before you take KISQALI, tell your health care provider if you:

- have any heart problems, including heart failure, irregular heartbeats, and QT prolongation
- have ever had a heart attack
- have a slow heartbeat (bradycardia)
- have problems with the amount of potassium, calcium, phosphorus, or magnesium in your blood
- have fever, chills, or any other signs or symptoms of infection
- have liver problems
- have any other medical conditions
- are pregnant, or plan to become pregnant. KISQALI can harm your unborn baby
  - If you are able to become pregnant, your health care provider should do a pregnancy test before you start treatment with KISQALI.
  - Females who are able to become pregnant and who take KISQALI should use effective birth control during treatment and for at least 3 weeks after the last dose of KISQALI.
  - Talk to your health care 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 health care provider right away.
- are breastfeeding or plan to breastfeed. It is not known if KISQALI passes into your breast milk. Do not breastfeed during treatment with KISQALI and for at least 3 weeks after the last dose of KISQALI

Please see Summary of Important Information on the following page.

Tell your health care provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. KISQALI and other medicines may affect each other, causing side effects. Know the medicines you take. Keep a list of them to show your health care provider or pharmacist when you get a new medicine.

What should I avoid while taking KISQALI?

Avoid eating grapefruit and avoid drinking grapefruit juice during treatment with KISQALI since these may increase the amount of KISQALI in your blood.

The most common side effects of KISQALI include:

- neutropenia
- nausea
- infections
- fatigue
- diarrhea
- leukopenia
- vomiting
- hair loss
- headache
- constipation
- rash
- cough

KISQALI may cause fertility problems if you are male and take KISQALI. This may affect your ability to father a child. Talk to your health care provider if this is a concern for you.

Tell your health care provider if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of KISQALI. For more information, ask your health care provider or pharmacist. 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.

SUMMARY OF IMPORTANT INFORMATION

What is KISQALI® (ribociclib)?

KISQALI is a prescription medicine used in combination with:

- an aromatase inhibitor to treat pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer that has spread to other parts of the body (metastatic), as the first endocrine-based therapy; or
- fulvestrant to treat postmenopausal women with HR-positive, HER2-negative metastatic breast cancer as the first endocrine-based therapy or with disease progression following endocrine therapy

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

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

KISQALI may cause serious side effects, including:

Lung problems. KISQALI may cause severe or life-threatening inflammation of the lungs during treatment that may lead to death. Tell your health care provider right away if you have any new or worsening symptoms, including:

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

Severe skin reactions. Tell your health care provider or get medical help right away if you get severe rash or rash that keeps getting worse; reddened skin; flu-like symptoms; skin pain/burning; blistering of the lips, eyes, or mouth; or blisters on the skin or skin peeling, with or without fever.

Heart rhythm problems (QT prolongation). KISQALI can cause a heart problem known as QT prolongation. This condition can cause an abnormal heartbeat and may lead to death. Your health care provider should check your heart and do blood tests before and during treatment with KISQALI. Tell your health care provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or if you feel dizzy or faint.

Liver problems (hepatobiliary toxicity). KISQALI can cause serious liver problems. Your health care provider should do blood tests to check your liver before and during treatment with KISQALI. Tell your health care provider right away if you get any of the following signs and symptoms of liver problems:

- yellowing of your skin or the whites of your eyes (jaundice)
- dark or brown (tea-colored) urine
- feeling very tired
- loss of appetite
- pain on the right side of your stomach area (abdomen)
- bleeding or bruising more easily than normal

Low white blood cell counts (neutropenia). Low white blood cell counts are very common when taking KISQALI and may result in infections that may be severe. Your health care provider should check your white blood cell counts before and during treatment with KISQALI. Tell your health care provider right away if you have signs and symptoms of low white blood cell counts or infections such as fever and chills.

Your health care provider may tell you to decrease your dose, temporarily stop, or completely stop taking KISQALI if you develop certain serious side effects during treatment with KISQALI.

What should I tell my health care provider before taking KISQALI?

Before you take KISQALI, tell your health care provider if you:

- have any heart problems, including heart failure, irregular heartbeats, and QT prolongation
- have ever had a heart attack
- have a slow heartbeat (bradycardia)
- have problems with the amount of potassium, calcium, phosphorus, or magnesium in your blood
- have fever, chills, or any other signs or symptoms of infection
- have liver problems
- have any other medical conditions
- are pregnant, or plan to become pregnant. KISQALI can harm your unborn baby
  - If you are able to become pregnant, your health care provider should do a pregnancy test before you start treatment with KISQALI.
  - Females who are able to become pregnant and who take KISQALI should use effective birth control during treatment and for at least 3 weeks after the last dose of KISQALI.
  - Talk to your health care 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 health care provider right away.
- are breastfeeding or plan to breastfeed. It is not known if KISQALI passes into your breast milk. Do not breastfeed during treatment with KISQALI and for at least 3 weeks after the last dose of KISQALI

What other medications might interact with KISQALI?

Tell your health care provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements (especially St. John's wort). KISQALI and other medicines may affect each other, causing side effects. Know the medicines you take. Keep a list of them to show your health care provider or pharmacist when you get a new medicine.

What should I avoid while taking KISQALI?

Avoid eating grapefruit and avoid drinking grapefruit juice during treatment with KISQALI since these may increase the amount of KISQALI in your blood.

What laboratory tests do I need if I am prescribed KISQALI?

Your doctor should check your heart rhythm, liver, and blood before you start KISQALI and periodically during your treatment with KISQALI. Your doctor may eventually stop checking some of these tests. If you are able to become pregnant, your health care provider should do a pregnancy test before you start treatment with KISQALI.

The most common side effects of KISQALI include:

- neutropenia
- nausea
- infections
- fatigue
- diarrhea
- leukopenia
- vomiting
- hair loss
- headache
- constipation
- rash
- cough

KISQALI may cause fertility problems if you are male and take KISQALI. This may affect your ability to father a child. Talk to your health care provider if this is a concern for you.

Tell your health care provider if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of KISQALI. For more information, ask your health care provider or pharmacist. 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.

General information about the safe and effective use of KISQALI

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use KISQALI for a condition for which it was not prescribed. Do not give it to other people, even if they have the same symptoms you have. It may harm them. You can ask your health care provider or pharmacist for more information about KISQALI.

For more information, go to www.kisqali.com or call 1-844-KIS-QALI (1-844-547-7254).

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‘Landmark’ FDA Approval of Tibsovo May Improve Outcomes for Some Patients

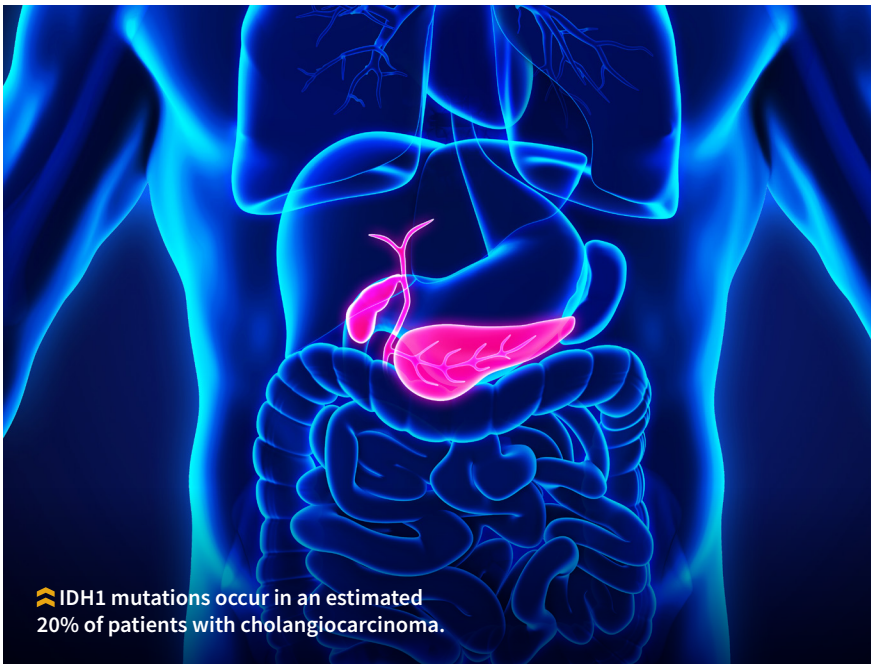
This urgently needed treatment option is the first and only targeted therapy approved for patients with previously treated cholangiocarcinoma with an IDH1 mutation.

By ANTONIA DEPACE

PATIENTS LIVING WITH cholangiocarcinoma with an IDH1 mutation may have better survival outcomes with the recent Food and Drug Administration (FDA) approval of Tibsovo (ivosidenib).

Tibsovo was approved based on findings from the randomized phase 3 ClarIDHy clinical trial. It is the first targeted therapy for patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an IDH1 gene mutation and the third drug approved overall for the hard-to-treat disease. Cholangiocarcinoma is a rare, aggressive cancer of the bile ducts within and outside the liver, with IDH1 mutations occurring in approximately 20% of cholangiocarcinoma cases, according to Dr. Rachna T. Shroff, a researcher on the trial. Shroff added that 20% is “a significant chunk of this population.”

“This is a landmark approval. This is a disease that, for the longest time, we had no FDA-approved therapies,” said Shroff, an associate professor of medicine at the University of Arizona and chief of gastrointestinal medical oncology at the University of Arizona Cancer Center in Tucson, in an interview with *CURE*®. “In the setting of a locally advanced and metastatic disease, it carries a dismal prognosis and, historically, even though there are 8,000 cases of cholangiocarcinoma a year, it was treated almost like an orphan disease with very little interest in terms of drug development.”



» IDH1 mutations occur in an estimated 20% of patients with cholangiocarcinoma.

Findings from the trial demonstrated statistically significant improvement in progression-free survival (time during and after treatment when the patient lives without disease worsening) with Tibsovo (2.7 months) versus placebo (1.4 months). The most common side effects reported were fatigue, nausea, abdominal pain, diarrhea, cough, decreased appetite, vomiting, anemia, rash and ascites (abdominal swelling caused by an accumulation of fluid).

“Tibsovo is actually a very well-tolerated therapy. … I can’t even tell you how happy patients were to be on a pill and to not have IV »

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(chemotherapy)," Shroff said. "I think it's important to point out that a lot of the side effects that patients were talking about are side effects that also come from this disease, from cholangiocarcinoma. So abdominal pain — ascites, I mean — these are things that, unfortunately, a lot of our patients live with."

She added that having the option of taking a pill rather than undergoing IV chemotherapy seemed to help patients both psychologically and emotionally. "It's just so much more palatable to take a pill," she said.

The approval of Tibsovo highlights the importance of biomarker testing, said Shroff. Before the approval, patients with IDH1-mutated cholangiocarcinoma were treated similarly to patients without the mutation and given combination chemotherapy of gemcitabine and cisplatin in the frontline setting, which had low response rates and low progression-free survival.

"It speaks to the importance of doing biomarker testing on every single cholangiocarcinoma patient. I cannot underscore it enough to patients to advocate for that and to providers to know that we should be doing it at this point," she said, adding that knowing if a patient has an IDH1 mutation can also help to better plan for second- and third-line treatments.

Shroff noted that although the IDH1 mutation is not prognostic for cholangiocarcinoma when predicting outcomes on specific treatments, knowing that the mutation responds to a targeted therapy is a huge step forward.

"As completely cheesy as it sounds, I was tearing up when this approval came ... because in January of 2020, we had zero drugs FDA approved for (cholangiocarcinoma), and we have three now," she said. "And that's just unbelievable to see and to think about what that means for our patients."

'The Future Is Promising' for Relapsed/Refractory MCL

More selective BTK inhibitors like Brukinsa may give patients who progressed on prior therapies another option with potentially fewer and more manageable side effects. *By* DARLENE DOBKOWSKI, M.A.

BRUTON TYROSINE KINASE (BTK) inhibitors have been a major focus of research for the treatment of patients with relapsed/refractory mantle cell lymphoma (MCL), and the recent Food and Drug Administration (FDA) approval of Brukinsa (zanubrutinib) may give patients another option with potentially fewer, more manageable side effects.

DR. PREETESH JAIN

BTK, which plays a critical role in the development of B cells, is a clinically validated target in these patients. Previously, the FDA approved the BTK inhibitor Imbruvica (ibrutinib) for this patient population.

"(Imbruvica) has shown very good results; however, the side effect profile of (Imbruvica) results in a fraction of patients who discontinue due to intolerance, especially cardiovascular side effects," said Dr. Preetesh Jain, an assistant professor in the department of lymphoma and myeloma at The University of Texas MD Anderson Cancer Center in Houston, in an interview with *CURE*®. "Atrial fibrillation (irregular heartbeat) is a major concern. Therefore, more selective BTK inhibitors with less chance of side effects are being investigated."

Data have shown promise for Brukinsa, especially regarding side effects.

"(Brukinsa) appears to have more benefit for patients with regard to less atrial fibrillation, hypertension (high blood pressure) and other cardiac effects," Jain said. "(Brukinsa) is easier to take. It has (fewer) side effects, less dose-reduction probability and a good tolerability. The patients can stay on it for a longer time. … This means most patients can continue and maintain remission on (Brukinsa) without encountering major safety issues."

Brukinsa provides patients with MCL a second-generation BTK inhibitor besides Calquence (acalabrutinib).

"(Brukinsa) does not have any (drug-drug interactions) like (Calquence) and, similar to (Calquence), demonstrates an improved safety profile compared to the first-generation medication (Imbruvica)," Dr. Tycel J. Phillips, an assistant professor of medicine at University of Michigan Rogel Cancer Center in Ann Arbor, told *CURE*®. "(Brukinsa) as well could potentially be given once daily in situations where patient compliance is of concern."

Data from a phase 1/2 study published in *Blood Advances* this »

year demonstrated similar results in 32 patients with relapsed/refractory MCL treated with Brukinsa. After a median follow-up of 18.8 months, patients achieved an overall response rate of 84% and a complete response rate of 25%. The median progression-free survival (time when a patient's disease does not worsen) was 21.1 months, with a median time to response (length of time it took a patient's disease to respond to treatment) of 2.8 months.

"(These findings) continue to reenforce that the agent has an improved safety profile and tolerability compared to (Imbruvica)," Phillips said. "Efficacy-wise, the publication supports that (Brukinsa) maintains a high efficacy rate in all populations, given that the original data reported on a Chinese-only cohort of patients."

In the original study, published in *Clinical Cancer Research* in 2020, researchers assessed the effects of Brukinsa in 86 Chinese patients with relapsed/refractory MCL. A 160-milligram, twice-daily dose resulted in an objective response rate (patients with tumor size reduction over a period of time) of 84% and a complete response rate (disappearance of all signs of cancer from treatment) of 68.6% after a median follow-up of 18.4 months.

"Given that the treatment of MCL is different in China compared to the U.S., Europe and Australia, this helps to ensure that the efficacy of the drug was not impacted by these differences," Phillips said about comparing the original data with the newer data.

In the study published this year, the most common side effects of Brukinsa were bruising (37.5%), diarrhea (43.8%), constipation (31.3%) and upper respiratory tract infection (31.3%). At least one side effect considered severe or worse occurred in 59.4% of patients and included pneumonia (9.4%), anemia (12.5%), neutropenia (lower levels of a type of white blood cell, which may indicate infection; 9.4%) and muscle pain (9.4%).

> Most patients can continue and maintain remission on (Brukinsa) without encountering major safety issues.
>
> —DR. PREETESH JAIN

"Patients can also develop other low-grade side effects including fatigue, skin rash (and) headaches," Jain said. "However, the clinical severity and management of side effects highly depends on many other factors: patient age, comorbidities (the presence of two or more diseases or medical conditions) and organ function."

Jain added that side effects in most patients can be managed.

Despite the positive data emerging from studies focused on Brukinsa for the treatment of MCL, more research is needed in this area, including for those who may not respond to this therapy or become resistant to it.

"There still remains an unmet need for some patients, as the efficacy of the agent is no different from the others in the class, which means that approximately 15% to 20% of patients will not respond to BTK (inhibitors), and, as such, combinations to improve outcomes are being explored," Phillips said.

Jain added, "The efficacy and toxicity profile of (Brukinsa) in (the) frontline setting in (patients with mantle cell lymphoma) is being investigated in both (older), transplant-ineligible and frontline young patients in combination with rituximab (Rituxan) and venetoclax (Venclexta). Longer follow-up and randomized studies are needed before confirming the superiority of (Brukinsa) over (Imbruvica)."

As more study results become available demonstrating the possibility of additional treatment options for this patient population, Phillips and other oncologists remain hopeful.

"New treatment options for MCL have continued to expand, which has led to better outcomes for our patients," Phillips said. "Hopefully, we will be able to cure this cancer, but until that time, if we can continue to have promising agents like (Brukinsa) enter this space, the future is promising."

For the treatment of **mantle cell lymphoma**

BRUKINSA® (zanubrutinib) is a BTK inhibitor that was designed to completely block BTK

- Mantle cell lymphoma (MCL) is caused by rapid growth and spread of cancerous B cells
- Bruton's tyrosine kinase (BTK) is a protein that signals to cancerous B cells, helping them to grow and spread
- Blocking BTK can help stop this signaling

BRUKINSA has been shown to block 100% of BTK in blood cells and 94% to 100% of BTK in lymph nodes when taken at the recommended total daily dose of 320 mg. The significance of completely blocking BTK on treatment responses has not been established.

BRUKINSA is a BTK inhibitor for adults with mantle cell lymphoma who have received at least 1 prior therapy. BRUKINSA was approved based on response rate. There is ongoing evaluation to confirm clinical benefit for this use. It is not known if BRUKINSA is safe and effective in children.

IMPORTANT SAFETY INFORMATION

What should I tell my healthcare provider before taking BRUKINSA?

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

- have bleeding problems
- have had recent surgery or plan to have surgery. Your healthcare provider may stop BRUKINSA for any planned medical, surgical, or dental procedure.
- have an infection
- have or had heart rhythm problems
- have high blood pressure
- have liver problems, including a history of hepatitis B (HBV) infection.
- are pregnant or plan to become pregnant. BRUKINSA can harm your unborn baby. If you are able to become pregnant, your healthcare provider may do a pregnancy test before starting treatment with BRUKINSA.
  - **Females** should not become pregnant during treatment and at least 1 week after the last dose of BRUKINSA. You should use effective birth control (contraception) during treatment and for at least 1 week after the last dose of BRUKINSA.
  - **Males** should avoid getting female partners pregnant during treatment and for at least 1 week after the last dose of BRUKINSA.
- are breastfeeding or plan to breastfeed. It is not known if BRUKINSA passes into your breast milk. Do not breastfeed during treatment with BRUKINSA and for at least 2 weeks after your last dose of BRUKINSA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking BRUKINSA with certain other medications may affect how it works and can cause side effects.

What are the possible side effects of BRUKINSA?

BRUKINSA may cause serious side effects, including:

- **Bleeding problems (hemorrhage)** that can be serious and may lead to death. Your risk of bleeding may increase if you are also taking a blood thinner medicine. Tell your healthcare provider if you have any signs or symptoms of bleeding, including:
  - blood in your stools or black stools (looks like tar)
  - pink or brown urine
  - unexpected bleeding, or bleeding that is severe or you cannot control
  - vomit blood or vomit that looks like coffee grounds
  - cough up blood or blood clots
  - increased bruising
  - dizziness
  - weakness
  - confusion
  - changes in your speech
  - headache that lasts a long time
- **Infections** that can be serious and may lead to death. Tell your healthcare provider right away if you have fever, chills, or flu-like symptoms.
- **Decrease in blood cell counts.** Decreased blood counts (white blood cells, platelets, and red blood cells) are common with BRUKINSA, but can also be severe. Your healthcare provider should do blood tests during treatment with BRUKINSA to check your blood counts.
- **Second primary cancers.** New cancers have happened in people during treatment with BRUKINSA, including cancers of the skin. Use sun protection when you are outside in sunlight.
- **Heart rhythm problems (atrial fibrillation and atrial flutter).** Tell your healthcare provider if you have any of the following signs or symptoms:
  - your heartbeat is fast or irregular
  - feel lightheaded or dizzy
  - pass out (faint)
  - shortness of breath
  - chest discomfort

The most common side effects of BRUKINSA include:

- decreased white blood cells
- decreased platelet count
- rash
- diarrhea
- upper respiratory infection
- decreased red blood cells (anemia)
- bruising
- cough

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

What is BRUKINSA?

BRUKINSA is a prescription medicine used to treat adults with mantle cell lymphoma (MCL) who have received at least one prior treatment for their cancer.

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

Please see full Prescribing Information at BRUKINSA.com.

LEARN MORE AT BRUKINSA.COM

Brukinsa® zanubrutinib 80mg capsules

Understanding the Variability of a Rare Blood Cancer

An expert discusses two primary unmet needs in myelofibrosis, current treatments and new approaches to this complex disease.

By RYAN MCDONALD

MORE FOCUS IS NEEDED ON the development of new drugs that treat low blood counts and new therapies that eradicate the disruption to bone marrow in patients with myelofibrosis, according to an expert.

In an interview with *CURE*®, Dr. Ann Mullally, an associate professor of medicine at Harvard Medical School and a physician-scientist at Brigham and Women's Hospital and Dana-Farber Cancer Institute in Boston, discussed this rare blood cancer, who is at higher risk and indicators of the disease. She also noted some unmet needs in treating myelofibrosis and some exciting developments on the horizon.

Q: Can you explain what myelofibrosis is and who is at higher risk?

A: Myelofibrosis is a type of blood cancer that is uncommon. Like all cancers, it's associated with aging, so it's most common in people in their 60s and older. Sometimes, however, younger patients can get it.

It's primarily a problem in the bone marrow. The bone marrow is the factory that makes blood for the body. All the cells in our blood originate in the bone marrow, and myelofibrosis arises when mutations happen within the blood-forming cells — called hematopoietic stem cells — and alter the behavior of those cells. They result in a scarring of the bone marrow. And that's where the name comes from, fibrosis. There's a scarring in the bone marrow, and that has consequences. Patients can have low blood counts. Then their bodies try to make blood in other sites, particularly the spleen.

Patients can require blood transfusions. Scarring (fibrosis) in the bone marrow can result in an enlarged spleen because the bone marrow is not very good at making blood anymore, and the spleen tries to make blood to compensate.

Q: Are there other symptoms of myelofibrosis?

A: Myelofibrosis is a type of myeloproliferative neoplasm, or MPN. And sometimes these MPNs can show up as incidental findings. Somebody can go to their primary care doctor, get (blood drawn), and (the results) can come back abnormal. In general with myelofibrosis, that's a more uncommon way for it to present. Most times people present with some type of symptoms including low blood counts, fatigue, weight loss, fevers, sweats and abdominal pain.

With myelofibrosis, it's more common that people develop symptoms that trigger tests that result in the diagnosis. In other (MPNs), it can be that you just have a blood count and something incidental shows up, but with myelofibrosis, it is more common for people to have symptoms that precipitate getting a blood test drawn.

Q: What are some available treatment options?

A: There are things that we look at when somebody comes to the clinic. We try to focus on the patient's main problem. Some people come in, and their main problem is that their spleen is very big and it's uncomfortable, their blood counts are elevated, and they're losing weight. In a situation like that, something like a JAK2 (Janus kinase 2) inhibitor can be very helpful because it can bring down the blood counts, it can shrink the spleen, and it can help patients gain weight.

Other patients may have very low blood counts. In those patients, we focus on blood transfusions to maintain their red blood cell count. Sometimes we use medicines like recombinant erythropoietin to try to stimulate their bone marrow to make its own red blood cells. There are some newer drugs being developed in this area, but we have (fewer) tools in our toolkit in that situation.

In a situation where somebody is of an age where they would be considered eligible to get a stem cell transplantation — generally considered up to age 70 — and if they've had treatment and the disease has progressed on a JAK2 inhibitor or other treatments, then we consider stem cell transplantation in certain situations. But that's a big decision because there are substantial risks associated with it.

We're trying to weigh the risks of the myelofibrosis and of it causing the patient further problems versus the risk associated with transplant. There's tremendous variability in myelofibrosis from patient to patient, in terms of the underlying biology of their disease and the problems that

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they face — and how we address them — and it's an individualized approach. But it can change over time.

In the beginning, a patient can have a certain problem, then it can change and become a different problem. Patients come back to the clinic on a regular basis and are constantly being evaluated. One very optimistic and positive thing is that we're developing new treatments. We have several JAK2 inhibitors. We have two approved by the (Food and Drug Administration), we have more coming in advanced-phase clinical trials, and we have a lot of drugs that are separate from targeting the JAK/STAT pathway that are also in clinical trials. That gives us more options. If a patient were to progress, for example, on a JAK2 inhibitor, then there can be options in terms of clinical trials or new drugs that are available and can be helpful.

Q: What are some developments we can expect in the next year or so?

A: I think there will likely be approval of additional JAK2 inhibitors, on top of the two that we have, and there are slight differences between them. And, in general, having more drugs is always better because sometimes there are some idiosyncrasies, and some patients just don't react well to one drug and might react well to another drug.

If patients progress and the JAK2 inhibitor is no longer working, then in general, we have a lot of clinical trials that add (another) agent to the JAK2 inhibitor. And those are generally things that are distinct and separate from the JAK/STAT pathway, (which) we think is good because you're sort of targeting a different mechanism of action. If the cell is no longer responding to the JAK2 inhibitor, now we can target a different distinct pathway. And several ongoing trials of agents look to have clinical activity in myelofibrosis.

This interview has been edited for clarity and conciseness.

To read the full story, **SCAN** the QR code. »

LEARN MORE ONLINE
SCAN HERE to learn more about our Ambassador program and to read more ambassadors' stories.

INTRODUCING THE *CURE*® AMBASSADOR PROGRAM

This program connects individuals at every stage of the cancer experience with others who have been on the same journey.

THE *CURE*® AMBASSADOR PROGRAM was created this year to help connect readers with patients, survivors, caregivers and others that they identify with and want to hear from. In particular, ambassadors have big social media followings and may be some familiar faces (or voices) who have their work recognized. This program allows ambassadors to share their experiences through written pieces and video blogs and participate in *CURE*® events, enabling them to connect with individuals at every stage of the cancer experience.

What follows are some excerpts from recent stories shared by ambassadors on our website.

> "I do not know why this happened to me, but I do believe there is a purpose now. One of the most frustrating things about my diagnosis is the lack of knowledge about it. The majority of the time, I find myself educating people about what happened to me because nobody has ever heard of molar pregnancies and the cancer they can cause. Even in the medical world, a lot of mistakes are made because most doctors and nurses just simply never see one in their career."
>
> — ***MICHELLE VELEZ,*** a Las Vegas news anchor who developed stage 4 metastatic choriocarcinoma due to her third pregnancy

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"And now, as deemed healthy again and cancer-free, I had to go back to a normal life. And I gained a new perspective while I was going through this journey and a new sense of gratefulness. But I was a changed person. I am a changed person. So I had to make the decision: 'Do I want to go back to work? Do I want to go back to New York City? Do I want to have the same friends? Do I want to live the life that I was previously experiencing?' And these were really, really big decisions."

— NINA LUKER, age 25, director of partnerships at Shuttlerock and a stage 4 diffuse large B-cell lymphoma survivor

"Cancer is often referred to as a six-letter word, much akin to those four-letter words that are frowned upon, but it can be so much more. This journey has taught me to savor the little things like sunrises over the mountains, the sound of waves crashing on the beach and hugs from those we love. It has introduced me to the most authentic people that I would not have met otherwise and taught me the importance of experiences over things. Life after cancer can be amazing if we open our eyes to see it.

— LACEY BUCHORN, a long-distance runner and 13-plus year chronic lymphocytic leukemia survivor who shares her journey openly on social media

"I can give you chapter and verse about my particular type of cancer. And now my sense of empathy is so keen that when I say to someone virtually or literally holding their hand, 'I get it,' I really do. And I know there are many of you out there hopefully watching this who get the same experience, who have had the same experience.

— ROB PAULSEN, the voice of Pinky in "Pinky and the Brain" and Yakko in "Animaniacs," among others, who was diagnosed with stage 3 metastatic squamous cell carcinoma of the throat in 2016

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In patients with CSCC that has spread or cannot be cured by surgery or radiation:

LIBTAYO works with your immune system to help treat advanced CSCC

In 1 clinical trial of 137 patients with CSCC that had spread or could not be cured by surgery or radiation treated with LIBTAYO*:

46% 63 out of 137 patients saw an improvement in their advanced CSCC.

Responses to LIBTAYO lasted 6 months or longer in **50 out of 63 patients (79%)** and 12 months or longer in **34 out of 63 patients (54%)**.

In the same clinical trial, in a separate group of 56 patients with CSCC that had spread who took LIBTAYO at the recommended dose†:

41% 23 out of 56 patients saw an improvement in their advanced CSCC.

Responses to LIBTAYO lasted 6 months or longer in **15 out of 23 patients (65%)**.

In this trial, responses lasted between 2 months and more than 2 years (24.2+ months); plus sign (+) denotes ongoing at last assessment.

*Patients were dosed by body weight.
†LIBTAYO 350 mg over a 30-minute infusion every 3 weeks.
CSCC=cutaneous squamous cell carcinoma.

LIBTAYO may not work for everyone.

**LIBTAYO Surround® offers support and resources to patients prescribed LIBTAYO.
If you think LIBTAYO may be right for you, talk to your doctor.**

What is LIBTAYO?

LIBTAYO (Lib-TIE-oh) is a prescription medicine used to treat people with a type of skin cancer called cutaneous squamous cell carcinoma (CSCC) that has spread or cannot be cured by surgery or radiation.

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

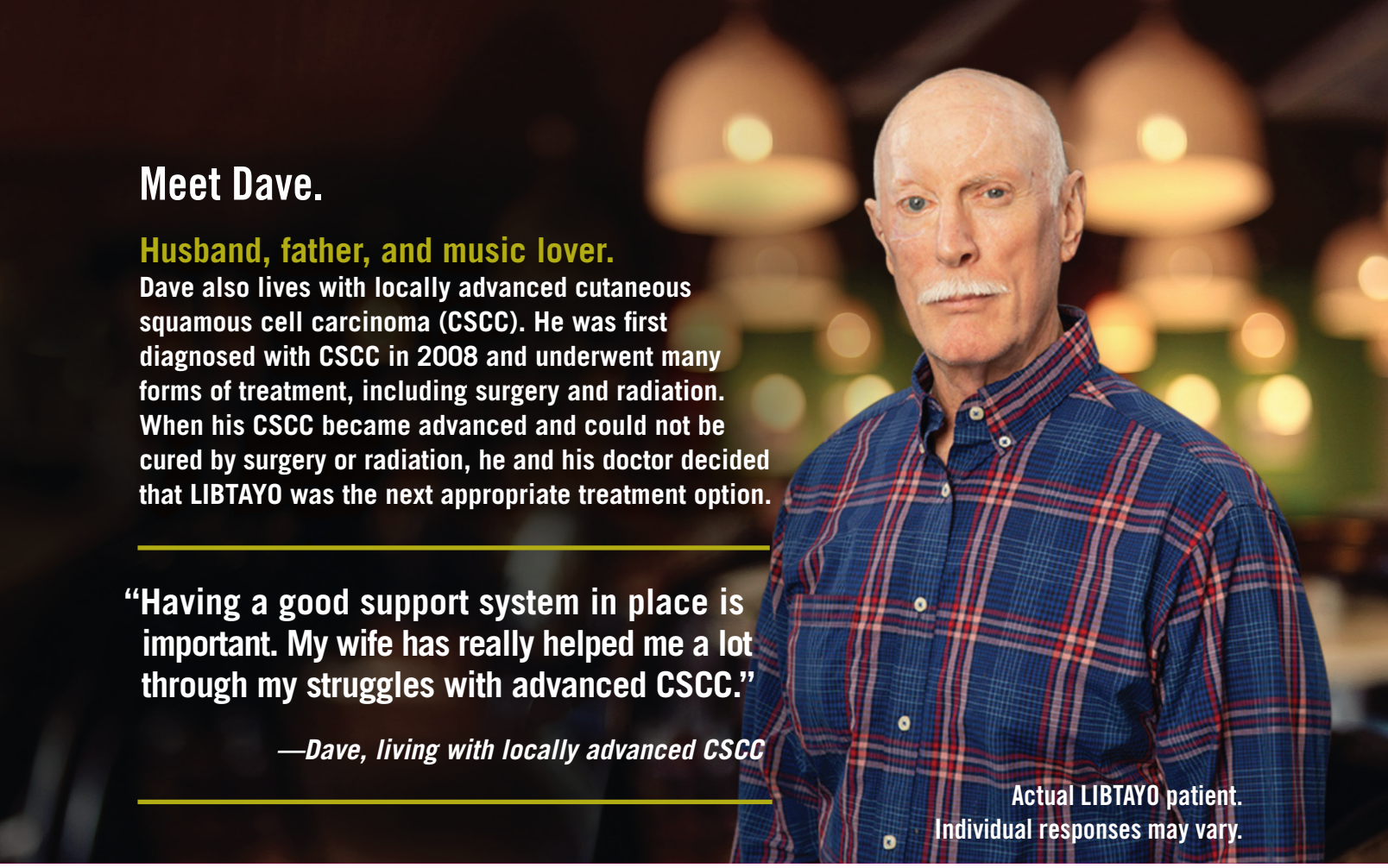
Important Safety Information

What is the most important information I should know about LIBTAYO?
LIBTAYO is a medicine that may treat certain cancers by working with your immune system. LIBTAYO can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:

- **Lung problems:** cough, shortness of breath, or chest pain
- **Intestinal problems:** diarrhea (loose stools) or more frequent bowel movements than usual, stools that are black, tarry, sticky or have blood or mucus, or severe stomach-area (abdomen) pain or tenderness
- **Liver problems:** yellowing of your skin or the whites of your eyes, severe nausea or vomiting, pain on the right side of your stomach area (abdomen), dark urine (tea colored), or bleeding or bruising more easily than normal
- **Hormone gland problems:** headache that will not go away or unusual headaches, eye sensitivity to light, eye problems, rapid heartbeat, increased sweating, extreme tiredness, weight gain or weight loss, feeling more hungry or thirsty than usual, urinating more often than usual, hair loss, feeling cold, constipation, your voice gets deeper, dizziness or fainting, or changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness
- **Kidney problems:** decrease in your amount of urine, blood in your urine, swelling of your ankles, or loss of appetite
- **Skin problems:** rash, itching, skin blistering or peeling, painful sores or ulcers in mouth or nose, throat, or genital area, fever or flu-like symptoms, or swollen lymph nodes
- **Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with LIBTAYO. Call or see your healthcare provider right away for any new or worsening signs or symptoms, which may include:** chest pain, irregular heartbeat, shortness of breath or swelling of ankles, confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs, double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight, persistent or severe muscle pain or weakness, muscle cramps, low red blood cells, or bruising
- **Infusion reactions that can sometimes be severe.** Signs and symptoms of infusion reactions may include: nausea, chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, feel like passing out, fever, back or neck pain, or facial swelling

Please see additional Important Safety Information and Brief Summary of full Prescribing Information on the following pages.



To learn more about Dave and other patient stories, visit MeaningfulStories.com

Important Safety Information (continued)

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including (continued):

- **Rejection of a transplanted organ.** Your healthcare provider should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had
- **Complications, including graft-versus-host disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic).** These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with LIBTAYO. Your healthcare provider will monitor you for these complications

Getting medical treatment right away may help keep these problems from becoming more serious. Your healthcare provider will check you for these problems during your treatment with LIBTAYO. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with LIBTAYO if you have severe side effects.

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

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have received an organ transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. LIBTAYO can harm your unborn baby

Females who are able to become pregnant:

- Your healthcare provider will give you a pregnancy test before you start treatment
- You should use an effective method of birth control during your treatment and for at least 4 months after your last dose of LIBTAYO. Talk with your healthcare provider about birth control methods that you can use during this time
- Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with LIBTAYO

- are breastfeeding or plan to breastfeed. It is not known if LIBTAYO passes into your breast milk. Do not breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO

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

The most common side effects of LIBTAYO include muscle or bone pain, tiredness, rash, and diarrhea. These are not all the possible side effects of LIBTAYO. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Regeneron Pharmaceuticals and Sanofi at 1-877-542-8296.

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 Brief Summary of full Prescribing Information on the following pages.

REGENERON | SANOFI GENZYME

IMPORTANT PATIENT INFORMATION ABOUT LIBTAYO® (cemiplimab-rwlc) INJECTION

Please speak with your healthcare provider regarding LIBTAYO. Only your healthcare provider knows the specifics of your condition and how LIBTAYO may work with your overall treatment plan. If you have any questions about LIBTAYO (pronounced Lib-TIE-oh), speak with your healthcare professional. Prescription Only.

What is the most important information I should know about LIBTAYO? LIBTAYO is a medicine that may treat certain types of cancers by working with your immune system. LIBTAYO can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:

Lung problems.
- cough
- shortness of breath
- chest pain

Intestinal problems.
- diarrhea (loose stools) or more frequent bowel movements than usual
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- yellowing of your skin or the whites of your eyes
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Hormone gland problems.
- headache that will not go away or unusual headaches
- eye sensitivity to light
- eye problems
- rapid heartbeat
- increased sweating
- extreme tiredness
- weight gain or weight loss
- feeling more hungry or thirsty than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Kidney problems.
- decrease in your amount of urine
- blood in your urine
- swelling of your ankles
- loss of appetite

Skin problems.
- rash
- itching
- skin blistering or peeling
- painful sores or ulcers in mouth or nose, throat, or genital area
- fever or flu-like symptoms
- swollen lymph nodes

Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with LIBTAYO. Call or see your healthcare provider right away for any new or worsening signs or symptoms which may include:
- chest pain, irregular heartbeat, shortness of breath or swelling of ankles
- confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- persistent or severe muscle pain or weakness, muscle cramps
- low red blood cells, bruising

Infusion reactions that can sometimes be severe. Signs and symptoms of infusion reactions may include:
- nausea
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- itching or rash
- flushing
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- dizziness
- feel like passing out
- fever
- back or neck pain
- facial swelling

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- have received an organ transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. LIBTAYO can harm your unborn baby

Continued on following page

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- Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with LIBTAYO.

• are breastfeeding or plan to breastfeed. It is not known if LIBTAYO passes into your breast milk. Do not breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO.

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 LIBTAYO?
- Your healthcare provider will give you LIBTAYO into your vein through an intravenous (IV) line over 30 minutes.
- LIBTAYO is usually given every 3 weeks.
- Your healthcare provider will decide how many treatments you will need.
- Your healthcare provider will do blood tests to check you for side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of LIBTAYO?
LIBTAYO can cause serious side effects, including:
- **See "What is the most important information I should know about LIBTAYO?"**

The most common side effects of LIBTAYO include muscle or bone pain, tiredness, rash, and diarrhea.

These are not all the possible side effects of LIBTAYO.
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 LIBTAYO. Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about LIBTAYO, talk with your healthcare provider. You can ask your healthcare provider for information about LIBTAYO that is written for health professionals.

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This is a brief summary of the most important information about LIBTAYO. For more information, talk with your healthcare provider, call 1-877-542-8296, or go to www.LIBTAYO.com

SPEAKING OUT

UVEAL MELANOMA

PROMISE ON THE HORIZON

AIM AT MELANOMA FOUNDATION
Reshaping the Future Together

In our "Speaking Out" video series, on behalf of Aim at Melanoma, *CURE*® talked with Dr. Sunandana Chandra about new treatments that are under evaluation for uveal melanoma.

By KRISTIE L. KAHL AND DARLENE DOBKOWSKI, M.A.

DR. SUNANDANA CHANDRA

UVEAL MELANOMA, sometimes referred to as intraocular (within the eye) melanoma, is the most common primary intraocular malignancy in adults, according to the National Cancer Institute. Despite this, uveal melanoma is rare, affecting approximately 4.3 patients per million people in the U.S.

Formation of uveal melanoma begins within the wall of the eye, particularly the middle of three layers. This middle layer contains the iris (the colored part of the front of the eye), choroid (blood vessels that bring nutrients and oxygen to the eye) and ciliary body (ring of tissue that changes a lens' shape).

Some factors that may increase a patient's risk for uveal melanoma are White race/ethnicity, light eye color, the ability to tan and fair skin. Beyond this, study results have not shown consistent evidence that links exposure to ultraviolet light or sunlight to uveal melanoma.

Dr. Sunandana Chandra, an associate professor of medicine at Northwestern University Feinberg School of Medicine in Chicago, has conducted research with her team focused on melanoma, including uveal melanoma.

As part of its "Speaking Out" video series, *CURE*® talked with Chandra, on behalf of Aim at Melanoma, about the current standards of care for uveal melanoma, treatments being studied and what patients can expect in the future.

Q: Can you explain what uveal melanoma is and how common it is?

A: Uveal melanoma is a melanoma that arises in the eye. It's not spread to the eye from other organs. It involves specific structures in the eye — namely, the iris, the ciliary body or the choroid. Together these encompass what we call uveal melanoma. And it is very, very rare. It affects approximately 2,000 adults in the United States every year.

Q: What are the signs and symptoms of this type of melanoma?

A: Signs and symptoms include blurred vision, floaters, flashing lights (and) misting of the eye. But it is

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important to know that sometimes it may not cause any symptoms at all, and instead, (it) is found on routine ophthalmic exams. So it's very important for us to see our optometrist or (ophthalmologist) on a routine basis.

Q: What are the current standards of care or the main types of treatment for uveal melanoma across its different stages?

A: In localized disease where the uveal melanoma has not spread to distant sites, the mainstays of therapy are usually radiation and surgery. In metastatic disease, meaning that uveal melanoma has spread to other organs in the body, clinical trials should be considered whenever possible, and immunotherapy may also be used for metastatic or stage 4 uveal melanoma.

Q: What new treatments are being evaluated in clinical trials?

A: In uveal melanoma, immunotherapy is being studied in the preventive setting, as (are) targeted therapies such as ... tyrosine kinase inhibitors. And in the metastatic uveal melanoma setting ... a recent phase 3 clinical trial known as (IMCgp100-202 randomly assigned patients to either) a new drug called tebentafusp (or) to their doctor's choice of either chemotherapy or immunotherapy. And the trial showed a survival benefit for patients who received tebentafusp, which is extremely exciting and very promising for this rare subtype of melanoma.

Q: What do patients have to look forward to?

A: Melanoma is being understood more and more, I think, compared to about a decade ago. The armamentarium of therapy options we have now (is) greater than ever before. And I think it's only going to increase, (and treating melanoma) requires a lot of multidisciplinary care, meaning between the medical oncologists, the surgical oncologist, the dermatologist (and) the radiation oncologist, not to mention our radiology colleagues and our pathology colleagues.

And together, I think we have made some great strides in understanding melanoma (and) understanding why some melanomas don't respond to some therapies. And I think there's a lot of promise on the horizon, looking at these newer therapies in novel combinations. So I do think that the next few years will show a lot of promise in the way we treat our (patients with melanoma).

JOIN THE MOVEMENT TO ACCELERATE CANCER RESEARCH

Right now, most clinical information is not regularly shared with the researchers who are trying to uncover new information about cancer every day, **but you can help change that.** Patients can help accelerate research **by sharing their data and unique experiences.**

When patients stand together with researchers, they can unlock new discoveries and treatments. People with all types of cancer may be eligible to **join Stand Up To Cancer, Count Me In and more than 7,500 patients who have already participated in this mission** to accelerate the pace of cancer research.

Find out more and sign up to join the movement at StandUpToCancer.org/CountMeIn

Uzo Aduba
Stand Up To Cancer Ambassador

Photo By
Matt Sayles

STAND UP TO CANCER®

Count Me In