FOR PATIENTS, SURVIVORS & THEIR CAREGIVERS

cure®

Cancer Updates, Research & Education®

ADVANCES IN SECOND OPINIONS

Second opinions may enhance your treatment plan or even change your course.

ALSO INSIDE

BREAST CANCER
Sharing journeys from patient, caregiver and health care provider perspectives

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Expanding treatment for basal cell carcinoma with immunotherapy

LUNG CANCER
Targeting a specific genetic mutation for non-small cell lung cancer

KIDNEY CANCER
Discussing 'new standards of care' for cancer subtype

LIVER CANCER
Tag teaming cancer care with multidisciplinary approach

CHRONIC LYMPHOCYTIC LEUKEMIA
Improving progression-free survival with combination treatment

curetoday.com

SPRING 2021 · VOL.20 NO.2

For adults with advanced melanoma,
KEYTRUDA could be your first treatment option.

"I want to share my story

so that other people with advanced melanoma can see there are options." – **Summer,** *a real patient*

Summer thought she had melanoma figured out, but when it returned she realized there was a lot she still didn't know. She wasn't sure what to do next, but after talking with her doctor she started treatment with **KEYTRUDA**.

Ask your doctor today if KEYTRUDA is right for you.

KEYTRUDA is a prescription medicine used to treat a kind of skin cancer called melanoma.
KEYTRUDA may be used when your melanoma has spread or cannot be removed by surgery (advanced melanoma).

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; 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.

KEYTRUDA will not work for everyone. Results may vary.

Watch Summer's TRU story at
keytruda.com/summer

IMPORTANT SAFETY INFORMATION *(continued)*

- **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 used 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.

These are not all the possible side effects of KEYTRUDA. Talk to your health care provider 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 read the adjacent Important Information About KEYTRUDA and discuss it with your oncologist.

Having trouble paying for your Merck medicine?

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

MERCK

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

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, irritability, or forgetfulness

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

Continued on the next page.

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, and headache.

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-2011r036 as revised November 2020.

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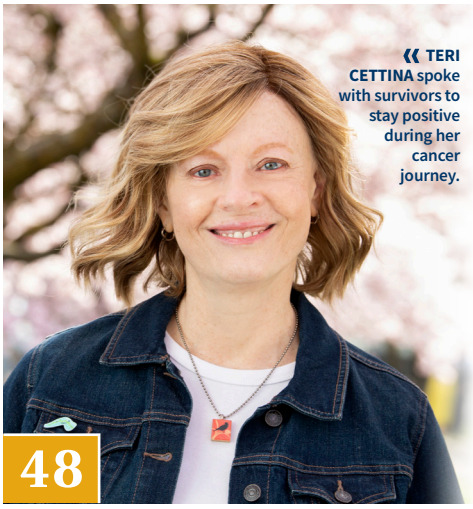
CURE® CONTENTS

SPRING ISSUE · 2021

» JASON PIKE sought a second opinion for a rare sarcoma after learning it would be a risky surgery.

« LORENZO COHEN implemented his studies of the gut microbiome into his personal life.



« TERI CETTINA spoke with survivors to stay positive during her cancer journey.

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is proud to be partners with a number of leading advocacy groups across the country, giving them national reach and visibility for their cutting-edge initiatives, programs, content, research and thought leadership.

You May Have Second Thoughts When Receiving a Cancer Diagnosis

IT GOES WITHOUT SAYING that receiving a diagnosis of cancer can catch people off guard. What if you want another expert to review your records to make sure the diagnosis is correct? Getting an appointment with another oncologist quickly, especially during the COVID-19 pandemic, can be a challenge.

Luckily, obtaining a second opinion has become easier with advances in telehealth and other virtual technologies, which allow patients to share their medical records and test results with physicians and pathologists to potentially improve treatment plans. Some cancer centers have launched second-opinion programs to help patients obtain care at a location closer to their homes. In this issue of *CURE*®, we speak with two patients who sought second opinions for rare and aggressive cancers. One patient details his journey after receiving a diagnosis of a rare sarcoma that spread across his abdominal cavity; his first doctor told him they could offer only palliative care, whereas another doctor was able to operate on him due to his specialization in treating rare sarcomas. Another patient obtained a second opinion regarding treatment for triple-negative breast cancer because her original treatment plan resulted in very low blood counts. Her alternate treatment plan from a different oncologist was more tolerable. We also spoke with several experts who emphasize the importance of second opinions to learn about all of the opportunities for your type of cancer.

> **"Staying positive can be fostered in so many ways, such as surrounding yourself with people you love."**

Also inside, a feature examines the power of positive thinking during and after cancer treatment. We spoke with patients who learned how beneficial optimism can be, especially since cancer and depression are biochemically linked. Staying positive can be fostered in many ways, such as surrounding yourself with people you love, focusing on the encouraging aspects of life and working with a therapist.

Read on and you'll meet an oncologist who learned how to balance being a caregiver for his wife, who received a diagnosis of stage 3 triple-negative breast cancer, with being a doctor for his patients. He and his wife wrote a book focused on their experiences during this challenging time. They share how important it is to communicate with your family and your care team to hopefully attain the best outcomes.

This issue also covers implications of several recent treatment approvals from the Food and Drug Administration for skin and kidney cancer, in addition to important targets for the treatment of non-small cell lung cancer that may be on the horizon.

MIKE HENNESSY SR.
Chairman and Founder

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Our Microbiome: A Reflection of Ourselves?

THE PAST DECADE HAS BROUGHT about a tremendous amount of professional and societal interest in the microbiome — the bacteria and other microorganisms that colonize different parts of our body, ranging from the skin to the intestines/colon, mouth and even the ducts of the breast. Intriguingly, each person's microbiome possesses the uniqueness of a fingerprint. But the concept is not "new age" at all; it is mentioned in the writings of one of the founders of the field of microscopy himself, Antonie van Leeuwenhoek. In the 1670s, van Leeuwenhoek reported distinctions of the microbiota from the mouth or feces among individuals and even differences based on illnesses. As it became clear that certain pathogenic bacteria — and later viruses — could cause distinct diseases, it also was recognized that normal colon bacteria such as E. coli (noting that some strains of E. coli can cause serious sickness) could be probiotic — that is, something that maintains the normal harmony. During some battles in World War I, more soldiers were lost to dysentery, an infection of the intestines, than to enemy fire. A specific strain of E. coli was discovered in an infantryman who survived a trench epidemic, and the strain was shown to antagonize harmful bacteria that were likely causing the scourge.

> **"Our gut microbiome often mirrors our health."**

Fast forward to the third millennium, when modern genomic analysis has revolutionized how we identify and classify microbes by sequencing their DNA. We can more easily determine what is causing an infection (although it's not always possible) and what populations of bacteria reside in body compartments. Using gene sequencing and bioinformatic tools, we can assess bacterial diversity in a specific habitat (alpha diversity), and variations in different regions (beta diversity). As you will read in this issue of *CURE*®, our gut microbiome often mirrors our health. Our microbiome interacts with and even sculpts our immune system. Each of us has a unique immune system with an inventory of activated T cells that can directly kill invaders (pathogens and cancer cells among them) and B cells that make antibodies that fit like a lock and key to inactivate bacteria and viruses and bring on additional waves of attack by other arms of the immune system.

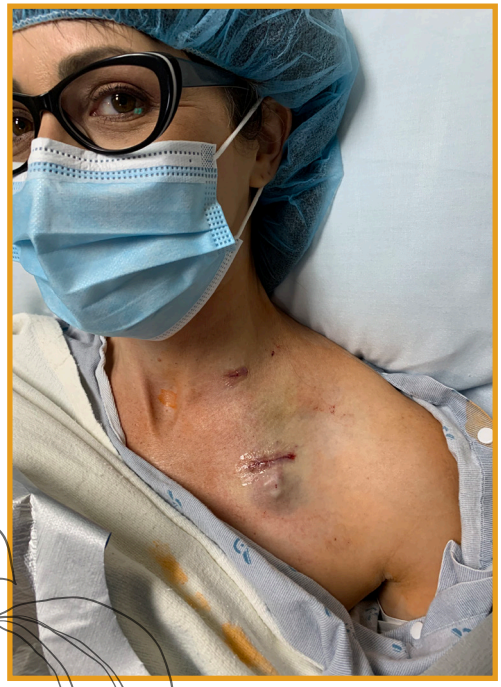
As we teach immune systems to attack cancer and develop drugs to reverse the dampening effects that cancer cells have to evade immunity, we are recognizing that some people have a more "trained" or "fit" immune system. This may be due to the experiences and exposure gained over one's lifetime, including interactions with the microbiome, which is an ever-present companion in many areas of our body. Not surprisingly, sophisticated analyses can predict which gut microbiome profile may lead to better outcomes to immunotherapy for patients with advanced melanoma. Trials are underway to transplant "good profile" colonic flora in patients receiving cancer immunotherapy. We invite you to read this and other fascinating breakthroughs that we are witnessing at accelerated paces — in this case, discoveries coming from within.

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

'Cheers to Pete': An Ode To A Cancer Port

A cancer survivor pens an ode to her port that has made her journey much less stressful. *By* MARISSA HOLZER

Meet Pete, he's my port.
Makes my lab draws very short.
Use the cream,
it works like a dream.
No pain.
Thank you, lidocaine.
My ever-ready vein,
keeps those nurses and lab techs sane.
Easy-Peasy.
Never queasy.
Should have done this years ago,
instead of having my veins blow.
So, this is Pete.
I think that he is pretty neat.
He works like a charm,
since I only have one good arm.
A power port,
it's my last resort.



Oh, the metastatic breast cancer life.
Once again, I'm under the knife.
Hoping to make things simple,
although Pete, he looks like a giant pimple,
implanted under my skin
because I'm thin.
But he'll get the job done.
Multiple poking now becomes one.
Digging no more.
Labs are no longer a chore.
Cheers to Pete,
for keeping things short and sweet.
Such a relief
to save so much grief.
No heads shaking,
no arm aching.
Now I'm less stressed,
thank you, Pete, you're the best.

PHOTO COURTESY OF HOLZER; FLORAL ARTWORK BY BABEER / STOCK.ADOBE.COM

Join Triage Cancer for a FREE educational conference!

This event covers key information needed to help navigate practical issues, minimize the financial burden of a cancer diagnosis, and reduce stress.

WHO SHOULD ATTEND?

Individuals diagnosed with cancer, caregivers, health care professionals, and advocates will learn about:

- Being an Empowered Patient and Advocate
- Health Insurance: Understanding Your Options & Using Your Coverage
- Practical Tools for Managing Medical Bills, Your Financial Health, & Estate Documents
- Employment Issues: Working Through Treatment and Taking Time Off
- Disability Insurance: Options, Applications, & Appeals

...and more!

Saturday, May 15, 2021

This program will be offered online.

7:30am – 3:30pm PT | 9:30am-5:30pm CT | 10:30am-6:30pm ET

Register at: **TriageCancer.org/Conferences**

Triage Cancer is a national, nonprofit organization that provides education on the practical and legal issues that may impact individuals diagnosed with cancer and their caregivers, through free events, materials, and resources.

TRIAGE CANCER

Doctor's Experience as Caregiver Is Helping Educate Others

A gynecologic oncologist who has spent her career helping patients during their cancer journeys goes a step further to educate women on how to advocate for themselves and possibly prevent cancer before it occurs.

By DARLENE DOBKOWSKI, M.A.

DR. VALENA WRIGHT HAS specialized in gynecologic oncology for the past 25 years. When her sister Debbie received a diagnosis of ovarian cancer, Wright gained a new perspective on what patients and their families go through.

After her sister died from ovarian cancer in 2016 at age 55, Wright decided to teach others what could be learned from her sister's experience by writing "It's Time You Knew." In the book, Wright speaks with her patients about their cancer journeys, discusses major takeaways from their experiences and explores ways to potentially reduce their risk for cancer, among other topics.

CURE® spoke with Wright about what women need to know to protect themselves from women-related cancers and the importance of potentially preventing the disease.

> "It's really important to be an advocate for your own health and consider genetic testing. — *DR. VALENA WRIGHT*

DR. VALENA WRIGHT

Q: *CURE*®: What inspired you to write your book?

A: Wright: My family story really inspired me to write the book. I'm a gynecologic oncologist, so I've trained both in obstetrics and gynecology and then (did my) fellowship in women's cancer surgery and chemotherapy. I take care of women who have different gynecologic cancers, which include ovarian cancer, uterine cancer, (cervical) cancer, vulvar cancers; those are the most common. When you study and practice all of these years and a member of your family receives a diagnosis of ovarian cancer, which is the most serious or difficult to treat, you see things from a different perspective. I learned so much from being with my sister during her battle with ovarian cancer. I was disappointed in some of the interactions that she had with the medical system. And I thought, if I wrote our story it could help other people avoid some of the same problems. There are a lot of things about ovarian cancer that aren't well understood, but the more that women understand and know about ovarian cancer, (the more it will help) them learn what they can do to avoid ever having to deal with that diagnosis.

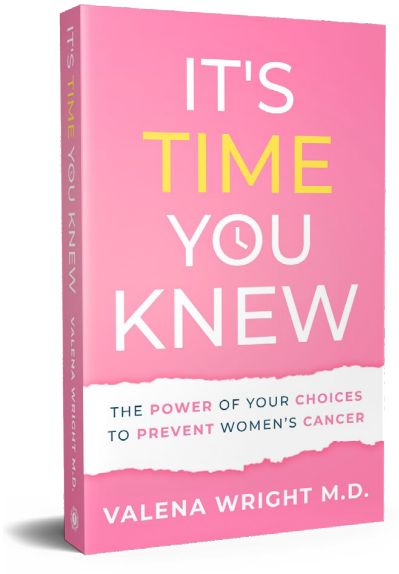
Q: What were some of the things you wish were different about your sister's communication with her doctor, and what do you want women to take away from this book?

A: A lot of times with ovarian cancer, it's really difficult to diagnose. … It can take up to two years of women (having) symptoms before they receive a diagnosis. And it's always been controversial — whether the symptoms aren't clear, if there are no symptoms that are recognized early or if it's a problem (related to cysts).

When my sister first received her diagnosis, she was living in Germany and she was told she had an abnormal cyst on her ovary. She didn't follow up right away because she was in the middle of traveling. When she came back to Canada, a follow-up ultrasound showed the cyst had enlarged dramatically. Because of that, her doctors recognized something was really wrong and that she should have surgery.

With ovarian cancer, some of the symptoms are very subtle, such as an increase in urinary frequency. … Often the symptoms are more related to digestion, such as a little bit of bloating, feeling full. (With) these symptoms, people don't think of the ovary. If people have those symptoms, they end up sometimes being triaged into gastroenterology, to colonoscopies, to urology, but people don't think about it in the differential diagnosis.

PHOTOS COURTESY OF WRIGHT



"IT'S TIME YOU KNEW" can be purchased on Apple Books, Amazon, Books-A-Million and Barnes & Noble.

There are some tests that can help diagnose ovarian cancer. Ultrasound and a tumor marker called CA 125 are our two best tools. If (my sister) had understood the importance of follow-up at that first visit, maybe she wouldn't have had a delay. I think it was six months from her first abnormal ultrasound to follow-up. Part of that was not having symptoms that she recognized, but even if you have no symptoms or no recognized symptoms, sometimes medical tests will come back abnormal. Just because you feel fine doesn't mean you should ignore an abnormal medical test; it means something requires follow-up, and not (following) up can put your health at risk.

When someone has ovarian cancer, they should consider genetic testing. The reason for that is up to 20% of ovarian cancers have a familial component. If you do genetic testing, you can identify yourself as being at increased risk if you have (what) we call a deleterious gene mutation. Debbie didn't have (genetic testing) with the other testing that was done. It was several years ago, so the testing is better now. But family history alone, even without genetic testing, shouldn't be ignored because there are some gene mutations that we just haven't studied or identified as being deleterious yet.

With that knowledge, in women who are at high risk for ovarian cancer (and) have a gene mutation, you can do risk-reducing surgery to decrease the risk of ovarian cancer, which is removal of the fallopian tubes and ovaries. Fortunately, my younger sister Shirley did that and was so lucky to receive a diagnosis, when she had no symptoms, of a very early precursor to ovarian cancer. It's called fallopian tube carcinoma in situ, which is a microscopic tumor in the fallopian tube that is impossible, really, to diagnose. When researchers looked at women with gene mutations who were undergoing this risk-reducing surgery, it was discovered that a lot of what we call ovarian cancer actually starts in the distal end of the fallopian tube as a microscopic lesion. It spills those cells into the abdominal pelvic cavity. And those cells can land on the ovary, creating a mass that is then attributed to the ovary, even though it really started in the fallopian tube.

She was very fortunate because she didn't require any further treatment or chemotherapy. I'm so glad she's with us today. … Because we know so much more now, it's really important to be an advocate for your own health and consider genetic testing.

There's a lot we're learning based on genetics and advances in the field. It's difficult for doctors to keep up on all the different aspects of care. If you do have a positive family history, it's really important to talk about it with your family members and see if you qualify for genetic testing. It doesn't mean you have to have risk-reducing surgery, but perhaps it will mean that you would be screened differently. And if you don't know or if you don't explore that option, you might miss an opportunity that could actually have a huge impact and save your life.

That background was really the motivating factor for me to write this book, because I want women to understand their risk and what their options are.

Q: Throughout your book, you focus on a variety of women-related cancers. Why do you find it so important to cover this topic with a broader approach?

A: The numbers of women affected by breast cancer is higher than the number of women with these other cancers. When we look at health and health outcomes, medicine wants to divide everything up into body parts or different areas, but our health is really a constellation of many things and it's not … one system. I think obesity is such a good example of that because it affects all of our body parts in different ways. There's risk of obesity and the comorbidities that we've seen associated with it. Even the COVID-19 pandemic highlights that.

Having more of an emphasis on health and lifestyle interventions to prevent risk rather than waiting for cancer to develop and playing catch up is another reason I thought this book was really important. Nobody wants to receive a diagnosis of cancer, and it's not just (that), it's the ability to have good health. That's probably our most important asset because without good health we're really limited in our ability to enjoy life in many different ways. Knowing over time (the) actions that you can take to prevent cancer over a lifetime, it really adds up.

This interview has been edited for clarity and conciseness.

FIRSTLINE

compiled *by* JESSICA SKARZYNSKI

Cancer Survivor Reenlists in the Navy After Completing Her Last Treatment Session

"BEING IN THE NAVY IS AMAZING. It's an honorable thing to serve my country and I've loved every minute of doing my 13 years," Carol Ortiz, a resident of Mesa, Arizona, said.

Navy Chief Ortiz was diagnosed with invasive stage 3 breast cancer after a serious bike accident during a triathlon in 2019. Ever dedicated to her post, Ortiz continued to work full time as a recruiter for the Navy while undergoing surgery, chemotherapy, radiation and drug therapy.

After being medically cleared to return, and with her reenlistment date fast approaching, Ortiz considered the move to reenlist for another six years "a double salute to cancer."

"To fight stage 3 and then be told you have no evidence of disease, I think part of … that is being positive the whole time and having the support that I've had — that's what really has gotten me through it," she said.

"Significant Portion" of Alex Trebek's "Jeopardy!" Wardrobe Donated to The Doe Fund

THE NONPROFIT, WHICH provides opportunities and training to people with histories of homelessness, incarceration and substance abuse, aims to help underserved Americans get back on their feet, and Alex Trebek's wardrobe will be given to those who participate in Ready, Willing & Able, the organization's reentry program.

"During his last day on set, Alex extolled the virtues of everyone opening up their hands and their hearts to those who are suffering," Mike Richards, the show's executive producer, said in a "Jeopardy!" news release. "Donating his wardrobe to those who are working to rebuild their lives is the perfect way to begin to honor that last request."

ALEX TREBEK

Childhood Cancer Survivor Chosen for First All-Civilian Space Mission

AFTER OVERCOMING BONE CANCER at age 10, Hayley Arceneaux, now 29, is poised to become the youngest American in space when she boards SpaceX's Dragon spacecraft in late 2021. She was selected by billionaire and civilian pilot Jared Isaacman, who will serve as the Inspiration4 mission leader.

Arceneaux, who works at St. Jude Children's Research Hospital in Memphis, Tennessee — where she was treated as a child — had dreamed of becoming an astronaut. But the steel rods in her leg from cancer treatment led her to believe that dream would never come true. That is, until Isaacman invited her to join the team and serve as "an inspiration to people all over the world," as he stated on Twitter. "Not just those with dreams of going to space, but to all people who need hope when encountering life challenges," he tweeted. Isaacman hopes to raise $200 million for the hospital from the mission.

"Being the youngest American to go to space is such an honor, but, honestly, what I'm more excited about is being the first pediatric cancer survivor to go to space," Arceneaux said. "I would just love to inspire my patients to dream big and to not limit themselves. And I really hope to show them while I'm in space that absolutely anything is possible."

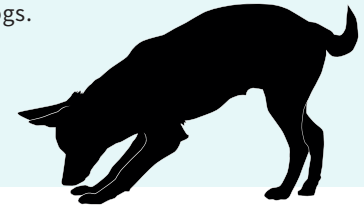
Dogs Trained to Detect Prostate Cancer May Help Smartphone App Development

AN INTERNATIONAL RESEARCH program that trained dogs to detect prostate cancer by sniffing urine samples has found that the dogs correctly identified positive samples of the most lethal prostate cancers 71% of the time.

Florin, a Labrador retriever, and Midas, a vizsla, were trained by Medical Detection Dogs, a charity based in Buckinghamshire, England. One of the group's founders, Dr. Claire Guest, said the dogs have "enormous potential."

"The dogs have been able to identify these very aggressive cancers. This could lead to lifesaving work in the future that would enable us to understand the difference between other diseases of the prostate and those that will go on to kill men," she said.

The project is so promising that Florin was brought to the United States to team up with scientists from the Massachusetts Institute of Technology in the hopes of building a smartphone app to replicate the sniffing ability of the dogs.



ALEX TREBEK: KRIS CONNOR / STRINGER / GETTY IMAGES ENTERTAINMENT / GETTY IMAGES SOUTH AMERICA; ANCHOR: MAXAV / STOCK.ADOBE.COM; DOG: KAROLINA / STOCK.ADOBE.COM

What Is IBRANCE® (palbociclib)?

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

Important Safety Information for Patients

IBRANCE may cause serious side effects, including:

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

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

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

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

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

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

The most common side effects of IBRANCE include:

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

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

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

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

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

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

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

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

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

Please see Important Facts About IBRANCE on the following page.

To learn more, talk to your doctor.

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

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

IBRANCE® palbociclib 125 mg tablets

IBRANCE®
palbociclib | 125 mg tablets

IMPORTANT FACTS

IBRANCE® (EYE-brans)
(palbociclib)

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

What is IBRANCE?

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

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

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

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

IBRANCE may cause serious side effects, including:

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

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

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

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

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

What should I tell my healthcare provider before taking IBRANCE?

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

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

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

How should I take IBRANCE tablets?

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

What are the possible side effects of IBRANCE?

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

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

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

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

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

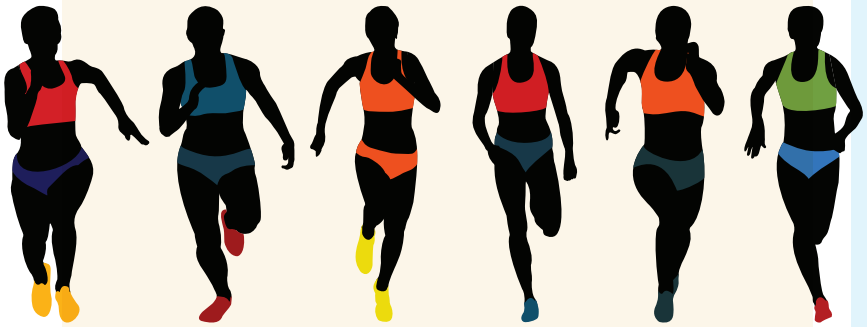
Keep IBRANCE and all medications out of the reach of children.

Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

To learn more, talk to your doctor.

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

Pfizer



Ovarian Teratoma Survivor Sets Her Sights on the Olympics

AT AGE 14, DANA GIORDANO thought the mass in her stomach was just a sign of weight gain. But when a piercing stomachache that wouldn't go away landed her in Boston Children's Hospital, doctors found a 5½-pound cancerous tumor. The surgery to remove it was successful, but it left her weakened and feeling without purpose — until she rediscovered running.

Giordano became an All-American in the 2-mile and 3,200-meter races in high school, and she was named a three-time All-American and seven-time Ivy League champion at Dartmouth College. After missing an invitation to the 2016 U.S. Olympic trials, she was determined to make it on her next attempt in December 2020, where she finished fourth in the 5,000-meter race, qualifying her for the Olympic trials later this year.

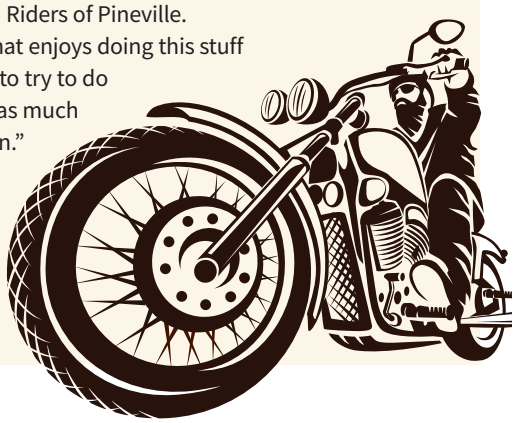
"I'm betting on myself above all else," Giordano says. "I've always dreamt of representing my country at the highest level."

Motorcycle Club Helps Ovarian Cancer Survivor Pay for Medical Bills

THE CHRISTIAN RIDERS OF PINEVILLE and Taboo Harley-Davidson in Alexandria, Louisiana, held a benefit ride in March for Doris Norris, 60, and her husband, Terry, to help pay for medical bills and other expenses they incurred while traveling to Shreveport where Norris received treatment for ovarian cancer.

"Whatever it takes to help Terry and Doris," said Ken Coody, president of the Christian Riders of Pineville. "We've got a great club that enjoys doing this stuff right here so we're going to try to do the best we can to make as much money for them as we can."

Norris, who took part in the ride with her husband, has completed her final treatment.



High School Kayaking Team Raises More Than $1 million to Help Fight Cancer

THE CASTAWAYS AGAINST CANCER team at Christopher Columbus High School in Miami was founded by teacher Steve O'Brien in 2000 after his mother's death from cancer. Each summer, the team paddles from Miami to Key West over the course of seven days to raise money for cancer research.

In 21 years of kayaking, the team has raised more than $1.2 million for the cause. Team members are preparing for their 2021 trek, which kicks off June 12. The team is partnering with the University of Miami Sylvester's Comprehensive Cancer Center for the second year in a row.

"Steve O'Brien's vision to 'light a candle instead of cursing the darkness' after his mother's death inspires all the Castaways to fundraise with passion and paddle with vigor," said team captain Eric Pino, a teacher and coach at the school who is a graduate of the class of 2000.

"We paddle for every person who has heard the words, 'You have cancer.' It's that simple. We kayak, you donate and we all pray for a cure."

Young cancer Survivor Interviews Aaron Rodgers for Fundraiser

ITZEL MERCADO, A GREEN BAY Packers fan, had the opportunity to interview her favorite player through the "50 Faces of Cancer" fundraiser for the Vince Lombardi Cancer Foundation. The conversation between Mercado and quaterback Aaron Rodgers premiered online on March 11.

Ten-year-old Mercado received her final round of chemotherapy in February after receiving treatment for leukemia for more than two years. She rang the bell to celebrate becoming cancer free at Children's Wisconsin on March 16.

"I feel more free now that I'm done with that, because that was really tough to go through," Mercado told WISN-TV.

AARON RODGERS

The donna Foundation
CARING FOR THOSE WITH BREAST CANCER

Shattering Myths Helps Patients With Cancer Become Advocates

Experts offer tips on how to be fearless about asking for better care and health policies. By RYAN MCDONALD

PATIENTS WITH CANCER NEED to rid themselves of certain beliefs to be better advocates for their health and the health of others, according to Dr. Carolyn McClanahan.

"When we think of advocacy, to me, the biggest mistake people make is not doing advocacy (for) two reasons," McClanahan, a physician, financial planner and founder of Life Planning Partners, said during The DONNA Foundation's How to Be Fearless Virtual Seminar in February. "(People) think their voice doesn't matter and they think advocacy takes a lot of time. This is so untrue."

During the seminar, McClanahan was joined by Mike Panetta of Beekeeper Group, and Rebecca Kirch and Nicole G. Braccio of the National Patient Advocate Foundation (NPAF) to discuss how patients with cancer can be better advocates for themselves and others.

The goal of the session, McClanahan said, was to "shatter those two myths."

McCLANAHAN: Rebecca, what are the opportunities for patients and their families to influence health policies that matter to them?

KIRCH: One thing that we've learned at the (NPAF) is that — before we even (start talking about) accessing health care — any serious illness can cause all sorts of financial distress. You've probably heard that in the context of your work, in addition to your medical career, but person-centered care is something that needs to happen everywhere. … It's a matter of focusing on what patients and their caregivers need as people. Because first and foremost, people want to be treated as people; treat the person beyond their disease. So, the focus (is on) helping all sorts of influencers, whether it's legislators or health systems, the different types of audiences; for the patient and caregiver voice, (it's) helping build that echo chamber of understanding. You're right, it doesn't take a lot of time.

It just takes that committed, steady drumbeat of the same message for change, and that builds the echo chamber. That's certainly what (NPAF) tries to advance through its advocacy program in helping support advocates such as you, (to give you) the opportunities to be influencers of change.

McCLANAHAN: Nicole, share some real-world examples about what people have done to advocate and their successes.

BRACCIO: It's a very timely point to talk about a campaign that we just finished up in the fall but is coming back. (The) Get Covered campaign is one of NPAF's community campaigns. The focus is on helping people understand the importance of health insurance and how to pick the best plan. Our campaign largely started around the Affordable Care Act (ACA) exchanges, but we've also weaved in Medicare (and)

TARTILA / STOCK.ADOBE.COM

open enrollment, since the two overlap, and then with starting the new special enrollment period for the (ACA) exchanges. This is a great campaign that a lot of our volunteers have been involved in for several years. I'll share some of the examples of what people have done to help talk about the importance of health insurance.

Pre-pandemic, our volunteers held in-person info sessions in their communities; they posted flyers in places (such as) grocery stores and churches driving people to the government sites to purchase health care, such as healthcare.gov and the Medicare plan finder. They also share this information with doctors' offices.

So, it was truly a community effort in that people were identifying places and friends, family, neighbors they thought could benefit from this information. And, you know, they went out and conquered. And recently, over the past year, and with this last campaign in the fall, everything was virtual. Some great examples (are) our volunteers who created Facebook pages and really built their online communities and helped to drive people to the government sites that I mentioned, as well as guides that we at NPAF built to help people determine which plan to choose.

Our plan guides are kind of a step-by-step, here's what you need to do and think about, around what aspects of health insurance are important to you. (They help you prioritize) your needs, as well as compare plans and learn about what's out there and how to make that decision. Because we all know it can be very complicated … to figure out how to choose that one plan out of so many. And (although) it's not easy to quantify this work, we have, as Rebecca mentioned, that echo chamber with many other advocacy organizations in the field. We know that the success of the 2021 open enrollment period has surely been (affected) by all the volunteers and advocates who raise their voice to talk about health insurance with people in their communities.

McCLANAHAN: Mike is going to share with you tips and tools and how to effectively engage with politicians and other stakeholders.

PANETTA: At Beekeeper Group, we do a lot of work with different patient advocacy organizations in their efforts. And the things that I like to focus on when we talk about advocacy and engaging with stakeholders is really the need for personalized stories. We find that's the most effective tool; there's great research by the Congressional Management Foundation that shows that (personalized stories) are the No. 1 thing that changes the minds of decision makers in Congress, and I'm sure at the state level, as well.

During the pandemic, I've been watching a lot of "Parks and Recreation," and there's a great quote by Leslie Knope. She says something along the lines of, "The only things I have on my side are facts and science, and people hate facts and science." So, I joke that that's a great quote, because one of the things I always (tell the) groups that we work with is that facts are cheap. Everybody has facts. And I'm not saying they're not important, but everybody can have facts. If you're getting into an argument, and you're debating just on pure facts, you're never going to be as strong as if you're coming in with personalized stories. And the reason that we focus a lot on using stories in our advocacy is because they affect the different parts of the brain. There's this concept called narrative transportation in which you tell somebody a story, their guard goes down, and they're more apt to change their mind and have empathy with the characters (who) are in that story.

> **"The things that we work on specifically are driving email messages to decision makers. It's a great entry-level action."**
>
> — *MIKE PANETTA*

Having your advocates find ways to collect those stories and get those stories to decision makers is hugely important in the work to affect public policy. Those are the things that really change hearts and minds. So, when we work with advocacy organizations, there are a number of ways to influence Congress to influence the decision makers and legislators. There are great tools out there now. The things that we work on specifically are driving email messages to decision makers. It's great entry-level action. These tools are important because they match you to your specific legislators, which is key. All members of Congress and all politicians live and die by the feelings of their constituents.

Another thing that we're seeing a lot more of these days, (which) has been going on for years, is the engagement on social media, specifically legislative engagement on social media. What I mean by that is tagging the legislator on Facebook, Twitter or whatever platform they're on. When that happens, it hits their office in a different way. If you send a letter to a member of Congress, it goes through their normal legislative channels. When you do something like this on the social media side of things, it goes to the communication side of the House. So, you're sort of hitting on two fronts; you're coming through the regular channels »

of advocating through the platforms that collect constituent engagement, and then you're advocating publicly on social media channels. And by specifically tagging the legislator, their office gets pinged on that, and that's something that gets reported up the chain to the decision maker. I like to describe it as the 21st century equivalent of a letter to the editor because it's public and it's out there and everybody can see it.

One thing that we always like to encourage our groups to do as well is (be as) specific as you can with a bill number when something is in committee status; this is all going through staff filters. (As much as) you can, make it easy for the staff to take the next step to their boss. Also, publicly thank the people who are on your side, who are your champions. Thank them for their leadership, thank them for their engagement. Do that publicly on social media; include photos of them, if you can. (Deepen) that relationship, especially in this time of pandemic when it's hard to have those in-person meetings, to show that you're backing the people who support you.

McCLANAHAN: Rebecca, where can patient voices other than just talking to politicians be influential?

KIRCH: The short answer is everywhere with everyone. It starts with yourself. Self-advocacy is important, and it can be very intimidating in a doctor's office (or) a legislative meeting. Oftentimes, patients and caregivers can feel a bit overwhelmed or intimidated. It's a whole different experience and landscape for them. But what (is) so important for patients and families to know about advocacy is that you are your own expert of your lived experience. And you need to think of yourself and equip yourself with organizations (such as) The DONNA Foundation (and) the National Patient Advocate Foundation; we all have resources to help you feel more confident. Just like Beekeeper (Group) has tools to help people practice their narrative and tell their story.

You have a whole community; you're not alone in doing this sort of advocacy. … It's becoming more and more interesting, and there's more reception to patient and caregivers speaking out. You move from confidence to demanding what's right and bringing person-centered care to the forefront. There are opportunities to be on hospital, patient and family advisory councils (and) to participate in research studies or be advisers on those research studies to keep them true to their ultimate objective, which is improving the quality of care for people.

Health systems often (will) speak their own language. And we have to join together as a community of advocates to say, "You know what, your ultimate customer really is us. And we bring (expertise) about what the experience was, what could be different about it." … Our volunteers have said that feeling heard and understood in every setting is their top priority. And if they're not getting that as a measure of quality for them, then the health system isn't doing its job. The medical, nursing, social work communities need to help join with patients to make sure they're feeling heard and understood. (This) is the No. 1 aspect of good quality care. It's an advocacy message to shout from every rooftop among legislators, among hospital administrators, among researchers, among those who are developing the quality measures so that we actually measure (if) people (have) been trained to elicit from patients and families what matters to them most. When you think of that expertise that you bring, then it's much less daunting, the notion of calling and asking for change.

McCLANAHAN: Nicole, you're going to share with us resources for people so that they do feel more confident in raising their voice.

BRACCIO: An overarching resource that can help patients, caregivers and their families feel confident is the community in and of itself … When we bring advocates together for a variety of initiatives that NPAF hosts, we overwhelmingly get the response from people that it was just so great to be in a room or at a place where other people understand (their) experience. That camaraderie among advocates goes farther than you would think. (Among) particular resources that we've built as part of our campaigns and as part of all the advocacy work that we do, education is No. 1, and communication would be second.

We've built worksheets and resources on how to talk to your doctor and to (members of Congress) about what matters to you. We all know about white coat syndrome and people feeling (as though) they don't have enough time to share what really matters. So, we have resources that (give you prompts for) questions and things that you have every right to ask your physician, as well as other stakeholders. And then the other piece is that, with all our campaigns, we like to link to a specific policy issue or reform issue.

For our Get Covered campaign, we have a toolkit that has evolved over the years. It has social media copy that people can personalize and share with their online communities. (It also includes a) coordinated effort among all the advocates in our grassroots network to act on specific days. And then I'll just touch on one last point … story collection. We agree that is absolutely the No. 1 way to get your point across and to generate interest among policy makers and others. We have thought about different story prompts and interview questions that we would like our advocates to answer, as well as a platform to help them collect their stories, and send them to us.

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Treatments for Multiple Myeloma Are Transforming Lives

In the past five years, treatment options for patients with multiple myeloma have evolved and include targeted therapies and immunotherapies. An expert discusses some of these treatment options and more information on stem cell transplantation. By ANTONIA DePACE

IF YOU RECEIVE A DIAGNOSIS of multiple myeloma, the first step is to not panic. The second? To educate yourself as much as possible, according to Dr. Krina K. Patel, an associate professor in the Department of Lymphoma/Myeloma, Division of Cancer Medicine, at The University of Texas MD Anderson Cancer Center in Houston.

Patel, who presented treatment options for patients with new diagnoses of the disease during the *CURE*® Educated Patient® Multiple Myeloma Summit, spoke about new treatments for the cancer, what to expect during treatment and what's next.

Q: *CURE*®: How has treatment for multiple myeloma transformed over the past five years?

A: Patel: VRd (Velcade, bortezomib; Revlimid, lenalidomide; dexamethasone) — that's sort of our standard-of-care, induction therapy for myeloma — used to be considered a novel therapy. Before, we just had steroids and melphalan, which we've been using for probably decades to treat myeloma. But then we (discovered) targeted therapies such as Velcade, which is a proteasome inhibitor. It really goes after the machinery in the myeloma cells that makes all that protein we watch. I consider it a targeted therapy in that sense. … And then there's lenalidomide, an immunomodulatory drug that helps your immune system fight the myeloma. But it's also chemotherapy that works a little bit differently to kill that myeloma compared with Velcade. Steroids kill myeloma, but they also decrease inflammation that you might have. ... So, using that combination was really novel. Putting them together to synergize, to kill that myeloma, was actually a revelation to the induction treatment.

Q: What can patients expect from stem cell transplant?

A: It's an acute process for approximately six to eight weeks, and then it becomes more of a chronic kind of evaluation for three months. In the acute process, it takes approximately a week to collect your stem cells — that's usually done outpatient. You get high-dose growth factors to help those stem cells really come out, grow in your bone marrow and then come into your blood. And then, similar to a dialysis session, they use a machine to take those stem cells out. So, it's not a surgery; it's a procedure.

You have a line placed that they attach to one end of the machine and there is another line coming back in. As your blood goes through this machine, they take out the stem cells and they give you back everything else. It's connected to you, and it usually takes three to four days for most people. (You'll be connected to the machine) for a half day, each day, to get those stem cells collected, and then they freeze them and you take a few days off. … Once you've recovered from that, you get your high-dose chemotherapy. It's not really a transplant; it's high-dose chemotherapy, followed by stem cell rescue.

Once you complete your chemotherapy, two days later you get the stem cells. It's like a blood transfusion. They bring them to your bedside, they thaw them out a little — I call it a "flambé" because it puts patients a little bit at ease. We give it to you just like a transfusion. It only takes 30 to 40 minutes, maybe an hour. Then, it takes about two weeks for the stem cells to find the bone marrow and start regenerating your blood cells (white blood cells, red blood cells and platelets) again. Once those are closer to normal, patients are monitored for a couple more weeks with labs and continue some antibiotic and antiviral prophylaxis, as the white blood cells are still naive. Around three months post-transplant, patients start some type of maintenance therapy. Six months after transplant, they start receiving certain immunizations again. This is really when most people feel back to 100% themselves.

Q: What are some common misconceptions?

A: The biggest fear for many patients is when they hear that myeloma, for the majority of patients, is not curable. They think it's the end of their life, and I can imagine what it's like to hear that you have a disease that's not curable. But the big difference is that it's really treatable. And every few years we're actually extending survival for patients. Some of my patients are surviving for decades — not just years, but decades. And I know not everybody is in that category, but that's our goal: to give you the best quantity of life as well as quality of life.

The other misconception is that everybody with myeloma should get treated a certain way. … In myeloma, we have high risk versus standard risk, and patients (are treated) differently based on what their myeloma is. You want to individualize treatment to a certain degree, and that's why that expert opinion really matters.

This interview has been edited for clarity and conciseness.

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Tag Teaming Liver Cancer Care

As part of the "Speaking Out" video series, CURE® spoke with Dr. Laura M. Kulik about the basics of liver cancer, highlighting the need for a multidisciplinary approach to care.

By KRISTIE L. KAHL

WITH MORE THAN 40,000 cases of liver cancer diagnosed each year, it is vital that patients better understand their disease. Moreover, receiving care from a multidisciplinary team could change many patients' outcomes.

As part of the "Speaking Out" video series and on behalf of Blue Faery: The Adrienne Wilson Liver Cancer Association, *CURE®* spoke with Dr. Laura M. Kulik, a professor at Northwestern University's Feinberg School of Medicine in Chicago, about the types and stages of liver cancer, as well as treatment options with a multidisciplinary approach.

Q: *CURE®*: What are the types of liver cancers in adults? How do they differ from one another?

A: Kulik: That's an important question. I often hear people say, "Oh my, someone died of liver cancer," but most cancers in the liver will be metastatic, meaning they're coming from another organ. When people have primary liver cancer it means the cancer originated in the liver itself, it's not coming from somewhere else.

The (most commonly diagnosed type) of liver cancer is hepatocellular carcinoma, or HCC. The way I describe this to patients is the analogy of a tree: you have a tree with a trunk, branches, and then all the way up to the tiny leaves. If you have a cancer of the leaves, those are equivalent to the liver cells, and that's called hepatocellular carcinoma. That's a cancer that we see (more than) 80% of the time in people with underlying liver disease, specifically cirrhosis — which is in the scarring score that we use if someone has cirrhosis, that's the most scar tissue someone has.

Another type is cholangiocarcinoma, and that is cancer anywhere from the twigs to the branches to the main tree trunk, and that (involves) the drainage system of the liver, which is called our bile ducts. We are seeing this type of cancer also increase, especially if it is coming from the little (branches) where it's called intrahepatic cholangiocarcinoma, so you can see it on a scan as a mass within the liver.

And then there are other types of cancer that form more frequently in the larger bile ducts.

Q: How is liver cancer staged, and how do we define those stages?

A: There are different stages that are used in liver cancer. The most (common staging system) used by clinicians within the United States, and I would say in Europe, is the Barcelona Clinic Liver Cancer staging system, which breaks it down into five separate stages: very early, early, intermediate, advanced and very advanced.

These are decided based on multiple factors. It's how much tumor someone has present. It's how well they are performing. Are they doing their daily activities? Can they do everything on their own? Are they in bed, and, if so, what percentage of the time? How well is their liver actually functioning? I call this the report card of the liver.

Patients are given what's called a Child-Pugh report card. It's just like in school: it's an A, B or C, with A being the best. The worse the liver function, the (higher the) risk is of dying of liver disease. And, unfortunately, (liver failure) is a competing risk of death related to the cancer itself.

Q: Let's say a patient just received a cancer diagnosis. What are some questions that they should ask their health care team?

A: Important questions include what stage (is the cancer and) is this something that has the potential to be cured? Am I in the right place? Do I need to be sent somewhere else to get an opinion on the treatment of this liver cancer?

Q: With treatment, we often talk about a multidisciplinary approach in cancer care. Can you talk about how this approach plays a role in liver cancer and its treatment options?

A: The multidisciplinary approach is becoming the absolute standard not only (for treating) liver cancer but other cancers, as well. (The approach) is comprised of multiple experts in their area, predominantly in an HCC multidisciplinary conference, including:

- **A hepatologist,** who is experienced in the liver and the treatments of liver disease and how to improve potential function and treat the complications.

- **A surgeon,** who is involved in doing a resection, which means cutting out that piece of the liver that has the cancer and then the remaining liver remain. (This) includes a liver that has cirrhosis, because (patients are) at risk of getting cancer again in the future as a result of that.

- **An oncologist.** There has been a burst in the number of (Food and Drug Administration)-approved medications for liver cancer and the more advanced disease. This is generally in patients who have disease that's outside the liver, or what's called metastatic. (The cancer has moved beyond) the organ that it started in, or they have invasion into some of the main vessels within the liver, generally what's called the portal vein or the hepatic vein.

- **An interventional radiologist,** who does most of the local regional therapies.
- **A radiologist,** who helps interpret the films.

- **And, importantly, nurses.** I think the nurses are a key point, because these are the people who are on the phone with the patients, who are checking the patients out, who will be (saying), "Oh, I think we should do this, or we should do that for the patient," based on all these different things. And then the nurse will say, "I've been talking with them and they don't want to do transplant." This is the reason why their input is very important in making those decisions.

A multidisciplinary approach (brings in) the expertise, experience and knowledge from all these different people. It's similar to ... a football team. Instead of having 11 players on the team on the field, if you only have five players on the field you're not going to do as well in that game. With a multidisciplinary approach, you're going to get everyone to say what they think is the best for that patient.

Patients should be asking if there is a multidisciplinary cancer tumor board. If not, many of these communities are (working) with their local or closest transplant center. They're allowed to present the cases and then get that input. We can get that information for the patient and also potentially save them from a long drive. Or we can encourage them to make that trip because they are candidates for something that would benefit them.

Q: To bring it all together, what is your best piece of advice for a patient who has recently received a liver cancer diagnosis?

A: Well, first and foremost, I would say, "Don't panic." This is a very scary diagnosis. But I would say be your own advocate. And if you don't have that within you because you're overwhelmed or you just don't know (what to ask), assign someone to be your advocate. You really want to be asking (your physician) those questions that we've just covered: Am I a transplant candidate? Why am I not a transplant candidate? And if I had a donor, am I a living donor transplant candidate?

I've seen so many patients who have shown up and we start talking about a living donor; things have really changed now. This is a conversation we have very early on with people who have liver cancer. Before we would say, "Oh, they're going to get points on the waiting list. They'll get transplanted." More than 15 years ago, patients were transplanted generally within three months after being put on the list for liver cancer. That's not the case anymore. The waiting time is longer and, therefore, the longer you wait, the greater the chance that the cancer may grow to a point that transplant is no longer an option. So now we talk about the living donor much earlier than we used to in the past. I've seen so many patients … who say, "I was told I wasn't a candidate for living donor." And many times that may be due to a misunderstanding of how living donor transplant works, specifically in centers that don't do living donor (transplants). If (doctors at a center) don't have the expertise or the experience, it's going to be hard to counsel a patient about being a living donor candidate.

Speaking Out PRESENTED BY cure

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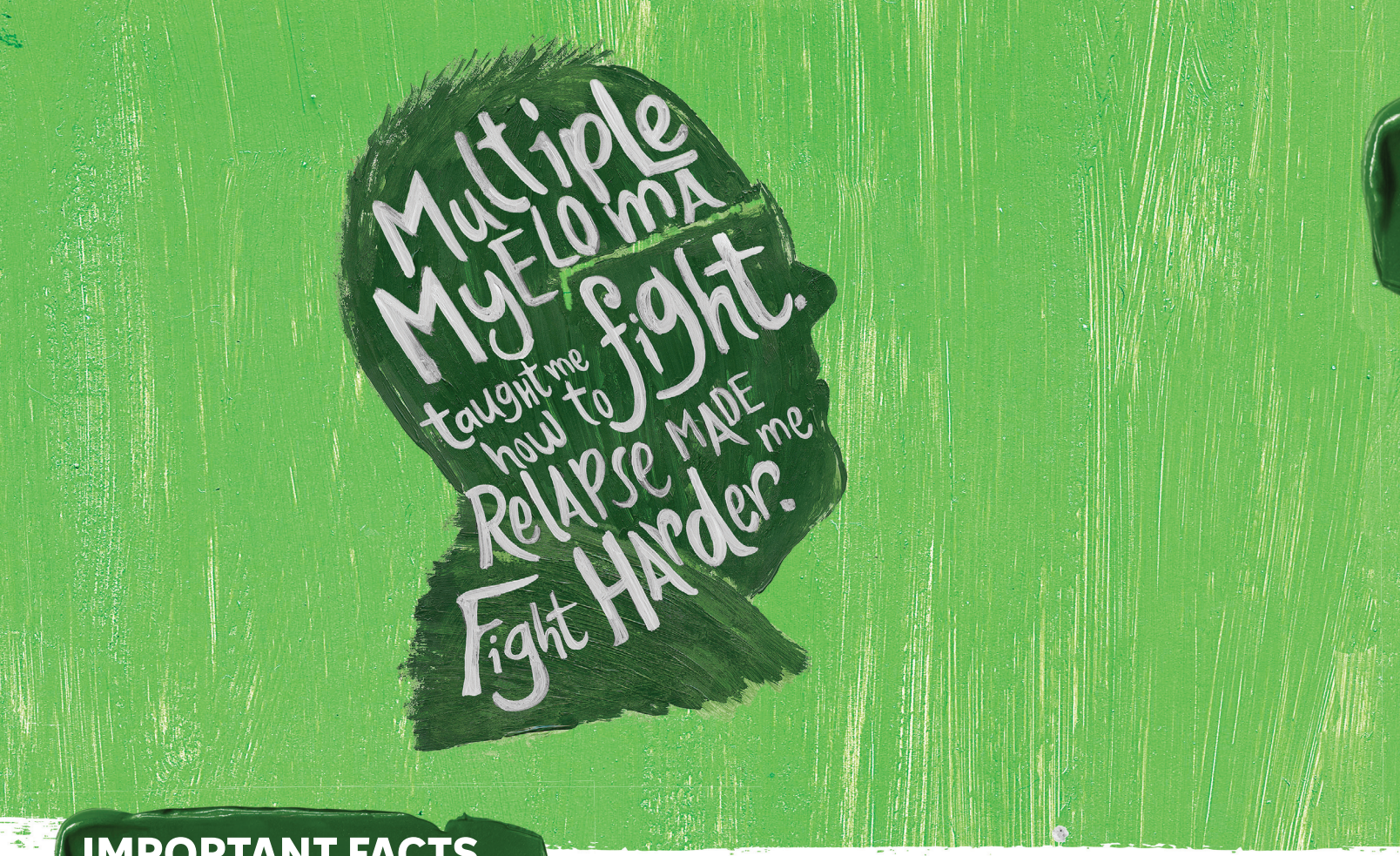

IMPORTANT FACTS ABOUT BLENREP

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.

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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.

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- Avoid wearing contact lenses during treatment with BLENREP unless directed by your eye specialist.

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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:

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- itching or rash
- shortness of breath, cough, or wheezing
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- dizziness
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- fever
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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.

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- 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.

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ADVANCES IN SECOND OPINIONS

Second opinions may enhance your treatment plan or even change your course.

By ARLENE WEINTRAUB

In 2019, after Jason Pike received a diagnosis of a rare sarcoma that had spread across his abdominal cavity, his doctors in San Diego told him it would be too risky to operate. Four rounds of chemotherapy didn't make a dent in the tumor, and Pike's doctors said they could only offer him palliative care.

So Pike sought a second opinion from an oncologist at the University of Southern California in Los Angeles who specializes in treating rare sarcomas and is known for performing delicate, complex surgeries. Pike found him by researching his particular type of tumor online and networking with other patients, some of whom he met in Facebook groups for sarcoma survivors. He ultimately switched his care, and in July 2019, Pike underwent an 18-hour surgery that involved removing his 20-pound tumor, one kidney, as well as portions of his pancreas, spleen, stomach, diaphragm, colon and surrounding muscle. »

There were some complications, and Pike had to file appeals to his insurance company to have the treatment reimbursed, but his disease is now stable. He's currently in a "holding pattern," and he will soon meet with his team to determine his future treatment plan.

Pike's message for other patients: Get a second opinion. "These are trained professionals, but they're not always right," says Pike, 48, an operations director for a medical devices distributor. "Do your research. Be your own advocate. It's your life."

Cancer experts have long preached the value of second opinions. And getting a second opinion is much easier now. Advances in telehealth and other virtual technologies — the adoption of which exploded during the COVID-19 pandemic — are allowing patients, physicians and pathologists to meet online and share medical records, pathology samples and other information to improve treatment plans.

A 2017 study by the Mayo Clinic found that 88% of patients who received second opinions ended up with a different or refined diagnosis. Experts from The University of Texas MD Anderson Cancer Center in Houston have previously noted that even in cases where the second opinion doesn't change the treatment plan, patients come away from the process feeling reassured they're on the right path.

The insights from second opinions can make a huge difference throughout the course of care, says Dr. Anees Chagpar, a professor in the department of surgery at the Yale School of Medicine in New Haven, Connecticut.

"Patients are often uneasy about how their doctor will feel about them getting a second opinion, but your doctor cares about you," Chagpar says. "They should have no objection to getting a second pair of eyes on your case, and often doctors will collaborate with each other so they can provide the best care."

In fact, your first step should be to ask your primary oncologist for a recommendation of where to go for a second opinion, suggests Dr. Efrat Dotan, associate professor of hematology and oncology at Fox Chase Cancer Center in Philadelphia. That's because you should seek the second opinion from an oncologist who specializes in your particular tumor type, Dotan says, and the physician who made your diagnosis is likely to know where to find such a specialist. Other good sources of referrals are online patient groups and nonprofits that are focused on specific cancers, such as the Sarcoma Foundation of America.

Knowing that patients may be anxious to start their treatments as soon as possible, several cancer centers will offer a second opinion within a day of receiving a request. These centers include Fox Chase, which takes requests for second opinions either online or by phone. Each case is handed to a nurse navigator who coordinates all appointments, secures copies of the patients' test results and other medical records, and shares the information with the team that will be providing the second opinion. Some centers will also offer reviews of the pathology and imaging tests, in some cases changing the diagnoses and recommended treatment course.

« **JASON PIKE** obtained a second opinion for a rare sarcoma after being told that it was too risky to operate on.

JENNY SIEGWART

"The navigators make sure patients are scheduled in a timely manner with all the right doctors, and they shepherd patients through the whole process," Dotan says. The entire process often can be done online, she adds. "I have had multiple visits on Zoom or other virtual platforms to give second opinions to patients who live quite far (away)," she says.

Stanford University in California launched its online second opinion program in 2018, and for some patients with cancer, it has resulted in coordinated care plans that may not have been possible in the past, says Dr. Kristen Ganjoo, an associate professor of oncology at Stanford who specializes in sarcoma.

For example, after Ganjoo met a patient from Nevada who had a rare sarcoma, she arranged for a surgeon to perform the surgery at Stanford.

JENNY SIEGWART

But she was able to do a follow-up consultation with the patient online, saving him 10 hours of driving back and forth from his home.

In other cases, Ganjoo has provided second opinions for out-of-town patients, then arranged for standard treatments such as chemotherapy to be done close to where they live. "If a community physician sends a patient to me for a second opinion, I can formulate a plan for that patient to be treated locally," she says. When patients get CT scans to check their progress, they can follow up with her by video chat. "I can review it with them and say, 'Your CT scan looks good, continue with the same therapy.' It can be reassuring for them to know that someone with sarcoma expertise is watching over them."

GAINING ACCESS TO CLINICAL TRIALS

The National Cancer Institute has selected 71 institutions around the country as "NCI-designated" cancer centers because of their focus on research aimed at developing new cancer treatments. It may be beneficial for patients to obtain second opinions from one of these centers because oncologists who practice there may be researchers in clinical trials of innovative treatments or may know about trials happening at other institutions.

"There's a lot of research right now, and what's amazing is some companies are developing drugs for rare sarcomas," Ganjoo says. "But you may need to get a second opinion from a sarcoma specialist to find the best clinical trial for you."

Although many oncologists recommend getting a second opinion before starting treatment, some patients can benefit from getting that second set of eyes on their case after they've completed one therapy and are moving to a second drug regimen or maintenance therapy.

Sarah Kelly sought her second opinion after she was treated for triple-negative breast cancer at a community hospital near Boston in 2015. She was pregnant when she received her diagnosis, and her first round of chemotherapy — along with the delivery of her daughter, induced at 38 weeks — went well. But when her oncologist treated her with a regimen of taxol and carboplatin, her blood counts dropped so low she had to skip some treatments. »

After SARAH KELLY had low blood counts from her first treatment regimen, she got a second opinion to see how else she can treat her aggressive triple-negative breast cancer.

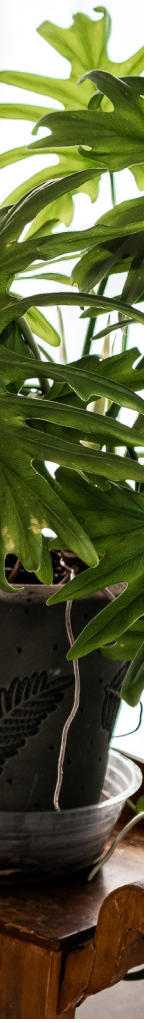
Knowing that triple-negative breast cancer is aggressive, Kelly decided to get a second opinion at Dana-Farber Cancer Institute in Boston. Her oncologist there recommended three high-dose treatments of taxol alone, followed by surgery to remove her tumor and nearby lymph nodes. The treatment was more tolerable for Kelly, and it worked; she has been free of cancer for six years. And she's confident she's getting her care from a cancer center that's staying on top of developments in triple-negative breast cancer.

> "It's important to understand all the options and opportunities for your kind of cancer. ... You're the CEO of your own cancer journey."
>
> — SARAH KELLY

"I took a long-term perspective in moving to Dana-Farber. I knew if there was a recurrence of my cancer, there would be clinical trials happening there and access to new types of treatments," says Kelly, 42, who went on to co-found SaltyGirl Beauty, a company that produces cosmetics using natural and organic ingredients.

Making a decision to switch to the cancer center that provided the second opinion can be difficult, but in some cases, it makes sense, Chagpar says. "Trust your gut," she says, and

DANI COURNOYER



your research. "Say you have a rare cancer, and your first doctor only sees one case of it every five or 10 years. Then you go for a second opinion at a place that sees five cases a week. You may feel more comfortable at that second institution where they have more expertise in your particular condition."

Chagpar was contacted by a patient with a rare cancer at the base of his skull, which his oncologist wanted to treat with surgery. "It would have been very risky. I found out where the national experts were and he got into a clinical trial of a chemotherapy treatment," she says. "He avoided surgery altogether and is doing remarkably well."

PREPARING FOR A SECOND OPINION

So what are the most important questions to ask during a second opinion? Dr. Charles LeVea, chair of pathology and laboratory medicine at Roswell Park Comprehensive Cancer Center in Buffalo, New York, recommends asking whether your case will be reviewed by a tumor board and, if so, who would serve on that board.

"Multidisciplinary tumor boards meet as a group, with pathologists, oncologists, surgeons and other people who would be taking care of the patients," LeVea says. "We project pathology slides on a screen so everyone understands the diagnosis and can discuss it." Some advanced cancer centers use new technology to convert tumor glass slides to digital images, which can then be run through algorithms that enhance details that might otherwise be missed — and that can lead to a more accurate diagnosis, LeVea says.

Dotan recommends asking what the standard of care for your cancer would be at the institution that's providing your second opinion. Depending on the tumor type, some cancer centers may have different strategies when it comes to surgery, chemotherapy, radiation and immunotherapy. "You want to know if the standard of care fits what you're being offered at your local site," she says. "If you find out that the place you go for a second opinion does something differently, that may be worth exploring."

Finally, if you're open to participating in a clinical trial, be sure to bring that up to your doctor during your second opinion appointment.

Kelly says she felt a bit guilty telling her first oncologist that she obtained a second opinion at Dana-Farber and decided to continue her treatment there. But in the end, she knew it was the right decision.

"It's important to understand all the options and opportunities for your kind of cancer," Kelly says. "As I always say, you're the CEO of your own cancer journey."

KELLY decided where to get her second opinion based on their access to new types of treatments.

DANI COURNOYER

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Patient portrayal

INDICATIONS AND IMPORTANT SAFETY INFORMATION

What is CABOMETYX?

CABOMETYX is a prescription medicine used to treat:

- People with kidney cancer (renal cell carcinoma). CABOMETYX may be used:
  - Alone to treat people with renal cell carcinoma (RCC) that has spread (advanced RCC)
  - In combination with nivolumab when your cancer has spread (advanced RCC), and you have not already had treatment for your advanced RCC
- People with liver cancer (hepatocellular carcinoma) who have been previously treated with the medicine sorafenib.

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

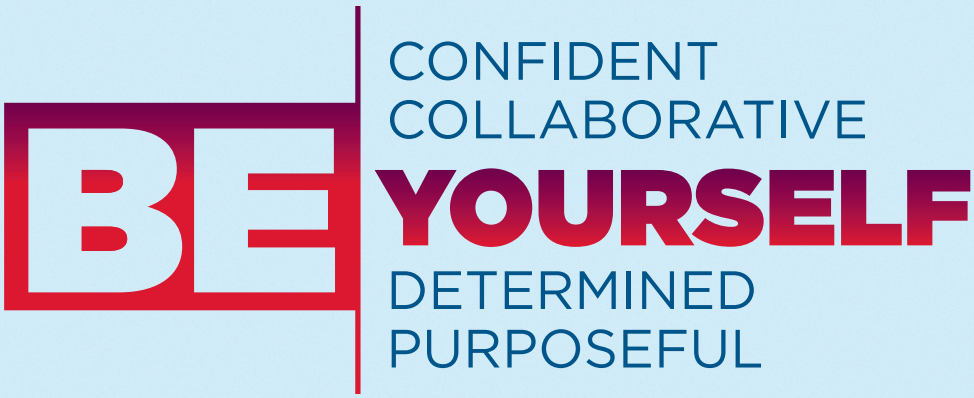
What are the possible side effects of CABOMETYX?

CABOMETYX may cause serious side effects, including:

Bleeding (hemorrhage). CABOMETYX can cause severe bleeding that may lead to death. Tell your healthcare provider right away if you get any signs of bleeding during treatment with CABOMETYX, including:

- Coughing up blood or blood clots
- Vomiting blood or if your vomit looks like coffee grounds
- Red or black (looks like tar) stools
- Menstrual bleeding that is heavier than normal
- Any unusual or heavy bleeding

A tear in your stomach or intestinal wall (perforation) or an abnormal connection between 2 parts of your body (fistula). Tell your healthcare provider right away if you get tenderness or pain in your stomach area (abdomen) that is severe or that does not go away.



Talk to your doctor about how CABOMETYX® + OPDIVO® may help you

CABOMETYX® (cabozantinib) tablets + OPDIVO® (nivolumab)

CABOMETYX.com

Blood clots, stroke, heart attack, and chest pain. Get emergency help right away if you get:

- Swelling or pain in your arms or legs
- Shortness of breath
- Feel lightheaded or faint
- Sweating more than usual
- Numbness or weakness of your face, arm or leg, especially on one side of your body
- Sudden confusion, trouble speaking or understanding
- Sudden trouble seeing in one or both eyes
- Sudden trouble walking
- Dizziness, loss of balance or coordination
- A sudden severe headache

High blood pressure (hypertension). Hypertension is common with CABOMETYX and sometimes can be severe. Your healthcare provider will check your blood pressure before starting CABOMETYX and regularly during treatment with CABOMETYX. If needed, your healthcare provider may prescribe medicine to treat your high blood pressure. Tell your healthcare provider if you develop severe headaches, nose bleeds, tiredness or confusion, vision changes, chest pain, trouble breathing, irregular heartbeat, or blood in your urine.

Diarrhea. Diarrhea is common with CABOMETYX and can be severe. If needed, your healthcare provider may prescribe medicine to treat your diarrhea. Tell your healthcare provider right away, if you have frequent loose, watery bowel movements.

A skin problem called hand-foot skin reaction. Hand-foot skin reactions are common and can be severe. Tell your healthcare provider right away if you have rashes, redness, pain, swelling, or blisters on the palms of your hands or soles of your feet.

Please see additional Important Safety Information and brief summary of full Prescribing Information on the following pages.

Liver problems. Liver problems may happen during treatment with CABOMETYX. When CABOMETYX is taken in combination with nivolumab, severe changes in liver function tests may happen more often than if you take CABOMETYX alone. Your healthcare provider will do blood tests to check your liver function before and during treatment with CABOMETYX.

Tell your healthcare provider right away if you develop symptoms of liver problems including: 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, bleeding or bruising more easily than normal.

Adrenal gland problems. Your healthcare provider will monitor you for this problem. Your healthcare provider may prescribe hormone replacement therapy or corticosteroid medicines if needed. Tell your healthcare provider right away if you develop any of the following signs or symptoms: extreme tiredness, dizziness or fainting, weakness, nausea, or vomiting.

Protein in your urine and possible kidney problems. Symptoms may include swelling in your hands, arms, legs, or feet. Your healthcare provider will check you for this problem during treatment with CABOMETYX.

Severe jaw bone problems (osteonecrosis). Your healthcare provider should examine your mouth before you start and during treatment with CABOMETYX. Tell your dentist that you are taking CABOMETYX. It is important for you to practice good mouth care during treatment with CABOMETYX. Tell your healthcare provider right away if you develop any symptoms of jaw problems, including: jaw pain, toothache, or sores on your gums.

Wound healing problems. Wound healing problems have happened in some people who take CABOMETYX. Tell your healthcare provider if you plan to have any surgery before or during treatment with CABOMETYX.

- You should stop taking CABOMETYX at least 3 weeks before planned surgery.
- Your healthcare provider should tell you when you may start taking CABOMETYX again after surgery.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS). A condition called reversible posterior leukoencephalopathy syndrome can happen during treatment with CABOMETYX. Tell your healthcare provider right away if you have headaches, seizures, confusion, changes in vision, or problems thinking.

Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with CABOMETYX if you have certain side effects.

The most common side effects of CABOMETYX include:

- Tiredness
- Decreased appetite
- Nausea
- Vomiting
- Weight loss
- Constipation
- Difficulty speaking

The most common side effects of CABOMETYX when used with nivolumab include:

- Tiredness
- Mouth sores
- Rash
- Low thyroid hormone levels (hypothyroidism)
- Pain in muscles, bones, and joints
- Decreased appetite
- Nausea
- Changes in the way things taste
- Stomach-area (abdominal) pain
- Cough
- Upper respiratory tract infections

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These are not all of the possible side effects of CABOMETYX. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

If your healthcare provider prescribes CABOMETYX in combination with nivolumab, also read the Medication Guide that comes with nivolumab.

Before you take CABOMETYX, tell your healthcare provider about all of your medical conditions, including if you:

- Have had a liver problem other than liver cancer.
- Have a recent history of bleeding, including coughing up or vomiting blood, or black tarry stools.
- Have an open or healing wound.
- Have high blood pressure.
- Plan to have any surgery, dental procedure, or have had a recent surgery. You should stop treatment with CABOMETYX at least 3 weeks before planned surgery.
- Are pregnant, or plan to become pregnant. CABOMETYX can harm your unborn baby.
  - If you are able to become pregnant, your healthcare provider will check your pregnancy status before you start treatment with CABOMETYX.
  - Females who are able to become pregnant should use effective birth control (contraception) during treatment and for 4 months after your final dose of CABOMETYX.
  - Talk to your healthcare provider about birth control methods that may be right for you.
  - If you become pregnant or think you are pregnant, tell your healthcare provider right away.
- Are breastfeeding or plan to breastfeed. It is not known if CABOMETYX passes into your breast milk. Do not breastfeed during treatment and for 4 months after your final dose of CABOMETYX.

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

What should I avoid while taking CABOMETYX?

Avoid drinking grapefruit juice, eating grapefruit or taking supplements that contain grapefruit or St. John's wort during treatment with CABOMETYX.

Please see additional Important Safety Information on the previous pages and brief summary of full Prescribing Information on the following pages.

EXELIXIS®

CABOMETYX® (cabozantinib) tablets

Consumer Brief Summary for
CABOMETYX® (Ka-boe-met-iks) cabozantinib tablets

Please read the Patient Information before you start taking CABOMETYX and each time you get a refill. There may be new information.

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How should I take CABOMETYX?

- Take CABOMETYX exactly as your healthcare provider tells you to take it.
- **Do not** take CABOMETYX with food. Take CABOMETYX at least 1 hour before or at least 2 hours after eating.
- Swallow CABOMETYX tablets whole.
- **Do not** crush CABOMETYX tablets.
- If you miss a dose and your next scheduled dose is in:
  - Less than 12 hours, take your next dose at the normal time. Do not make up the missed dose.
  - 12 hours or more, take the missed dose as soon as you remember. Take your next dose at the normal time.

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How should I store CABOMETYX?

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

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

General information about the safe and effective use of CABOMETYX.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use CABOMETYX for a condition for which it was not prescribed. Do not give CABOMETYX to other people, even if they have the same symptoms you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about CABOMETYX that is written for health professionals.

Manufactured for Exelixis, Inc. Alameda, CA 94502

For more information, go to www.cabometyx.com or call 1-855-292-3935.

This brief summary is based on CABOMETYX® (cabozantinib) Patient Information. Issued: 01/2021

EXELIXIS®

 02/2021 CA-1895

FOLLOW YOUR GUT:

Advances in Understanding Microbiomes Are Transforming Cancer Care

The gut microbiome plays an important role in how patients may respond to cancer treatments, and researchers are learning more about ways to alter it to benefit treatment outcomes.

By TARA HAELLE

On the same day in March 2018, three things happened in the life of Lorenzo Cohen, professor and director of the Integrative Medicine Program at The University of Texas MD Anderson Cancer Center in Houston. First, he and his wife signed off on the final draft of their book "Anticancer Living: Transform Your Life and Health With the Mix of Six," focused on cancer prevention and improving outcomes for those with cancer. Next, he received an email from the Melanoma Research Alliance telling him they would fund his study on lifestyle factors in patients with melanoma. Finally, he learned that the node that had been growing in his left armpit in recent weeks was stage 3 melanoma with unknown primary location. »

LORENZO COHEN implemented what he's studied for years into his own life to alter his gut microbiome.

TARA FLANNERY

"That means the immune system did what it had to do to knock out the (original tumor that began the cancer) but not soon enough before a few cells started to grow in the (armpit)," Cohen, who holds a postdoctorate degree, explains. He started taking a combination of Yervoy (ipilimumab) and Opdivo (nivolumab) as neoadjuvant immunotherapy — treatment given before surgery to shrink the tumor first. It was soon obvious the immunotherapy was working. "The nodes just started melting away," he says.

But he wanted to do more for his therapy. Cohen is an expert on lifestyle habits that reduce risk of cancer and improve outcomes in those with cancer, and he had studied how psychological factors influence hormones that then affect the immune system. He knew, for example, that chronic stress weakens the immune system and can alter the microenvironment around a tumor, making it more hospitable to cancer growth.

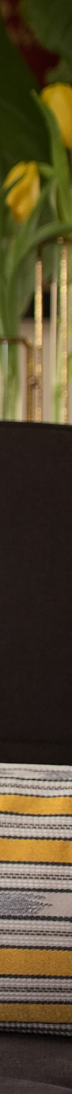
"Stress was the first thing I knew I had to manage better," he says. He doubled down on yoga, meditation and exercise because "the evidence is overwhelming that regular physical activity makes a huge difference on immune function and activation," he says. He also started taking a beta-blocker, a drug that lowers heart rate and blood pressure by blocking the effects of a stress hormone and potentially reducing the effect of stress within the tumor microenvironment. He then turned to his diet. Cohen was familiar with the research of his colleague, Dr. Jennifer Wargo, a surgical oncologist at MD Anderson who studies how melanoma patients respond to immunotherapy based on the bacteria in their guts. He planned to use current evidence to improve his own gut bacteria, but he would discover that trying to manipulate the makeup of bacteria in our bodies can be tricky.

MEET THE MICROBIOME

Wargo discovered early in her career that bacteria in pancreatic cancer tumors could break down chemotherapy into its inactive form. She began studying the millions of microbes that grow in a tumor alongside the cancerous cells, which is known as the tumor microbiome. Soon she was investigating the human gut microbiome, a community of organisms that has a far bigger effect on human health than researchers realized even a decade ago.

"In our bodies, there are hundreds of trillions of microbes that outnumber our cells," Wargo says, adding that only a fraction of cells in our bodies are human. The rest are bacteria, viruses, fungi and other microbes. "There are more microbial genes in our body than there are stars in the galaxy," she says. "It goes without saying that these microbes could have an impact on the way our body functions and how it may react to cancer treatment."

Scientists have learned that these bacteria can help break down food and fight illness, or they can cause inflammation



or contribute to chronic disease. It all depends on the balance of "good" and "bad" microbes in the gut, where the majority of the microbiome flourishes. Though researchers are still learning what makes a healthy microbiome, they know genetics, age, diet, lifestyle, medications, the environment and other factors can affect it. Antibiotics, for example, can wipe out good bacteria. Cancer treatments, including surgery, chemotherapy and radiation, also can disrupt the microbiome's balance.

Research into the microbiome has touched nearly every area of medicine, from gastrointestinal disorders to heart disease, autism to Alzheimer disease, obesity to cancer. But scientists are in the earliest stages of learning how to alter the microbiome or restore imbalances. One way to modify gut bacteria is increasing or decreasing probiotic intake — the microorganisms themselves — or prebiotics, the fibrous foods that feed the bacteria. For example, taking probiotic supplements or eating fermented foods rich with bacteria can sometimes offset the negative effects of antibiotics that kill off too much good bacteria.

Another option is a fecal microbiota transplant, in which fecal matter of a healthy donor (first screened for harmful, infectious germs) is transplanted into another person's gastrointestinal (GI) tract to restore the balance of healthy bacteria. This is done through a colonoscopy or through a pill or liquid. Fecal transplants are already the standard of care for recurrent Clostridium difficile infections, which occur in up to 10% of patients with cancer undergoing chemotherapy and 20% of all people with cancer.

But aside from those treatments, fecal transplants for other conditions are still only in trials, not treatment rooms, explains Dr. Saranya Chumsri, an oncologist specializing in breast cancer at Mayo Clinic in Jacksonville, Florida. "We're not quite there yet in the cancer world," she says, but scientists are making headway. Chumsri has been conducting studies with over-the-counter probiotics to learn whether these supplements or other microbiome restoration products can improve treatment responses in patients with breast cancer, but it's tricky to figure out the best combination of bacteria to offer.

"Studies show that if you have diverse gut microbiome — not just species but more diversity of the type of bacteria in the gut — it's actually more protective for cancer," she says. But it's not always as simple as taking pills from the store.

"The problem with over-the-counter probiotic capsules is that they break apart in the stomach," Chumsri explains. The stomach's low pH can kill the bacteria before it reaches the rest of the gut, so researchers are looking at other options.

> "I did not realize (the gut microbiome) was that important until I had cancer and needed to maintain a good gut balance."
>
> — DWAYNE COPELAND

ADVANCES IN GUT MICROBIOTA WITH MELANOMA

As scientists have learned how integral gut bacteria is to the immune system, the microbiome has received more attention in cancer research.

"Although our immune (system) originally evolved to fight microbes, it has actually become tolerant of some of them, and they shape how our immune system functions," Wargo says. "Depending on what the bugs look like, your gut can influence your response to immunotherapy."

Two studies in 2015 found that the microbiomes of mice can affect how well they respond to checkpoint inhibitor drugs and that researchers could change their microbiomes to improve the mice's response. More recent research involving patients with cancer has found that differences in gut bacteria composition are linked to survival rates after bone marrow/stem cell transplants and may be able to reduce GI side effects from cancer treatment.

"I see a lot of patients referred to me with diarrhea and colitis," says Dr. Pankaj Vashi, a gastroenterologist and vice chief of staff at Cancer Treatment Centers of America (CTCA) in Chicago. "If you give them doses of good bacteria (during) immunotherapy, it can reduce the incidence of colitis." Vashi has seen other patients experience lower levels of toxicity to immunotherapy for kidney or lung cancer if their gut microbiome has the right mix of bacteria.

The question is whether it's possible to modify patients' microbiomes to achieve better response rates or less toxicity with cancer treatments. The most progress with these experiments is seen in patients with melanoma.

A study published in 2017 by Wargo and colleagues examined the gut microbiome of 112 patients with melanoma receiving anti-PD-1 immunotherapy, which not only kill cancer cells directly but block a pathway that protects tumor cells from the components of the immune system that fight cancer. Patients who responded to the therapy had higher rates of diversity and more Ruminococcaceae bacteria. It was research such as this that inspired Cohen to see if he could improve the diversity of his microbiome.

"Your microbiome is totally dependent on what you eat," Vashi says. "If you eat a lot of fast foods and synthetic foods, you're going to have issues with your gut microbiome." Those who eat lots of fruits, vegetables, lentils and legumes, however, tend to experience fewer side effects and have better outcomes overall.

Cohen was already eating a mostly whole food vegan diet, with occasional eggs or cheese. But after receiving his diagnosis, he increased his intake of probiotic-rich foods and reduced his carbohydrates, having read that spikes in insulin »

COHEN experimented with his diet to learn what could impact the gut microbiome, which also played a role in his clinical research.

after eating carbs can negatively affect tumor microenvironments. He swapped out healthy grains such as oatmeal and quinoa for fermented foods such as miso, kombucha, sauerkraut, a liquid probiotic drink and nondairy yogurts fortified with extra bacteria.

He signed up as a participant in his own study — the one he was conducting with Wargo and others that had received funding the day he received his diagnosis — so he could analyze changes in his microbiome. Three months after his initial microbiome sample, he was startled to find less biodiversity in his gut than when he started. He stayed on the diet and analyzed another sample three months later: Again, it had less biodiversity than his first sample.

"I needed to do something, so I decreased the amount of probiotic food and increased healthy grains — quinoa, buckwheat, oatmeal, maybe 2 to 3 tablespoons a day of a healthy whole-grain mush," he says. Another three months later, his microbiome's diversity was better than it had been at the start of the study. Though he can't be sure of the exact cause, it seemed that increasing his healthy microorganisms with extra food-based probiotics while decreasing prebiotics led to dysbiosis, an imbalance in his gut bacteria, and a decrease in the diversity of his gut bacteria.

Cohen, Wargo and their colleagues presented preliminary findings of that study in 2019. Among 46 patients with melanoma, those who ate a high-fiber diet rich in whole grains, fruits and vegetables were five times more likely to respond to anti-PD-1 therapy than those who had a low-fiber diet. And those who took probiotic supplements tended to have lower microbiome diversity.

"What's interesting about the microbiome is that it's far more complex than we know," Cohen says. Cohen underwent surgery in June 2018 that removed the entire tumor and then continued taking Opdivo. He has had no evidence of disease since then.

The most recent breakthrough has replicated in humans a study previously done in mice. Two studies in February 2021 showed that fecal transplants from patients with melanoma who responded to checkpoint inhibitor therapy could turn some nonresponders into responders. In the phase 1 trial led by Dr. Gal Markel of the Sheba Institute in Israel, in which Wargo was involved, 10 patients with metastatic melanoma who had not responded to anti-PD-1 therapy received fecal transplants from patients who had responded. Two of the 10 patients then partially responded, and one had a complete response.

The other study, from the University of Pittsburgh Medical Center, involved 15 patients with advanced melanoma who had not responded to a combination treatment with Keytruda (pembrolizumab) and Opdivo. After undergoing fecal transplants and then further treatment with Keytruda, six of the 15 saw a reduction in tumor size or no more progression. Those six had higher amounts of bacteria previously linked to immunotherapy response. The researchers suspect the changes to a patient's gut microbiome may influence a tumor's microenvironment to make it more susceptible to immunotherapy, but this is only one possible explanation for why changing the gut microbiome appeared to improve responses. Currently approximately 40% of patients with advanced melanoma do not respond to immunotherapy, so researchers hope larger trials will show this treatment can increase how many patients respond.

USING DIET TO MAINTAIN A HEALTHY BALANCE

Research into modulating the microbiome has expanded to colorectal cancer, but doctors such as Vashi have been counseling their patients for years on how to find the right diet for their cancer, body type and health. One of those patients is Dwayne Copeland, a 57-year-old middle school teacher in Florence, Alabama. During the summer of 2010, while in Maryland for professional development, Copeland began feeling sick each afternoon. After he returned home, Copeland, also a football coach, began feeling sick during practice. When blood showed up in his stool, he called his family doctor. That October, he found out that he had colorectal cancer in all three

TARA FLANNERY

parts of his large intestine. The first oncologist he saw recommended immediate surgery but told him he had only one to three years to live, so Copeland got a second opinion at CTCA.

"They told me I did not have an expiration date. That was really good to hear," he says. He underwent 60 doses of chemo and 36 radiation visits before a total colectomy in January 2011, which left him with 3 inches of his rectum and 12-inch J-pouch — a surgery that allows a person to have control over their bowels without a complete colon — that enabled him to continue his active lifestyle without needing a colostomy bag. He also learned he has the hereditary condition MUTYH (MYH)-associated polyposis in which too many copies of the same cell are created, increasing the risk of colorectal cancer.

"It wasn't *if* I'd have cancer again, it was *when*," Copeland says. Vashi and his treatment team taught him what to eat to keep his microbiome balanced and reduce the likelihood of recurrence. As a science teacher, Copeland had read about the microbiome, "but I did not realize it was that important until I had cancer and needed to maintain a good gut balance," he notes. Though he no longer coaches, he walks six days a week, maintains muscle mass with body weight and dumbbell exercises, takes a probiotic supplement, eats an apple and banana every day, and eats plenty of whole wheat bread and fish.

"The one thing I refrain from is sugar," he says. "Anything (such as) desserts with a lot of sugar, that's a risk-reward thing for me because I know it'll cause problems with my gut bacteria." He can tell within 45 minutes of eating if his gut is rebelling against what he ate.

As researchers continue exploring the relationship between the microbiome and cancer treatment, each discovery brings up more questions. It's not clear how to determine which patients might benefit from a treatment that alters their microbiome, who the best donors are for fecal transplants, when patients should receive the transplant during treatment or what is the best method for fecal transplant. But it is clear from Cohen's experience that even seemingly positive changes in diet can backfire. And over-the-counter probiotics aren't necessarily beneficial, especially since they are not regulated by the Food and Drug Administration for quality.

"We haven't yet figured out a magic pill that can work, and currently we focus more on a whole foods-based approach," Wargo says. Her colleague, Nadim Ajami, executive director of scientific research for the Program for Innovative Microbiome and Translational Research at MD Anderson, points out that many probiotic supplements are a single organism. "We're also seeing with cancer patients that diversity is good," he says. "You wouldn't want to miss the opportunity to increase diversity, but that is not the only ingredient."

Vashi recommends that patients who want to learn more about ensuring a healthy microbiome should ask their oncologist for a referral. Many oncologists still haven't recognized the importance of probiotics, prebiotics and microbiome balance to cancer care, but they should be willing to refer patients to dietitians or others who are familiar with the evidence.

TARA FLANNERY

A well-rounded diet may affect a patient's gut microbiome, which can include a focus on whole foods, plants and high fiber.

Cohen pointed out the risks of making recommendations with incomplete evidence. After giving a lecture on the microbiome, he heard from a patient whose oncologist recommended taking probiotics based on Wargo's early findings. That was before the findings that patients with melanoma taking probiotic supplements had less diversity were presented.

"This well-intentioned physician was potentially harming a patient because he was getting just a little bit ahead of what the evidence actually showed," Cohen says. "There's never been a clinical trial of probiotic supplementation with melanoma patients to say it helps the gut. Maybe the fecal microbiome transplant may help, but you can't get that over the counter."

The key appears to be a well-rounded diet that doesn't tip too far in any direction. "Now the only recommendation we can really make is to try to achieve good gut health through a whole food, plant-centered, high-fiber diet," he says. "Healthy gut bacteria for the majority of people will thrive and grow and proliferate in a positive way if they're fed healthy foods."

IMPORTANT SAFETY INFORMATION

What is XPOVIO?

XPOVIO® (selinexor) is a prescription medicine used:

- in combination with bortezomib and dexamethasone to treat adult patients with multiple myeloma who have received at least one prior therapy.

It is not known if XPOVIO is safe and effective in children less than 18 years of age.

Your healthcare provider will do blood tests before you start taking XPOVIO, and often during the first 3 months of treatment, and then as needed during treatment.

XPOVIO can cause serious side effects, including:

- **Low platelet counts.** Low platelet counts are common with XPOVIO and can lead to bleeding, which can be severe and can sometimes cause death. Your healthcare provider may prescribe platelet transfusions or other treatments for your low platelet counts. **Tell your healthcare provider right away if you have any bleeding or easy bruising during treatment with XPOVIO.**
- **Low white blood cell counts.** Low white blood cell counts are common with XPOVIO and can sometimes be severe. You may have an increased risk of getting bacterial infections during treatment with XPOVIO. If needed, your healthcare provider may prescribe antibiotics if you have signs or symptoms of infection.
- **Serious infections.** Infections are common with XPOVIO and can be serious and can sometimes cause death. This includes upper or lower respiratory tract infections, such as pneumonia, and an infection throughout your body (sepsis). **Tell your healthcare provider right away if you have any signs or symptoms of an infection such as cough, chills, or fever during treatment with XPOVIO.**
- **Neurologic side effects.** XPOVIO can cause dizziness, fainting, decreased alertness, and changes in your mental status, including problems with thinking, seeing or hearing things that are not really there (hallucinations). These problems can sometimes be severe and life-threatening. **Tell your healthcare provider right away if you get any of these symptoms. Do not drive or operate heavy or dangerous machinery until you know how XPOVIO affects you. Take precautions to prevent a fall.**
- **Nausea, vomiting and/or diarrhea.** Nausea, vomiting and/or diarrhea can occur when you take XPOVIO and can sometimes be severe. You may be at risk for becoming dehydrated. Your healthcare provider may prescribe anti-nausea or anti-diarrhea medicines.
- **Loss of appetite and weight loss.** Loss of appetite and weight loss are common with XPOVIO. Tell your healthcare provider if you have a decrease or loss of appetite and if you are losing weight.
- **Decreased sodium levels in your blood.** Decreased sodium levels in your blood are common with XPOVIO. Your healthcare provider may talk with you about your diet and prescribe IV fluids or salt tablets.
- **New or worsening cataract, cloudiness, or loss of transparency of the lens in the eye.** New or worsening cataract are common with XPOVIO. If a cataract forms, your vision may decrease, and you may need eye surgery to remove the cataract and restore your vision. **Tell your healthcare provider right away if you have symptoms of a cataract such as double vision, blurred vision, or sensitivity to light or glare.**

Common side effects of XPOVIO include:

- tiredness
- weakness
- low red blood cell count (anemia). Symptoms may include tiredness and shortness of breath
- constipation
- shortness of breath
- increased blood sugar
- changes in body salt and mineral levels in your blood
- changes in kidney and liver function blood tests

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

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

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

- have or have had a recent or active infection
- have or have had bleeding problems
- are pregnant or plan to become pregnant. XPOVIO can harm your unborn baby
- are taking prescription and over-the-counter medicines, vitamins, and herbal supplements

Ability to have children: XPOVIO may affect the ability of both women and men to have children. Talk to your healthcare provider if you have concerns about fertility.

Females who are able to become pregnant: Your healthcare provider will check to see if you are pregnant before you start taking XPOVIO. You should use effective birth control (contraception) during treatment with XPOVIO and for 1 week after your last dose, as XPOVIO can harm an unborn baby. Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with XPOVIO. Do not breastfeed during treatment with XPOVIO and for 1 week after your last dose of XPOVIO. It is not known if XPOVIO passes into your breast milk.

Males with female partners who are able to become pregnant should use effective birth control during treatment with XPOVIO and for 1 week after your last dose.

Please see the Medication Guide and the full Prescribing Information for XPOVIO.

To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1-888-209-9326 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Karyopharm® Therapeutics

XPOVIO®
(selinexor)

NEW INDICATION
FOR PATIENTS WITH MULTIPLE MYELOMA

Your doctor may prescribe XPOVIO, the only FDA-approved medication of its kind, as early as 1st relapse in multiple myeloma.

XPOVIO® (selinexor) is **now approved** in combination with other treatments (bortezomib and dexamethasone) to treat adult patients with multiple myeloma who have received at least one prior therapy.

LEARN MORE ABOUT TREATMENT AT XPOVIO.COM

PATIENT INFORMATION

XPOVIO® (x-PO-Vee-O)
(selinexor)
Tablets

XPOVIO® (selinexor)

What is XPOVIO?

XPOVIO is a prescription medicine used in combination with the medicines VELCADE® (bortezomib) and dexamethasone to treat adults with multiple myeloma (MM) who have received at least one prior treatment for their disease.

It is not known if XPOVIO is safe and effective in children less than 18 years of age.

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

XPOVIO can cause serious side effects, including:

- **Low platelet counts.** Low platelet counts are common with XPOVIO and can lead to bleeding which can be severe and can sometimes cause death. Your healthcare provider may prescribe platelet transfusions or other treatments for your low platelet counts.
  Tell your healthcare provider right away if you have any bleeding or easy bruising during treatment with XPOVIO.
- **Low white blood cell counts.** Low white blood cell counts are common with XPOVIO and can sometimes be severe. You may have an increased risk of getting bacterial infections during treatment with XPOVIO. Your healthcare provider may prescribe antibiotics if you have signs or symptoms of infection, or certain medicines to help increase your white blood cell count, if needed.

Your healthcare provider will do blood tests before you start taking XPOVIO, and often during the first 3 months of treatment, and then as needed during treatment to monitor you for side effects.

Your healthcare provider may change your dose of XPOVIO, stop your treatment for a period of time, or completely stop your treatment if you have certain side effects during treatment with XPOVIO.

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

What should I tell my healthcare provider before taking XPOVIO?

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

- have or have had a recent or active infection.
- have or have had bleeding problems.
- are pregnant or plan to become pregnant. XPOVIO can harm your unborn baby.
  Females who are able to become pregnant:
  - Your healthcare provider will check to see if you are pregnant before you start taking XPOVIO.
  - You should use effective birth control (contraception) during treatment with XPOVIO and for 1 week after your last dose.
  - Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with XPOVIO.

  Males with female partners who are able to become pregnant:
  - You should use effective birth control during treatment with XPOVIO and for 1 week after your last dose.
- are breastfeeding or plan to breastfeed. It is not known if XPOVIO passes into your breast milk.
  - Do not breastfeed during treatment with XPOVIO and for 1 week after your last dose of XPOVIO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Talk with your healthcare provider before taking any new medicines.

How should I take XPOVIO?

- Take XPOVIO exactly as prescribed by your healthcare provider.
- Your healthcare provider will prescribe dexamethasone with your XPOVIO treatment. Take dexamethasone exactly as prescribed.
- Your healthcare provider will tell you how much XPOVIO to take and when to take it. Do not change your dose or stop taking XPOVIO without talking to your healthcare provider first.
- Swallow XPOVIO tablets whole with water. **Do not break, chew, crush, or divide the tablets.**
- Be sure to take any medicines prescribed by your healthcare provider before and during treatment with XPOVIO to help prevent nausea and vomiting. Tell your healthcare provider if the prescribed medicine does not control your nausea and vomiting.
- It is important for you to drink enough fluids to help prevent dehydration and to eat enough calories to help prevent weight loss during treatment with XPOVIO. Talk to your healthcare provider if this is a problem for you. **See "What are the possible side effects of XPOVIO?"**
- If you miss a dose of XPOVIO, take your next dose at your next regularly scheduled day and time.
- If you vomit after taking a dose of XPOVIO, do not take an extra dose. Take your next dose at your next regularly scheduled day and time.
- If you take too much XPOVIO, call your healthcare provider right away.

What should I avoid while taking XPOVIO?

XPOVIO can cause neurologic side effects.

- **See "What are the possible side effects of XPOVIO?" below.**
- If you have any neurologic side effects with XPOVIO, **do not drive or operate heavy or dangerous machinery until your neurologic side effects go away.**
- **Avoid falling.** Use care as needed to avoid falling due to neurologic side effects.

What are the possible side effects of XPOVIO?

XPOVIO can cause serious side effects, including:

- **See "What is the most important information I should know about XPOVIO?"**
- **Nausea and vomiting.** Nausea and vomiting are common with XPOVIO and can sometimes be severe. Nausea and vomiting may affect your ability to eat and drink well. You can lose too much body fluid and body salts (electrolytes) and may be at risk for becoming dehydrated. You may need to receive intravenous (IV) fluids or other treatments to

help prevent dehydration. Your healthcare provider will prescribe anti-nausea medicines for you to take before you start and during treatment with XPOVIO. **See "How should I take XPOVIO?"**

- **Diarrhea.** Diarrhea is common with XPOVIO and can sometimes be severe. You can lose too much body fluid and body salts (electrolytes) and may be at risk for becoming dehydrated. You may need to receive IV fluids or other treatments to help prevent dehydration. Your healthcare provider will prescribe anti-diarrhea medicine for you as needed.
- **Loss of appetite and weight loss.** Loss of appetite and weight loss are common with XPOVIO and can sometimes be severe. Tell your healthcare provider if you have a decrease or loss of appetite and if you notice that you are losing weight at any time during treatment. Your healthcare provider may prescribe medicines that can help increase your appetite or prescribe other kinds of nutritional support. Your healthcare provider will monitor your appetite and weight before you start XPOVIO and often during the first 3 months, then as needed during treatment.
- **Decreased sodium levels in your blood.** Decreased sodium levels in your blood is common with XPOVIO but can also sometimes be severe. Low sodium levels in your blood can happen if you have nausea, vomiting, or diarrhea, you become dehydrated, or if you have loss of appetite with XPOVIO. You may not have any symptoms of a low sodium level. Your healthcare provider may talk with you about your diet and prescribe IV fluids for you based on the sodium levels in your blood. Your healthcare provider will do blood tests before you start taking XPOVIO, and often during the first 2 months of treatment, and then as needed during treatment to monitor the sodium levels in your blood.
- **Serious infections.** Infections are common with XPOVIO and can be serious and can sometimes cause death. XPOVIO can cause infections including upper or lower respiratory tract infections, such as pneumonia, and an infection throughout your body (sepsis). **Tell your healthcare provider right away if you have any signs or symptoms of an infection such as cough, chills or fever, during treatment with XPOVIO.**
- **Neurologic side effects.** XPOVIO can cause neurologic side effects that can sometimes be severe and life-threatening.
  - XPOVIO can cause dizziness, fainting, decreased alertness, and changes in your mental status including confusion and decreased awareness of things around you (delirium).
  - In some people, XPOVIO may also cause problems with thinking (cognitive problems), seeing or hearing things that are not really there (hallucinations), and they may become very sleepy or drowsy.
  - Taking other medicines that can cause dizziness or mental status changes during treatment with XPOVIO may increase your risk of neurologic side effects.

Tell your healthcare provider right away if you get any of these signs or symptoms.

- **New or worsening cataract, a cloudy or loss of transparency of the lens in the eye.** New or worsening cataract are common with XPOVIO. If a cataract forms, your vision may decrease, and you may need eye surgery to remove the cataract and restore your vision. **Tell your healthcare provider right away if you have symptoms of a cataract such as double vision, blurred vision, sensitivity to light or glare.**

Your healthcare provider may change your dose of XPOVIO, stop your treatment for a period of time, or completely stop your treatment if you have certain side effects during treatment with XPOVIO.

Common side effects of XPOVIO include:

- tiredness
- low red blood cell count (anemia). Symptoms may include tiredness and shortness of breath.
- increased blood sugar
- changes in body salt and mineral levels in your blood
- changes in kidney and liver function blood tests

XPOVIO may cause fertility problems in males and females, which may affect your ability to have children. Talk to your healthcare provider if you have concerns about fertility.
These are not all the possible side effects of XPOVIO.
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 XPOVIO?

- Store XPOVIO at or below 86°F (30°C).
- XPOVIO comes in a child-resistant blister pack.

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

General information about the safe and effective use of XPOVIO.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use XPOVIO for a condition for which it was not prescribed. Do not give XPOVIO to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about XPOVIO that is written for health professionals.

What are the ingredients in XPOVIO?
Active ingredient: selinexor
Inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, Opadry 200 clear, Opadry II blue, povidone K30, and sodium lauryl sulfate.
Manufactured for and marketed by: Karyopharm Therapeutics Inc., 85 Wells Avenue, Newton, MA, 02459
XPOVIO is a registered trademark of Karyopharm Therapeutics Inc. All other trademarks are the property of their respective owners.

For more information, call 1-888-209-9326 or go to www.XPOVIO.com.
Based on Medication Guide approved by the U.S. Food and Drug Administration, as revised in December 2020.

Karyopharm® Therapeutics

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Positive Thinking Is Powerful During and After Cancer Treatment

Channeling optimism during your cancer journey isn't just about living longer — it's about living better

By AMY PATUREL, MS, MPH

In the fall of 2018, Teri Cettina began feeling a mysterious pain around her ribs. "I thought I had done too many ab exercises at the gym," says the 55-year-old health writer from Portland, Oregon.

When Cettina visited her doctor, her blood and urine tests came back normal. But over the next several weeks, the pain worsened. Convinced her muscles were out of whack, she saw a physical therapist who did a 10-minute exam and told Cettina, "This is not musculoskeletal; it's not a rib thing. It's deeper — you need to see your doctor today."

Later that day, Cettina had a CT scan and received a diagnosis: pancreatic adenocarcinoma. Cettina's tumor was particularly troubling because it was entangled in her veins and branches of the aortic artery, making surgical removal virtually impossible. Such grim news would send even the most hopeful optimist into a tailspin. »

KIM NGUYEN

TERI CETTINA learned the importance of having a strong support system throughout her cancer journey.

> *I can't say for certain whether my optimism has kept me going, but it has taught me that good things can come from a bad situation.*
>
> — TERI CETTINA

Cancer and depression are biochemically linked, which complicates patients' ability to stay positive. "Something about the development of the cancer leads to a chemical imbalance in the brain that manifests as depression," says Dr. Allyson Ocean, associate professor of medicine at Weill Cornell Medical College in New York City. Left untreated, depression can interfere with patients' ability to fight the disease.

"Depression is a deactivating condition, meaning you tend not to do things," says Dr. William Dale, the Arthur M. Coppola Family Chair in Supportive Care at City of Hope Comprehensive Cancer Center in Duarte, California. "If you're depressed, you're more likely to skip an appointment or miss a medication and less likely to eat well, exercise and spend time with people who make you feel good."

Despite tough odds and toxic treatments, people do survive pancreatic adenocarcinoma. "There may be a single digit survival rate for this diagnosis, but that means at least one person survived," Cettina says. "I just keep saying to myself, 'What one person can do, another person can do.'"

Studies about whether optimism such as Cettina's improves cancer outcomes are largely inconclusive. It's not clear whether a glass-half-full mentality can help patients with cancer live longer. What scientists do know is that there are plenty of perks to positive thinking — some of which have nothing to do with survival rates.

FIND YOUR PEOPLE

Ever notice how your mood changes when you see someone you love? Positive friends support you when you need it, stick around when you want to discuss the hard stuff and bring out the best in you just by showing up. Turns out those same qualities are key when putting together your health care team.

"I learned early on that you need doctors who are willing to fight for you, who believe you can beat the disease," Cettina explains. "My first potential surgeon looked at me with sad eyes and told me I was going to get really sick very quickly and statistically had about 18 months to live."

A week later, Cettina met with a different oncologist for the first time. He didn't have great bedside manner. But he was logical, even hopeful, about Cettina's odds. He told her, "There's a 25% chance your cancer will respond to treatment to make surgical removal possible. That means 25 out of 100 people go through this treatment and come out of it. Why couldn't one of those four people be you?" Cettina knew she had found the right oncologist.

No matter your type of cancer or its stage, the messages you receive are critical, says Ocean, who co-founded Let's Win!, an innovative nonprofit dedicated to advancing pancreatic cancer research. "Our goal is to connect patients to the researchers, doctors and survivors who can give them reason to hope — not just because there *is* reason to hope, but because having a positive attitude enables patients to fight the disease in a stronger way."

While there are no data to suggest that staying on the sunny side improves outcomes, there's no doubt that if you

KIM NGUYEN

have hope, you're more motivated to try complementary treatments, ask questions and get second opinions. You're also more likely to advocate for yourself. For Cettina, that meant telling her health care team that she didn't want to hear about potential time frames or poor survival rates unless she specifically asked. She wanted to hear about pancreatic cancer survivors.

"I knew how bad the prognosis was because I'm a health writer," Cettina says. "So, I skimmed over the scary statistics and focused on researching hopeful stories about survivors. That became my coping mechanism." She found her first pancreatic cancer survivor on The University of Texas MD Anderson Cancer Center website, a middle-aged woman with stage 4 disease, just like Cettina. After the two connected via email and then phone, Cettina set out to find more survivors and learn everything she could about how they were beating the disease.

"Connecting with survivors is important," Ocean says. "They can give you tips based on their experience, direct you to clinical trials and help you formulate questions for your physicians that you may not have thought to ask."

In addition to assembling a team of experts who believe you can beat the disease and survivors who prove it can be done, it's important to convene support closer to home. After receiving her diagnosis, Cettina knew she needed more people in her corner.

"I hadn't been a big Facebook user, but I felt strongly that sharing this scary news with my network would somehow be helpful," Cettina says. "The response was incredible. Just reading positive words from friends and loved ones made me feel better." The outpouring of support — even from unexpected places — helped buoy her as she navigated rough waters.

BUILD RESILIENCE

In 1990, when Lonnie Reed was 40 years old, doctors gave her a breast cancer diagnosis. She elected to have a lumpectomy followed by radiation, and doctors followed her for several years before declaring her "cleared."

But 17 years later, the broadcast journalist turned state representative from Branford, Connecticut, noticed hypersensitivity in the same breast when she was snorkeling through a school of blue tang in the Cayman Islands. The cancer was back.

"This second primary made me angry and depressed. I had worked so hard to live a healthy life. I felt betrayed," Reed says. "The doctors said they had to do a mastectomy. I told them to take them both because my breasts were trying to kill me."

Reed's cancer was triple negative, which required a long course of chemotherapy. During treatment, she began re-evaluating her life. "I discovered I didn't have time or energy for people and activities that didn't fill my cup," Reed notes. She created a chart with two columns. In column A, she listed things that made her feel calm and happy. In column B, she listed the things that made her anxious or sad. Then she began the difficult work of pruning.

"Your time and energy have to be spent carefully when you have a serious illness (such as) cancer," Dale says. "Patients and families can get stuck thinking about what happened six months ago or questioning how a doctor missed a mass on a mammogram. Unfortunately, we can't change what happened a year ago, but we can do something right now that will make a difference. We can help people grab on to positive experiences and enjoy the life they have right now." »

LONNIE REED reevaluated her life to focus on the positive during her cancer treatment.

ATHENA BLUDÉ

Working with a therapist can help you not only cultivate gratitude but also challenge negative thought patterns. "I learned to ask myself: 'Do you have proof that a certain bad thing is going to happen?' If I don't have proof, the next question is, 'How do you feel when you believe this sad story?'" Cettina says. The idea is to recognize that these negative thought loops don't serve you. Sometimes that requires getting out of your head and finding a purpose bigger than beating cancer.

Forge new relationships, join a cause that's important to you or take a bucket-list trip that you've postponed. "Just don't stop having positive experiences because you're sick," Dale says. For Reed, that meant focusing her energy on environmental threats. Using her high-powered social connections in the media and political worlds, Reed not only fought to stop a dangerous gas plant project while undergoing chemotherapy treatment for her second bout of breast cancer, but she also ran for office.

"I had all of these people looking to me for leadership. That was really encouraging and made me feel present and empowered," she says. "It gave me purpose and with the support of a team of amazing people, we killed the plant proposed for Long Island Sound. I thought, if I can defeat a giant floating gas plant, I can defeat cancer."

After her last chemotherapy treatment, Reed traveled to Paris with her partner. When she returned from the trip, politicians from both sides of the aisle convinced her to run for a seat in the Connecticut House of Representatives — a seat she won in 2008.

CULTIVATE HEALING

The idea that you need to stay positive to effectively treat cancer can put a lot of pressure on an already overtaxed psyche. Amidst the barrage of "stay strong," and "you've got this," you may feel as though you need to hide your shock, pain, anger and grief from friends and family, and that takes a lot of energy.

ATHENA BLUDÉ

> *I had all these people looking to me for leadership. That was really encouraging and made me feel present and empowered.* ***It gave me purpose.***
>
> — LONNIE REED

"As a culture, we want to believe we can think ourselves out of cancer, that we can cause the cancer cells to go away," says Dr. Jana Bolduan Lomax, a licensed clinical health psychologist in Denver who specializes in coping with cancer and survivorship. "The reality is, we don't have that control, but we can create space for people to feel safe to be mad and angry, even if it's inconsistent with their identities."

People with late-stage disease often perform a delicate dance of trying to show people in their lives they're strong while also trying to prepare themselves for their death.

The best way to address both the desire to live and the desire to let go: Get palliative care (also termed supportive care) involved.

"People think when you have palliative care on board that you're giving up hope," Lomax says. "That's not the case at all. Instead, palliative care allows for better symptom management and enhanced quality of life." Research also suggests it may help you live longer.

Results from a study published in *Health Psychology* in 2017 demonstrated that patients with advanced cancer who were depressed and who received palliative care interventions lived longer than those who did not get palliative care services. Researchers suspect that palliative care not only plays a role in managing symptoms but also helps patients focus on what's most important to them: Finding joy despite a difficult diagnosis.

"Cancer takes up a huge slice of the pie. How can you reclaim some of the other slices of that pie?" Lomax says. For Reed, that meant laughter and music. She regularly indulged in all-out cancer laugh fests with her friends and created playlists of her favorite songs: Aretha Franklin's version of "Bridge Over Troubled Water," The Beatles' "Here Comes the Sun" and Bette Midler's "The Rose." "'The Rose' always made cry tears of hope, and I would end these customized concerts with Helen Reddy's 'I am Woman,'" she says.

Cettina's not-so-guilty pleasure is Netflix, especially shows such as "Outlander" and "Bridgerton."

"Watching period pieces takes me out of my life for a while," she says. She also regularly takes time out to tune into her body with qi gong classes, sound (and water) baths and journeys through the art of guided imagery, meditation and hypnosis. Although her goal with hypnosis was initially to alleviate the anticipatory nausea she experienced prior to chemotherapy, the therapist also harnessed the power of her mind to tackle big picture issues.

"He said things (such as) 'Your body is a healing machine,' 'Your body wants to return to its healthy state,' and 'You're going to surprise your doctors and cure this pancreatic cancer,'" Cettina says. "I didn't believe his words in the beginning, but I listened to them over and over, borrowing his optimism."

Six months after Cettina's diagnosis, her tumor had shrunk significantly. However, the presence of liver lesions meant she was not eligible for potentially curative surgery. Long-term survival felt impossible. "I really felt smashed at that point. I curled up into a ball for a few days and felt really bad," she says. But when Cettina emerged, she uncovered other treatment options she wouldn't have pursued if she had been eligible for surgery.

"I think people's mindset needs to be that they're not dying of cancer. They're living with cancer," Ocean says. "To live a life of happiness and positivity is like medicine, and I do think it can help change the trajectory of the disease, even if it's only a temporary change."

With cancer, doors will close. When they do, the key is to look for a proverbial window. Cettina already has outlived her initial life expectancy. "I already feel (as though) I've won the cancer lottery," she says. "I can't say for certain whether my optimism has kept me going, but it has taught me that good things can come from a bad situation. I've been lucky before. I could be again."

Off Our Chests

Dr. John Marshall and his wife, Liza, share their journey with breast cancer from the patient, caregiver and health care provider perspectives.

By KRISTIE L. KAHL AND GINA MAURO

IN NOVEMBER 2006, the lives of the Marshall family changed dramatically when their matriarch, Liza, was diagnosed with stage 3 triple-negative breast cancer. Her husband, Dr. John Marshall, had to learn to juggle being both a caregiver and a doctor.

The family, including the couple's two children, went through a long and stressful journey with Liza Marshall's cancer. In the book "Off Our Chests: A Candid Tour Through the World of Cancer," which will be released May 4, the Marshalls share their perspectives on this challenging time.

THE ANNOUNCEMENT

Although a cancer diagnosis comes as a shock to many, hearing the news from one's husband — John Marshall is chief of the Division of Hematology/Oncology at MedStar Georgetown University Hospital and a professor of medicine and oncology and director at the Ruesch Center for the Cure of Gastrointestinal Cancer at Georgetown Lombardi Comprehensive Cancer Center in Washington, D.C. — can come with a different set of emotions for both the patient and the caregiver.

In the chapter "The Announcement," Liza Marshall, who was then 43 years old, recounts when her husband called midmorning to go over the logistics of an upcoming holiday. He became distracted. What came next? Hearing these words from him: "You have breast cancer."

"I honestly thought he was joking when he first said it … And I said, 'You've got to be kidding me.' And he said, 'No.' I could hear this catch in his voice and (I knew he was) serious," Liza Marshall said. "That was the point at which I could hear panic in John's voice. But at the same time, he stepped in and said, 'OK, this is what we're doing next.' … So I was incredibly fortunate to have somebody there who immediately knew what the next steps were."

John Marshall added that it was a typical morning for him, going through a stack of results for patients undergoing testing for gastrointestinal cancer, until he came across his last name on a pathology report for breast cancer.

"The feeling that I had has never really left me … now, since experiencing that on the receiving side of things, I kind of know what it's like. So, (compared with) what I used to do, now I just feel so much more. And that's, again, part of why we wanted to share our story … for both the patient and the doctor, we really need to look at what we're doing. And the better we can talk to each other, the better we can understand each other (and) the better our outcomes (will be)."

DR. JOHN MARSHALL, and LIZA MARSHALL documented their emotional journey following Liza's diagnosis of triple-negative breast cancer in their memoir, "Off Our Chests: A Candid Tour Through the World of Cancer."

CAREGIVER OR ONCOLOGIST?

The Marshalls wrote "Off Our Chests" not only to tell their story but also to show the perspective of a cancer diagnosis from the patient, the caregiver and the oncologist.

Liza Marshall, who was used to making her own medical decisions as well as the decisions for her family's care, straddled a line between being her own advocate while utilizing the advice from her caregiver, who also happens to be an oncologist. Looking back, however, she joked that she is unsure they did so successfully.

"It was a day-by-day decision. I mean, I certainly relied a lot on John's knowledge — some of that was as an oncologist and some of that was as a caregiver," she said, adding that as the pair got further into her treatment journey, her husband made a conscious effort to take a step back, allowing her to make her own care decisions.

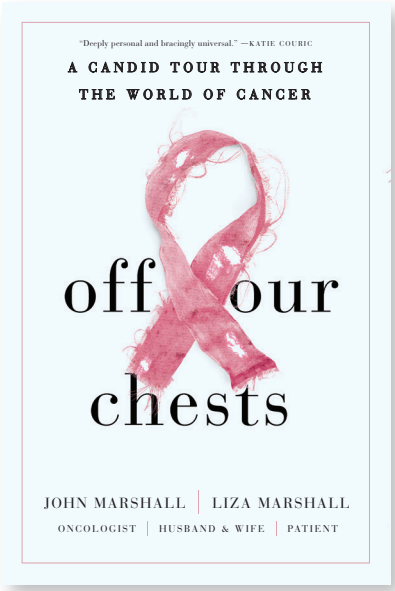
"I can't tell you to this day whether that was the right decision or not. I didn't want him telling me what to do, but, at the same time, I wanted him to tell me what to do. I'm not sure we succeeded in straddling the line, but we both did our best, which I suppose is all anybody can ask of each other."

John Marshall noted that his wife's desire to join a clinical trial gave him a different perspective. As he moved back and forth between being a supportive caregiver and a physician, he worried about a conflict of interest.

"One of the requirements of a (National Cancer Institute) Comprehensive Cancer Center is a certain percentage of patients need to go into clinical trials," he explained. "And so, my wife was contributing to our metrics … It really made me look, from my end, at what trials are all about. It made me look at our research operation and those sorts of things differently, having now experienced it as a consumer."

ADVICE FOR OTHERS

John Marshall hopes that the book shows others the empathy that health care providers feel. "I used to have this vision in my head that there was this half-built wall: I was on this side and the patient was on that side. And I could shake their hand and I could examine them. But they were over there. And I was over here. After our experience, I couldn't find that wall anymore," he said.



« To order a copy of "Off Our Chests: A Candid Tour Through the World of Cancer," visit Amazon.com.

"The emotional load that that takes (on a health care provider) is what leads to burnout. We have to watch ourselves … We have to acknowledge it's there. We're not superhuman, we are human. And what we do every day is the most human thing that you can do: care for others."

Liza Marshall hopes "Off Our Chests" offers patients and caregivers a straightforward and honest approach to cancer care.

"(John talked) about a wall … I'm over this wall, and I have no idea how I got here and why I'm here and what anything is on this side of the wall. So, we hope that, to a certain extent, it's just a lifting of the curtain (to educate you about) tests, conversations with your doctor, how to have conversations with your family," she said, adding that empathy is not only for the patients, but providers and caregivers, as well.

"It's a little bit of empathy for each other about situations that we're all in and recognizing that what people look like on the outside may not be what's going on with them on the inside, for caregivers, doctors, everybody."

CURE® and its sister publication, *OncLive*®, sat down with the Marshalls to discuss how a diagnosis of triple-negative breast cancer changed the lives of a patient and her gastrointestinal oncologist husband.

SCAN THE QR CODE

to watch the full interview

LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg

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

LIBTAYO helps your immune system fight 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 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

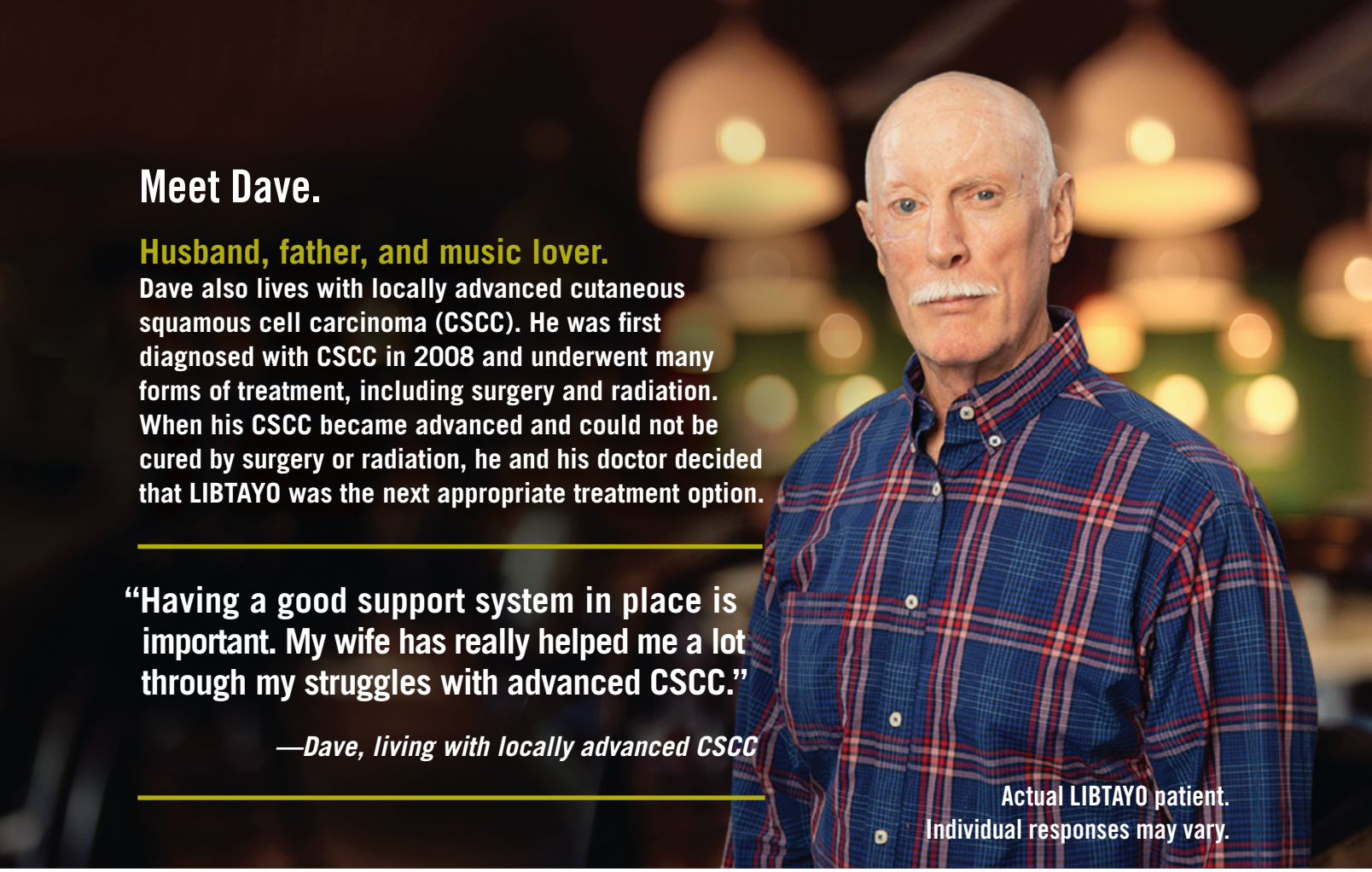
What is the most important information I should know about LIBTAYO?

LIBTAYO is a medicine that may treat a certain type of skin cancer 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 worse 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: 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.



Meet Dave.

Husband, father, and music lover.

Dave also lives with locally advanced cutaneous squamous cell carcinoma (CSCC). He was first diagnosed with CSCC in 2008 and underwent many forms of treatment, including surgery and radiation. When his CSCC became advanced and could not be cured by surgery or radiation, he and his doctor decided that LIBTAYO was the next appropriate treatment option.

"Having a good support system in place is important. My wife has really helped me a lot through my struggles with advanced CSCC."

—Dave, living with locally advanced CSCC

Actual LIBTAYO patient.
Individual responses may vary.

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 worse 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 tiredness, rash, diarrhea, muscle or bone pain, and nausea. 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.

What is LIBTAYO?

LIBTAYO 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.

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 a certain type of skin cancer 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 worse signs or symptoms, including:

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

Intestinal problems.
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- 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
- dark urine (tea colored)
- severe nausea or vomiting
- bleeding or bruising more easily than normal
- pain on the right side of your stomach area (abdomen)

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

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

Skin problems.
- rash
- painful sores or ulcers in mouth or nose, throat, or genital area
- itching
- skin blistering or peeling
- 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:
- chills or shaking
- dizziness
- itching or rash
- feel like passing out
- flushing
- fever
- shortness of breath or wheezing
- back or neck pain
- facial swelling

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.

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- 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-Barre 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 with LIBTAYO.
  - You should use an effective method of birth control during your treatment and for at least 4 months after the last dose of LIBTAYO. 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 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.

Continued on following page

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

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 tiredness, rash, diarrhea, muscle or bone pain, and nausea.

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.

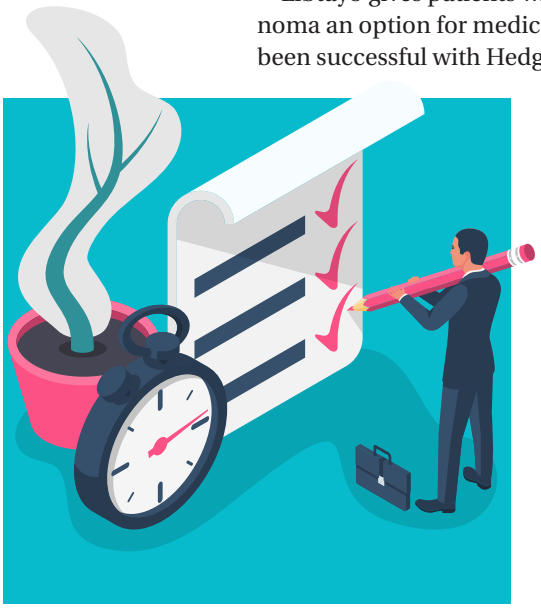
REGENERON | SANOFI GENZYME

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

Libtayo Gets 'Big Approval' for Treating Advanced Basal Cell Carcinoma

An expert spoke with CURE® about the FDA's recent approval of the immunotherapy to treat patients who previously had only one therapy option for advanced disease. By DARLENE DOBKOWSKI, M.A.

RECENTLY, THE FOOD AND DRUG Administration (FDA) approved Libtayo (cemiplimab-rwlc) to treat patients with advanced basal cell carcinoma previously treated with a Hedgehog pathway inhibitor or patients for whom Hedgehog pathway inhibitors were not appropriate, making it the first immunotherapy option for these patients. The FDA granted Libtayo full approval in locally advanced basal cell carcinoma and accelerated approval for the treatment of patients with metastatic basal cell carcinoma.



According to the American Cancer Society, basal cell carcinoma is the most common skin cancer type, making up approximately 80% of skin cancer diagnoses. There are an estimated 2 million new cases of basal cell carcinoma each year. Although most basal cell carcinomas are easily excised and 100% curable, there is a small proportion of tumors that become advanced or not easily amenable to resection or other therapy.

"Basal cell cancers are generally thought of as benign cancers, no big deal," Dr. Karl Lewis, professor of medicine at University of Colorado School of Medicine in Aurora, said in an interview with *CURE*®. "That's fortunately true for most basal cell cancers that develop, but it's such a common cancer that even a small percentage of these becoming problematic, either locally advanced or metastatic, it affects a significant number of people."

Before the FDA approval, patients with advanced basal cell carcinoma were treated with Hedgehog pathway inhibitors, which were originally "a really big breakthrough for this group of patients," Lewis said. "(Hedgehog pathway inhibitors were) able to get the tumor to shrink down in a large percentage of these patients and really change the course of the disease."

Hedgehog pathway inhibitors were the only option a few years ago for these patients. Unfortunately, not all patients with advanced basal cell carcinoma responded to the therapy. Also, patients often could not take these inhibitors long term despite responding to the treatment because of significant side effects such as fatigue, muscle spasms, hair loss and impaired sense of taste.

Libtayo gives patients with advanced basal cell carcinoma an option for medical treatment if they have not been successful with Hedgehog pathway inhibitors.

"They have an option that is trying to use their immune system to attack the cancer," Lewis said. "A good percentage of these patients will have their cancers shrink and ... controlled. For those (patients) that (Libtayo) works in, (as) for other cancers, immunotherapies tend to be durable, so they have the potential to get long-term benefit from their treatment."

Although most patients tolerate Libtayo well, some patients may experience significant toxicities or other autoimmune side effects. There is a risk that a patient's immune system may start attacking normal tissues in the body.

"It varies from patient to patient because all of our immune systems are different," Lewis said. "In one person, their immune system might have a predisposition to attack their liver. In somebody else, it might be their colon. We just don't know. Most of the side effects are relatively mild, but some can be severe, so we have to watch for that."

Lewis added that the FDA approval of Libtayo gives patients another therapy option for a disease that can be difficult to treat.

"The options for treating this disease historically have been extremely limited," Lewis said. "... Now we have two very good effective options, the Hedgehog inhibitors and the big approval of an immunotherapy in this disease. It's very exciting."

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Targeting a Specific KRAS Mutation May Change Treatment Landscape for Non-Small Cell Lung Cancer

Patients with non-small cell lung cancer and a KRAS G12C genetic mutation may benefit from treatment with an inhibitor targeting that mutation, although more research is needed to learn why more patients are not responding to the drug. By DARLENE DOBKOWSKI, M.A.

FINDINGS FROM THE RECENT CodeBreak 100 trial demonstrated that sotorasib, a KRAS G12C inhibitor, was effective in treating patients with non-small cell lung cancer (NSCLC) and the KRAS G12C mutation. The KRAS G12C mutation is the most common genetic mutation in these patients and has been gaining attention as a treatment target.

DR. VAMSIDHAR VELCHETI

"These treatments were quite effective in this population that's really hard to treat, and there are no good treatment options for these patients," Dr. Vamsidhar Velcheti, director of thoracic medical oncology at NYU Langone's Perlmutter Cancer Center in New York City, said in an interview with *CURE*®. "This is a good clinical validation of the impact of innovating this KRAS protein with drugs that are targeting this mutant protein."

The phase 2 CodeBreak 100 trial included 126 patients with locally advanced or metastatic NSCLC with a KRAS G12C mutation; they were treated with 960 milligrams of oral sotorasib once per day. Patients showed a median progression-free survival (time from treatment to disease worsening or progressing) of 6.8 months, and 80% of patients achieved disease control with sotorasib. The drug had a response rate of 37.1%, or the proportion of patients who had a partial or complete response to treatment.

The mutated RAS gene can induce growth of cancer cells and lead to rapid spread of these cells. Although the effects of the mutated RAS gene were discovered nearly 50 years ago, the road to developing new drugs to target KRAS hasn't been easy "because of the complexity of the biology of this mutation and how drugs work on this mutation," Velcheti said. Several clinical trials have assessed different types of drugs and approaches to target this gene mutation. Although there is not yet a successful treatment option, progress has been made over the past several years thanks to advances in medicinal chemistry.

"We've been able to develop newer drugs that interact with certain specific subtypes of mutant KRAS protein and help disrupt the KRAS signals in the cancer cell," Velcheti said. "These newer drugs that have been developed to specific types of mutations in KRAS can disrupt the signaling function of this mutant protein and thereby (lead) to death of the cancer cell, preventing it from growing and spreading."

Velcheti added that the safety profile of sotorasib is much better than the current standard treatments for patients with NSCLC, such as chemotherapy and immunotherapy. These standard treatments have many side effects that can lead to reduced blood counts, among other complications. Taking sotorasib may lead to liver function abnormalities, but severe side effects were observed in less than 5% of patients.

Adagrasib is another KRAS G12C inhibitor being studied for the treatment of patients with NSCLC. Currently, sotorasib is the KRAS G12C inhibitor that is the closest to receiving Food and Drug Administration (FDA) approval, with a Prescription Drug User Fee Act date of Aug. 16, 2021. The FDA is expected to decide by this date whether the drug should be approved to treat patients with NSCLC with the KRAS G12C mutation after receiving at least one previous systemic therapy.

Although KRAS G12C inhibitors seem to be a major advancement in treating patients with KRAS mutation, "the percentage of patients responding to the drug is still relatively low compared (with) the other types of gene mutations where we've seen patients respond really well to treatment," Velcheti said. "We're still trying to understand why that's the case. And there are a lot of clinical trials looking at novel innovative combinations with other potential drugs to improve the percentage of patients who would benefit from these drugs. There's a lot of active research going on, a lot of clinical trials evaluating these. I would strongly encourage patients to consider those clinical trials to potentially improve on the success of sotorasib."

PHOTO CREDIT: NYU LANGONE HEALTH

Imbruvica Plus Novel Agent May Improve Progression-Free Survival in Chronic Lymphocytic Leukemia

In patients treated with Imbruvica plus TG-1101, 83% had their tumors shrink or disappear versus 65% in those treated with Imbruvica alone.

By DARLENE DOBKOWSKI, M.A.

ADDING TG-1101 (UBLITUXIMAB) to Imbruvica (ibrutinib) to treat patients with relapsed or refractory high-risk chronic lymphocytic leukemia (CLL) led to a higher overall response rate compared with Imbruvica alone, according to results of a study published in *Lancet Haematology*.

TG-1101 is a novel anti-CD20 monoclonal antibody that targets an antigen commonly found on the surface of B cells and plays a role in CLL. Researchers assessed the addition of TG-1101 to Imbruvica, a drug that binds to a protein — Bruton tyrosine kinase (BTK) — within B cells, to see whether outcomes can be improved compared with Imbruvica alone.

DR. JEFF SHARMAN

> "BTK inhibitors have dramatically improved outcomes for patients with CLL, but particularly among those individuals with high-risk disease."
>
> — DR. JEFF SHARMAN

"BTK inhibitors have dramatically improved outcomes for patients with CLL, but particularly among those individuals with high-risk disease," said Dr. Jeff Sharman, medical director of hematology research for The US Oncology Network and director of research at Willamette Valley Cancer Institute and Research Center in Eugene, Oregon, in an interview with *CURE*®. "Nonetheless, patients with high-risk genetic risk factors still have inferior outcomes relative to patients without high-risk features. We wanted to determine if adding the novel anti-CD20 antibody (TG-1101) could improve outcomes among patients with relapsed/refractory CLL harboring high-risk features."

In this phase 3 trial, researchers analyzed data from 126 patients with relapsed or refractory CLL who previously received at least one therapy for their disease. These patients also had high-risk cytogenetics, or chromosomes, defined as the presence of a 17p deletion, 11q deletion or TP53 mutation.

"Patients with (17p deletion)/TP53 mutations have consistently demonstrated inferior outcomes," Sharman said. "In contrast, although early publications demonstrated less favorable outcomes among individuals with (11q deletion) treated with BTK inhibitors, more recent publications have questioned if this remains an adverse outcome."

Patients were assigned either Imbruvica with TG-1101 (64 patients) or Imbruvica alone (62 patients), which were both administered in 28-day cycles in outpatient settings. Imbruvica was given as a 420 milligrams oral dose once per day. TG-1101 was administered intravenously at varying doses throughout the first cycle, stabilizing at 900 milligrams per day on the first day of the second through sixth cycles. Both treatments were administered until unacceptable toxicity, disease progression or withdrawal of consent from the trial.

End points included overall response rate, which was defined as the percentage of patients who had a complete response or partial response to the therapy, in addition to those with a complete response with incomplete marrow recovery. Safety also was analyzed in patients throughout the trial.

During a median follow-up of 41.6 months, the overall response rate was 83% in patients given Imbruvica with TG-1101 versus 65% in those given Imbruvica alone. Researchers also monitored for progression-free survival based on the presence of certain high-risk cytogenetics.

"We show that adding (TG-1101) to (Imbruvica) provides clinically meaningful and statistically significant benefits to progression-free survival among patients with (17p deletion)/TP53 mutations," Sharman said. "We did not see similar improvements among patients with (11q deletion)."

Safety analyses included 117 of the patients who received at least one dose of treatment. Most side effects

continued on page 65 »

CALQUENCE®
(acalabrutinib) 100 mg capsules

YOU ARE NOT ALONE

with chronic lymphocytic leukemia (CLL)

CALQUENCE™ Connections is here for you—whether you are newly diagnosed, beginning a new treatment, or just seeking connections with other cancer patients.

Through the stories of patients on CALQUENCE and their caregivers, CALQUENCE Connections hopes to make you feel empowered while living with CLL.

SIGN UP TO MEET MEMBERS OF THE CLL COMMUNITY AT AN UPCOMING EVENT

Or visit CALQUENCEConnections.com for more information.

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

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.

Please read Brief Summary of Prescribing Information on adjacent page.

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.

CALQUENCE™ CONNECTIONS

AstraZeneca

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.

Distributed by:
AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850

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

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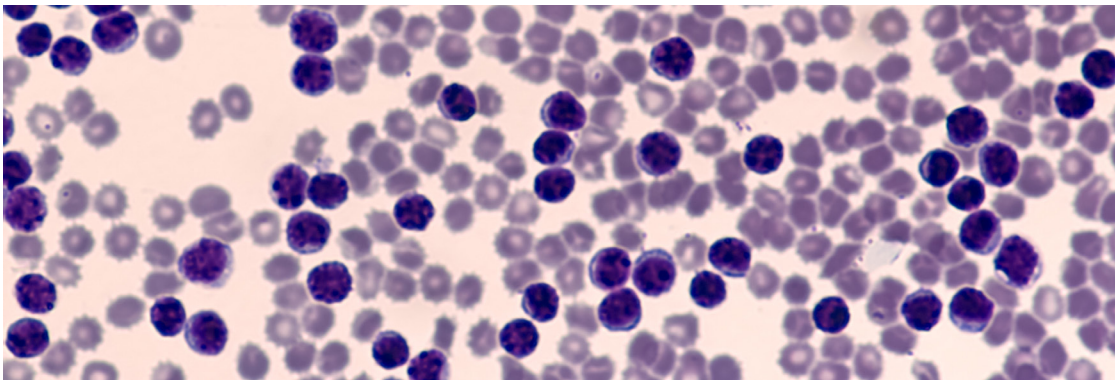


DAVID A LITMAN / STOCK.ADOBE.COM

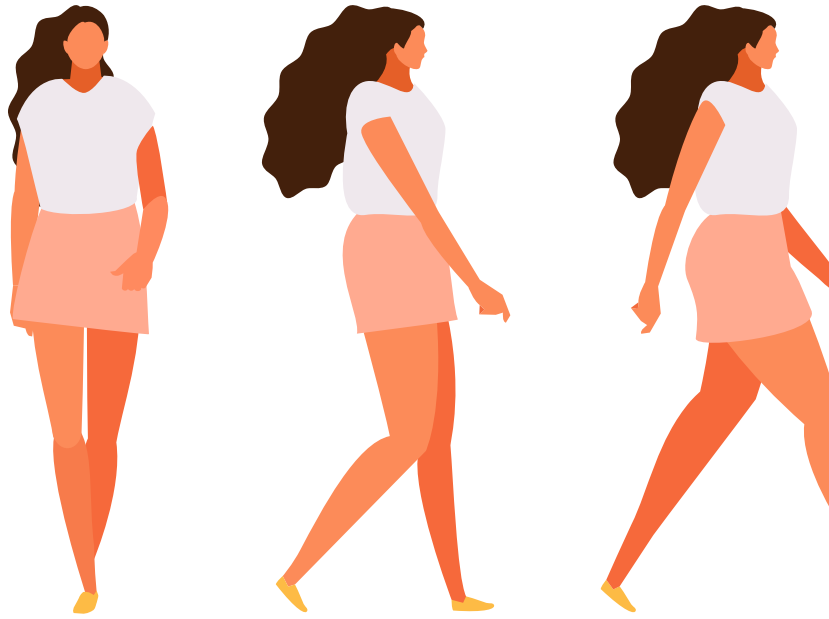
« An antigen commonly found on the surface of B cells and plays a role in CLL may be a target for potential treatment.

were grade 1 or 2, or mild to moderate. The most common grade 3 or 4 (severe to life-threatening) side effects observed in patients given Imbruvica with TG-1101 or Imbruvica alone included anemia (lack of red blood cells; 8% vs. 9%, respectively), neutropenia (low counts of neutrophils, a type of white blood cell; 19% vs. 12%) and diarrhea (10% vs. 5%). The most common serious side effects were atrial fibrillation (irregular heartbeat; 7% vs. 2%, respectively), pneumonia (10% vs. 7%), febrile neutropenia (fever during neutropenia; 5% vs. 2%) and sepsis (illness from the body's response to infection; 7% vs. 2%).

Two patients assigned Imbruvica with TG-1101 died, one of failure to thrive (symptoms including weight loss, poor nutrition, decreased appetite and inactivity) and one of cardiac arrest, although neither was associated with the treatment. In contrast, five patients assigned Imbruvica alone died of stroke, cardiac arrest, pneumonia, brain bleed, or an unexplained cause. The only death related to the treatment was the one caused by cardiac arrest.

Despite the findings of this trial, questions remain regarding the use of drugs such as TG-1101 in this specific patient population.

"The role of anti-CD20 antibodies added to (BTK) inhibitors (to treat these patients) remains unsettled," Sharman said. "Whether it is the nature of the (BTK) inhibitor or the type of anti-CD20 antibody that provides benefits remains uncertain."



Making Strides in Ovarian Cancer

Clinical trials are often the key to advancements in treating ovarian cancer. As part of its "Speaking Out" video series, CURE® spoke with Dr. Debra Richardson about what patients should know about joining a trial. By KRISTIE L. KAHL

MANY ADVANCES HAVE BEEN made in treating ovarian cancer treatment, such as the development and use of maintenance therapy in the past decade. Clinical trials made these developments possible, and patient participation and awareness of clinical trials are vital to their success.

On behalf of the National Ovarian Cancer Coalition, *CURE®* spoke with Dr. Debra Richardson, a gynecologic oncologist at the Stephenson Cancer Center and associate professor at the University of Oklahoma College of Medicine in Oklahoma City, about clinical trials in ovarian cancer, and what patients should know if they are interested in joining one.

Q: *CURE®*: How are clinical trials addressing the challenges that we see in ovarian cancer?

A: Richardson: There are lots of clinical trials going on right now trying to address every problem imaginable in ovarian cancer. We're looking at screening tests. We're looking at early diagnosis tests. We're looking at better treatments, treatments that will hopefully result in better cure rates. We're looking at new maintenance therapies. We're investigating immunotherapy. So, really, every avenue of ovarian cancer.

For recurrent ovarian cancer, we separate patients into platinum-sensitive and platinum-resistant groups. And that has to do with how long it's been since a patient's last platinum (chemotherapy treatment). If it's less than six months, they're considered platinum-resistant. If it's more than six months, they are considered platinum-sensitive. We're investigating how to maximally treat those patients, as well, and find new drugs to get approved so that we can continue to treat patients with ovarian cancer.

Q: Why is it important for patients to consider joining a clinical trial?

A: The National Cancer Institute recommends that all patients with cancer who are eligible for clinical trial be offered one. Unfortunately, we know that's not the case. And, in fact, about only 5% or so of (adult Americans with cancer) go on clinical trial. I think we have a lot to learn from our pediatric colleagues. More than 60% of children diagnosed with cancer go on clinical trial. If you look in the past, pediatric cancers were mostly lethal. Now there's a more than 85% cure rate. And that is from high participation in clinical trials. That's the only way to move the needle forward and find better treatments and increase the cure rate.

Q: How can patients learn more about a clinical trial that they might be eligible to join?

A: (Patients) should definitely talk to their physician, and hopefully their physician can give them information about clinical trials. There's also clinicaltrials.gov, where patients can put in their type of cancer, where they live and how far they might be willing to travel to see what types of clinical trials are potentially available. And then if they find some, they should contact the institution that's running that trial and speak to one of the clinical research nurses and get more information.

Q: Why is it important for a patient to talk to their doctor first about a clinical trial?

A: Clinical trials are not a one-patient-fits-all (approach). (Patients) might find something online that you think is really exciting or interesting but is not the appropriate clinical trial for you, for whatever reason. Your physician will know about your particular case, your diagnosis and whether a clinical trial may be a good fit for you. (Your physician) can also put it in context of what is the current standard of care and what are the potential risks and benefits of that clinical trial.

Q: Can you help to negate some misconceptions that we often hear about clinical trials?

A: The guinea pig (misconception is one) I hear a lot. But the truth is, guinea pigs don't have any say, they're just put in a cage and given drugs. Human beings have a say. We do what's called an informed consent where

we have a conversation about risks, benefits and alternatives. You have the right, if you participate in a clinical trial, to revoke consent at any time and withdraw from the trial if you don't think it's the right fit for you. Now, obviously, we don't want a lot of people to sign up for clinical trials and then not complete them. But there are certainly rights that are respected for humans participating in clinical trials.

Regarding the placebo (misconception), the only way that you would ever be randomized to a drug versus placebo is if the placebo is the standard of care. In other words, when we were first looking at maintenance therapy for ovarian cancer, the standard of care was that after you completed chemotherapy (you would) not get any further treatment. And that's how it was ethical to give placebo only, because we didn't know if the other drug would be beneficial. Drugs certainly have the potential for side effects. The only way to really investigate what is the benefit from the drug we're giving you (is to use) a placebo because we know when we put people on clinical trials, they actually do better than patients (not on a clinical trial), even if they only get the standard care on the trial. They tend to do better on clinical trial than if they get sooner care off trial. We're not entirely sure why that is, but it may be all the extra visits or monitoring that you get on a clinical trial that you may not get ordinarily, for example.

> **"(High participation in clinical trials) is the only way to move the needle forward and find better treatments and increase the cure rate."** — *DR. DEBRA RICHARDSON*

In clinical trials, when you're talking about being potentially randomized, that means either a flip of a coin or, if there are three arms, it might be picking straws, in that you don't choose and your physician doesn't choose. It's generated by the computer randomly so that we can try to control for factors that we're not aware of that might affect the study's outcome. The only way that you're getting on a clinical trial such as that is if it's standard-of-care versus our new drug.

Q: To bring it all together, what is your best advice for a patient who might be considering joining a trial?

A: I would say definitely discuss it with your physician. See what your options are. You're given a consent form when you're considering a clinical trial. They tend to be long, about 20 to 25 pages. I definitely recommend that you read through it. They are supposed to be written in a language that the average patient can understand. Involve your family members or your caregivers in that decision, as well. Make a list of questions and make sure that all your questions are answered to your satisfaction.

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.

Live longer with KISQALI.

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

In premenopausal women, the median OS was not reached for KISQALI + a nonsteroidal aromatase inhibitor (NSAI) + goserelin vs 40.7 months for an NSAI + goserelin. KISQALI + an NSAI + goserelin delayed disease progression for a median of 27.5 months vs 13.8 months for an NSAI + goserelin.

In postmenopausal women, median OS was not reached for KISQALI + fulvestrant vs 40 months for those taking fulvestrant alone. KISQALI + fulvestrant delayed disease progression for a median of 20.5 months vs 12.8 months for fulvestrant alone.

Ask your doctor if KISQALI can help you live longer and visit KISQALI.com.

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

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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).

NOVARTIS

KISQALI® ribociclib 200 mg tablets

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

Cabometyx-Opdivo Is 'One of the New Standards of Care' in Treating Kidney Cancer Subtype, Expert Says

A new treatment option for patients with advanced renal cell carcinoma was recently approved by the FDA. By RYAN MCDONALD

THE FOOD AND DRUG ADMINISTRATION'S (FDA)'s recent approval of Cabometyx (cabozantinib) plus Opdivo (nivolumab) for the treatment of advanced renal cell carcinoma provides patients with another therapy option and should become one of the new standards of care, according to Dr. Toni Choueiri.

"If we go back 10 to 15 years ago, a patient with metastatic kidney cancer really did not have much (in terms of treatment) options," Choueiri, director of the Lank Center for Genitourinary Oncology and director of the Kidney Cancer Center at Dana-Farber Cancer Institute in Boston, said in an interview with *CURE*®.

Drugs targeting vascular endothelial growth factor were approved as single agents to treat patients with renal cell carcinoma starting around 2005 and 2006, according to Choueiri. Then, in late 2015, single-agent immune checkpoint inhibitors started receiving approval to treat these patients. Recently, however, the FDA has started to approve combination therapies to treat renal cell carcinoma.

The combination of Cabometyx plus Opdivo becomes the third immunotherapy/vascular endothelial growth factor doublet treatment approved by the FDA, according to Choueiri.

"(Cabometyx and Opdivo) is certainly going to become one of the new standards of care," he said.

The approval was based on results of the CheckMate 9ER trial, which showed that the Cabometyx-Opdivo combination induced a superior progression-free survival (the time from treatment to disease progression or worsening), overall survival and overall response rate in patients compared with the chemotherapy Sutent (sunitinib).

Patients who received the combination achieved a median progression-free survival of 16.6 months compared with 8.3 months for those who received Sutent. Moreover, the combination induced a confirmed overall response rate of 55.7% compared with 27.1% for Sutent. A median overall survival was not reached in either treatment group.

QUALITY OF LIFE

Data recently presented at a medical conference also showed that treatment with the combination was more associated with improved quality of life than Sutent was.

CRYSTAL LIGHT / STOCK.ADOBE.COM

This newly approved combination therapy for advanced renal cell carcinoma adds another treatment option for patients.

The results showed that patients who received Cabometyx plus Opdivo experienced a delay in deterioration and a significant decreased risk for confirmed deterioration in health-related quality of life scores, including disease-related kidney cancer symptoms.

"There (are) some intriguing quality of life data that showed that this regimen also has a better quality of life," Choueiri said. "These (are) what we call patient reported outcome; the voice of the patient (is) very important."

Overall, Choueiri said, he's happy to have another combination regimen approved to treat these patients and that treatment advances are extending survival.

"The picture is that people with metastatic kidney cancer today — because of these drugs, whether single agent or combination — are living way longer, and that's what the message should be," Choueiri concluded.

Finding Ways to Manage Helpless Anger

A caregiver recalls how an unexpected side effect of her daughter's breast cancer treatment stirred up feelings of helpless anger. By DEBBIE LEGAULT

I KNOW THAT CANCER IS A never-ending story, the gift that keeps on giving, the (insert your cliché here). I have accepted that once I heard the words "Mom, it's cancer" from my 27-year-old daughter, my life was changed forever. I know things will go up and down, but today, if I could, I would throw a hundred dishes against a wall, screaming at the top of my lungs. Because just when she started to feel like herself again, a cancer treatment side effect has come along to say…

"Hey, remember you had cancer?"

Adrienne has had significant issues with her skin since she was a baby. We were very apprehensive about how her skin would react to the six weeks of radiation treatments she had in January and February 2020, and we felt particularly blessed when her side effects were very minimal. This is why I am so angry today, more than a year after she finished her treatments, she has been diagnosed with radiation recall dermatitis, which is an uncommon inflammatory reaction of the skin at the previous site of radiation.

DEBBIE LEGAULT

Adrienne had a lot of uncommon things happen during radiation, some of which made us laugh out loud. Tubes came loose from machines in a way the technicians had never seen before. Her lips swelled up like a bad lip job in reaction to something on the mouthpiece. Managing these issues, including strapping ice packs to her face with a headband, brought out the humor.

She found out only after going back for a recheck with the radiation oncologist a year later that there was a specific parking structure for the department and we had parked as far away as possible for every day of the six weeks of treatment. But when it came to side effects, short and long term, in comparison with chemotherapy, we both came out of there thinking it had been a walk in the park.

The kicker is that the cancer-fighting hormonal treatment Soltamox (tamoxifen) she's taking to prevent recurrence could be the culprit that initiated the skin reaction she's having, but coming off it is not an option. A dermatologist did a biopsy to make sure the diagnosis was accurate and has prescribed a more intensive cream to put on the affected areas to ease her discomfort. It's one more thing to add to the list of medical stuff she has to do that constantly reminds her she had cancer.

I was recently reflecting on the grief cycle and how I wished with all my heart that it was linear, that you would go through the steps from beginning to end, one and done. Unfortunately, that's not how it works, and I find that the stage I get pulled back into most often is anger. I wish I could deny what is happening, but I don't have that luxury because of the ongoing impact cancer has on my daughter's life.

Most of my life, I have been able to take an objective look at a situation and tamp my reaction down to mild annoyance. But this type of anger comes on so fast and furious, I don't seem to have time to even look at it before I'm ready to punch a wall.

I'm not very good at dealing with this kind of helpless anger. If the world were not locked down because of the pandemic, I would go to a thrift store and buy up all their random dishes and put them in a box for just such occasions. My family is stuck at home with me, so I have nowhere to go inside to simply stand and scream at the top of my lungs about how unfair this is, about how she did nothing to deserve it, that I just want it to be over. So, when I'm feeling as though I'm going to explode, in a semblance of outward calm, I put on my headphones, turn on my audiobook and clean or organize something.

Not just an obvious something, but one of those chores you put off because "nobody sees it anyway." Like lying on the floor cleaning the baseboards under the counters. Or using a toothbrush to get out those little bits of something that accumulate in the hinges of things. Or pulling out family photos and writing down on the back of the pictures the who, where, when for future generations. Anything to put the genie back in the bottle for a few more moments of peace.

How often does this happen, you ask? Right now, we have the cleanest house in town. C

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Nominate your **Lung Cancer Hero** today!

CURE® is now accepting nominations to recognize our 2021 Class of Lung Cancer Heroes®, individuals who go above and beyond to make a difference in the lives of those affected by lung cancer. Each hero is nominated by patients, caregivers, and fellow health care professionals for their heroic contributions in the field of lung cancer, or in the individual lives of people with lung cancer.

Submit yours by June 30, 2021.

Three Lung Cancer Heroes®, along with their nominators, will be interviewed by *CURE*® and honored at a special reception to be held later in 2021. More details will be announced as they become available.

Submit your essay today at **curetoday.com/LCH21**

CURE®, Takeda, Lung Cancer Heroes®, and the advocacy community are dedicated to bringing together the lung cancer community to end the stigma, inform, connect, and empower anyone who has been impacted by lung cancer.

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

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