FOR PATIENTS, SURVIVORS & THEIR CAREGIVERS

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Virtual reality headsets can relieve anxiety and pain in those affected by cancer

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SPRING 2020 · VOL.19 NO.2

KEYTRUDA IS BREAKING THROUGH BARRIERS IN ADVANCED LUNG CANCER TREATMENT.

FOR TODAY

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

KEYTRUDA also has **more FDA-approved uses** for advanced lung cancer than any other immunotherapy.

FOR THE FUTURE

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

Ask your doctor if KEYTRUDA is right for you. **Visit keytruda.com/lung**

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

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

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

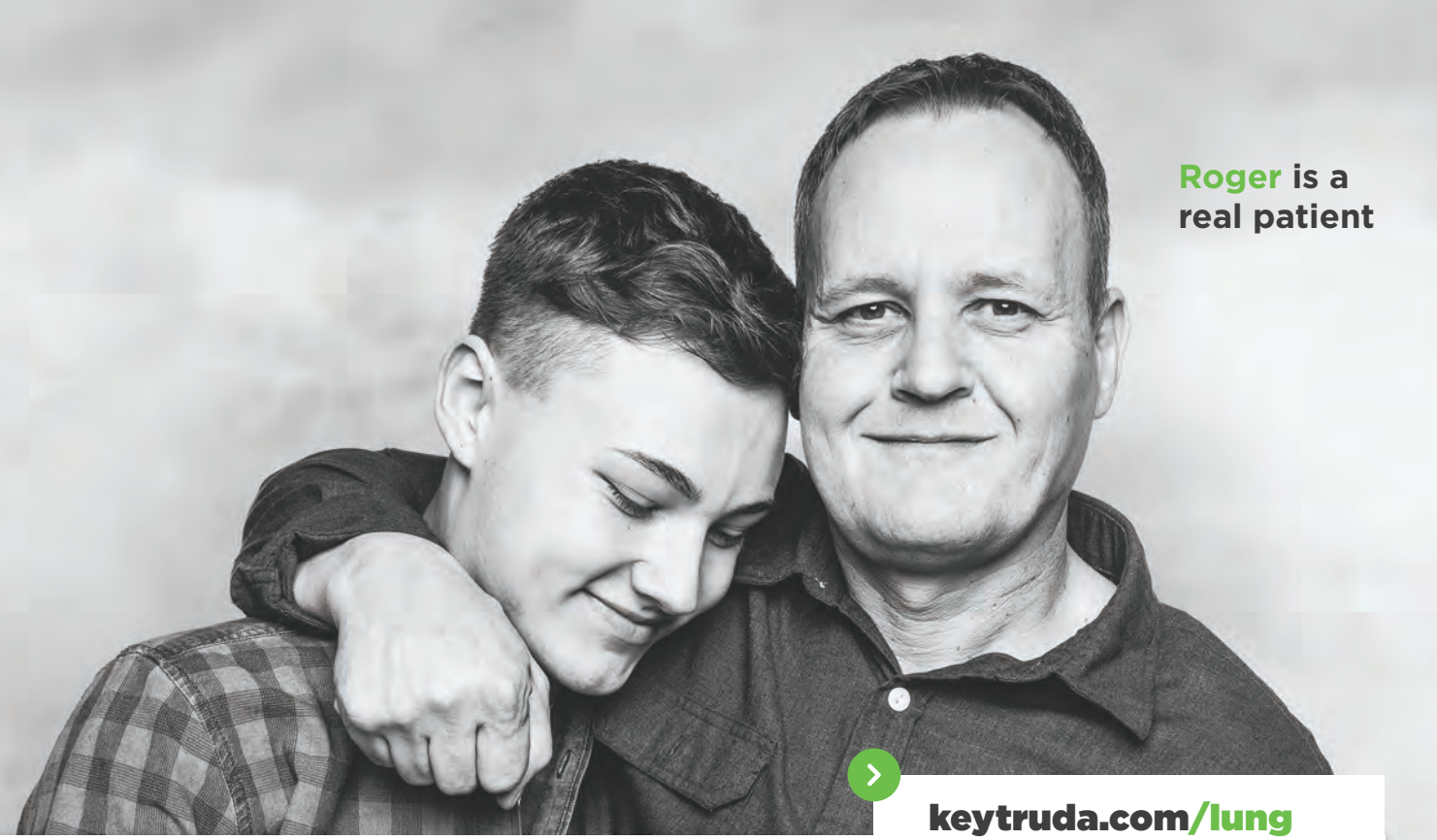
IMPORTANT SAFETY INFORMATION

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

Call or see your doctor right away if you develop any symptoms of the following problems or these symptoms get worse:

- **Lung problems (pneumonitis).** Symptoms of pneumonitis may include shortness of breath, chest pain, or new or worse cough.
- **Intestinal problems (colitis) that can lead to tears or holes in your intestine.** Signs and symptoms of colitis may include diarrhea or more 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, including hepatitis.** Signs and symptoms of liver problems may include yellowing of your skin or the whites of your eyes, nausea or vomiting, pain on the right side of your stomach area (abdomen), dark urine, or bleeding or bruising more easily than normal.
- **Hormone gland problems (especially the thyroid, pituitary, adrenal glands, and pancreas).** Signs and symptoms that your hormone glands are not working properly may include rapid heartbeat, weight loss or weight gain, increased sweating, feeling more hungry or thirsty, urinating more often than usual, hair loss, feeling cold, constipation, your voice gets deeper, muscle aches, feeling very weak, dizziness or fainting, or headaches that will not go away or unusual headache.
- **Kidney problems, including nephritis and kidney failure.** Signs of kidney problems may include change in the amount or color of your urine.
- **Skin problems.** Signs of skin problems may include rash, itching, blisters, peeling or skin sores, or painful sores or ulcers in your mouth or in your nose, throat, or genital area.
- **Problems in other organs.** Signs and symptoms of these problems may include changes in eyesight; severe or persistent muscle or joint pains; severe muscle weakness; low red blood cells (anemia); swollen

Important Safety Information is continued on the next page.



Roger is a real patient

keytruda.com/lung

IMPORTANT SAFETY INFORMATION *(continued)*

lymph nodes, rash or tender lumps on skin, cough, shortness of breath, vision changes, or eye pain (sarcoidosis); confusion, fever, muscle weakness, balance problems, nausea, vomiting, stiff neck, memory problems, or seizures (encephalitis); and shortness of breath, irregular heartbeat, feeling tired, or chest pain (myocarditis).

- **Infusion (IV) reactions that can sometimes be severe and life-threatening.** Signs and symptoms of infusion reactions may include chills or shaking, shortness of breath or wheezing, itching or rash, flushing, dizziness, fever, or feeling like passing out.
- **Rejection of a transplanted organ.** People who have had an organ transplant may have an increased risk of organ transplant rejection if they are treated with KEYTRUDA.
- **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 severe and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with KEYTRUDA. Your doctor will monitor you for the following signs and symptoms: skin rash, liver inflammation, abdominal pain, and diarrhea.

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

Before you receive KEYTRUDA, tell your doctor if you have immune system problems such as Crohn's disease, ulcerative colitis, or lupus; have had an organ transplant or plan to have or have had a bone marrow (stem cell) transplant that used donor stem cells (allogeneic); have lung or breathing problems; have liver problems; or have any other medical problems.

If you are pregnant or plan to become pregnant, tell your doctor. KEYTRUDA can harm your unborn baby. If you are able to become pregnant, your doctor will give you a pregnancy test before you start treatment. Use effective birth control during treatment and for at least 4 months after the final dose of KEYTRUDA. Tell your doctor right away if you think you may be pregnant or you become pregnant during treatment with KEYTRUDA.

If you are breastfeeding or plan to breastfeed, tell your doctor. 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 doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

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

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

These are not all the possible side effects of KEYTRUDA. Tell your doctor if you have any side effect that bothers you or that does not go away. For more information, ask your doctor or pharmacist.

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

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

Having trouble paying for your Merck medicine?
Merck may be able to help. www.merckhelps.com

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

MERCK

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

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

Call or see your doctor right away if you develop any symptoms of the following problems or these symptoms get worse:

Lung problems (pneumonitis). Symptoms of pneumonitis may include:
- shortness of breath
- chest pain
- new or worse cough

Intestinal problems (colitis) that can lead to tears or holes in your intestine. Signs and symptoms of colitis may include:
- diarrhea or more bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdomen) pain or tenderness

Liver problems, including hepatitis. Signs and symptoms of liver problems may include:
- yellowing of your skin or the whites of your eyes
- nausea or vomiting
- pain on the right side of your stomach area (abdomen)
- dark urine
- bleeding or bruising more easily than normal

Hormone gland problems (especially the thyroid, pituitary, adrenal glands, and pancreas). Signs and symptoms that your hormone glands are not working properly may include:
- rapid heart beat
- weight loss or weight gain
- increased sweating
- feeling more hungry or thirsty
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- muscle aches
- feeling very weak
- dizziness or fainting
- headaches that will not go away or unusual headache

Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include:
- change in the amount or color of your urine

Skin problems. Signs of skin problems may include:
- rash
- itching
- blisters, peeling or skin sores
- painful sores or ulcers in your mouth or in your nose, throat, or genital area

Problems in other organs. Signs and symptoms of these problems may include:
- changes in eyesight
- severe or persistent muscle or joint pains
- severe muscle weakness
- low red blood cells (anemia)
- swollen lymph nodes, rash or tender lumps on skin, cough, shortness of breath, vision changes, or eye pain (sarcoidosis)
- confusion, fever, muscle weakness, balance problems, nausea, vomiting, stiff neck, memory problems, or seizures (encephalitis)
- shortness of breath, irregular heartbeat, feeling tired, or chest pain (myocarditis)

Infusion (IV) reactions that can sometimes be severe and life-threatening. Signs and symptoms of infusion reactions may include:
- chills or shaking
- flushing
- fever
- shortness of breath or wheezing
- dizziness
- feeling like passing out
- itching or rash

Rejection of a transplanted organ. People who have had an organ transplant may have an increased risk of organ transplant rejection. Your doctor 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 severe and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with KEYTRUDA. Your doctor will monitor you for the following signs and symptoms: skin rash, liver inflammation, stomach-area (abdominal) pain, and diarrhea.

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

What should I tell my doctor before receiving KEYTRUDA?

Before you receive KEYTRUDA, tell your doctor if you:
- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have received an organ transplant, such as a kidney or liver
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have lung or breathing problems
- have liver problems
- have any other medical problems
- are pregnant or plan to become pregnant
  - KEYTRUDA can harm your unborn baby.

  Females who are able to become pregnant:
  - Your doctor 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 doctor about birth control methods that you can use during this time.
  - Tell your doctor 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 doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How will I receive KEYTRUDA?
- Your doctor will give you KEYTRUDA into your vein through an intravenous (IV) line over 30 minutes.
- KEYTRUDA is usually given every 3 weeks.
- Your doctor will decide how many treatments you need.
- Your doctor will do blood tests to check you for side effects.
- If you miss any appointments, call your doctor 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.

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, and mouth sores.

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.

In children, feeling tired, vomiting and stomach-area (abdominal) pain, and increased levels of liver enzymes and decreased levels of salt (sodium) in the blood are more common than in adults.

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

Tell your doctor if you have any side effect that bothers you or that does not go away. 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 KEYTRUDA

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about KEYTRUDA, talk with your doctor. You can ask your doctor or nurse for information about KEYTRUDA that is written for healthcare professionals.

For more information, go to www.keytruda.com.

Based on Medication Guide usmg-mk3475-iv-2001r029 as revised January 2020.

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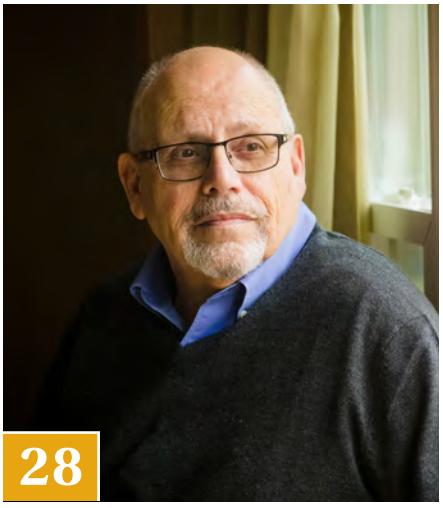

COVER IMAGE: ANDREAOBZEROVA / ADOBE STOCK / ADAPTED BY RAY PELESKO; THIS PAGE (TOP TO BOTTOM): JOE APPEL; MAGEN PORTANOVA SCARBORO; HEATHER ESPOSITO

IF YOU'VE PROGRESSED ON HORMONE THERAPY AND KNOW THAT YOU HAVE A PIK3CA GENE MUTATION, PIQRAY MAY BE THE RIGHT TREATMENT FOR YOU.

Ask your doctor about PIQRAY—the first and only treatment that specifically targets PIK3CA mutations in HR+, HER2- mBC, after progression on hormone therapy. PIK3CA mutations are common and linked to cancer growth.

PIQRAY affects cancer cells, but can also affect healthy cells.

INDICATION

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

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

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

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

IMPORTANT SAFETY INFORMATION

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

PIQRAY may cause serious side effects, including:

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

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

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

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

  Females who are able to become pregnant:

  - Your health care provider will check to see if you are pregnant before you start treatment with PIQRAY
  - You should use effective birth control during treatment with PIQRAY and for 1 week after the last dose. Talk to your health care provider about birth control methods that may be right for you during this time
  - If you become pregnant or think you are pregnant, tell your health care provider right away

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

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

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

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

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

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

These are not all of the possible side effects of PIQRAY. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see Summary of Important Information on the following page.

SUMMARY OF IMPORTANT INFORMATION

WHAT IS PIQRAY USED FOR?

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

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

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

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

WHO SHOULD NOT TAKE PIQRAY?

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

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

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

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

  Females who are able to become pregnant:
  - Your health care provider will check to see if you are pregnant before you start treatment with PIQRAY
  - You should use effective birth control during treatment with PIQRAY and for 1 week after the last dose. Talk to your health care provider about birth control methods that may be right for you during this time
  - If you become pregnant or think you are pregnant, tell your health care provider right away

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

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

WHAT OTHER MEDICATIONS MIGHT INTERACT WITH PIQRAY?

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

WHAT ARE THE POSSIBLE SIDE EFFECTS OF PIQRAY?

PIQRAY may cause serious side effects, including:

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

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

These are not all of the possible side effects of PIQRAY. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

WHAT LABORATORY MONITORING TESTS DO I NEED WHEN TAKING PIQRAY?

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

GENERAL INFORMATION ABOUT THE SAFE AND EFFECTIVE USE OF PIQRAY

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

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

NOVARTIS

PIQRAY® (alpelisib) tablets

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cure®

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During COVID-19 Pandemic, Heed the Advice of Health Experts When Seeking Cancer Care

THIS ISSUE COMES TO you during times that are uncertain for everyone, but perhaps especially for those in the cancer community.

As cases of the new coronavirus, also known as COVID-19, continue to multiply and hospitals divert their resources to handle the crisis — as well as do their best to protect vulnerable individuals from infection — the face of cancer care is changing, and this can cause anxiety. Patients whose treatments are postponed may worry about cancer's progression, while individuals who must continue going to hospitals for lifesaving treatment are likely concerned about catching the infectious disease. Meanwhile, with many facilities banning visitors to help control the virus' spread, patients who are hospitalized are soldiering on without the emotional boost a familiar face can bring.

"In this issue of *CURE*®, we share advice from experts around the country about how patients with cancer should handle medical care during the COVID-19 pandemic."

In this issue of *CURE*®, we share advice from experts around the country about how patients with cancer should handle medical care during the COVID-19 pandemic. We also offer insights into the changed face of cancer care from Dr. Len Lichtenfeld, deputy director of the American Cancer Society, as well as a look at how clinical trials may be altered during this time.

We can only hope that the social distancing, handwashing and other measures encouraged by health care leaders will soon begin to ease these challenges for people with cancer and their families.

Elsewhere in the issue, we explore the growing use of virtual reality in cancer care. Doctors or nurses might use this technology to help patients visualize their own disease, its location in the body and the way it will be treated. Virtual reality also can present patients with scenes or games to distract them from the discomforts of treatment. In our article, we look at how this technology is being used in cancer care today and might be applied in the future.

In another feature, we consider the dangers associated with nonalcoholic fatty liver disease and strategies for preventing this condition, an increasing cause of liver cancer. In other news related to specific cancer types, we bring you a variety of findings from doctors and patient advocates at the recent Miami Breast Cancer Conference® and look at why lifesaving screening for lung cancer is being vastly underused.

Finally, we report on lifestyle issues, including chemo brain, dietary supplements and how to thrive while in the infusion chair.

We hope these discussions will better acquaint you with the latest trends in patient care, including practices that have changed due to the spread of COVID-19 and how those adjustments might affect you. With knowledge comes the ability to make sound medical decisions, and that can make an enormous difference.

As always, thank you for reading.

MIKE HENNESSY SR.
Chairman and Founder

The First Step Toward Preventing Liver Cancer Is Being Aware of the Precursors to its Development

MANY CANCER TYPES DEVELOP in a seemingly random and mysterious manner, with no connection to obvious risk factors, leaving patients wondering if they developed the disease because of something they did — or didn't do.

On the other end of the spectrum is liver cancer. Although some cases arise without any apparent precursors, many are linked to some insult to the liver. These include past or ongoing hepatitis infection, significant use of alcohol and, increasingly, nonalcoholic fatty liver disease (NAFLD), which tends to be associated with obesity. The common element in these factors is that they lead to inflammation and fibrosis (scarring) of the liver, which raises the risk of cancer.

It might sound ominous that 25% of Americans have NAFLD, but the good news is that the condition is a modifiable risk factor for liver cancer: It appears to be reversible through dietary changes and exercise. This means that, in many cases, prevention of liver cancer may be in the hands of patients — and not only those who know they have NAFLD. By losing weight when a doctor recommends it, patients may well reverse a case of fatty liver they didn't know they had, potentially averting cancer.

Still, it's ideal to know whether NAFLD is present so that patients can change their lifestyles with purpose and doctors can monitor their progress. This requires some investigation because the condition is typically "silent," causing no symptoms. In particular, it's reasonable for doctors to consider testing blood for elevated liver enzymes in patients who are overweight, have symptoms of liver disease, have type 2 diabetes, drink alcohol regularly or have been exposed to hepatitis. Other less common diseases cause fibrosis or the more advanced condition of cirrhosis, and these patients are also at risk of liver cancer. Finally, a smaller group of patients have inherited genetic mutations that predispose them to NAFLD, so those with a family history of that condition or liver cancer should ask their doctors about getting evaluated.

When doctors find that a patient's liver enzymes are elevated, their follow-up likely will include additional blood tests and imaging. Although CT scanning is an option after causes such as hepatitis have been ruled out, a new approach is FibroScan, a specialized ultrasound device that vibrates the liver to measure stiffness due to scar tissue.

Patients and doctors should keep NAFLD front of mind, because we may have seen just the beginning of its upward trend. Although the obesity epidemic may finally be tapering off, we can expect its long-term effects to remain. That certainly seems true when we consider that NAFLD is now the fastest-rising cause of liver cancer in Western countries.

The first step toward controlling the incidence of NAFLD is making people aware of it, an effort that should be undertaken by public health outlets, primary care physicians, oncologists and patients. It's up to everyone individually to take stock of personal health issues and, if risk factors are present, ask about screening. With members of the public aware and advocating for themselves, we may reduce the incidence of both NAFLD and liver cancer.

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

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Battling Cancer — And Social Security

In February of 2014, I was diagnosed with metastatic breast cancer. At the age of 45, cancer had spread through my body into my lymph nodes, liver and both hip bones. My prognosis was only a 27% chance to live five years. I had a young son, so decided to fight by keeping normalcy in his world. I chose to throw on my wig and continue working at my stressful 40-hour-a-week administrative job. My treatment regimen included surgery, biopsies, scans every four months and intravenous chemotherapy every three weeks — for the rest of my life, or until my body can no longer tolerate it. I have had over 80 rounds of chemotherapy in less than six years.

Praise God, I am blessed to have been in remission since July 2014! I exceeded the five-year prognosis, but have to be realistic knowing that I have even less than a 27% chance of living 10 years. Unfortunately, I am forced to spend over a year of my time left in this world fighting Social Security.

I can no longer work due to daily exhaustion. My first attempt to get Social Security disability benefits was filed in June 2019. I was turned down in August 2019. I retained an attorney and appealed the decision. Seven months later in January of 2020, I had a hearing and was notified in February 2020 that I had lost my appeal. At the recommendation of my attorney, I am appealing again. I provided my medical statements and records, and my attorney told me to expect a 12 month or longer wait for a decision. My husband and I are afraid to go so long with missed income, in fear of having to file for bankruptcy. I cannot even apply for unemployment. The attorney did say we could request to have my case rushed, but only if hospice is called in for me. Really?

There has to be a better way to screen out those trying to abuse our system. I would much rather work than have to request Social Security benefits, however God sometimes has different plans for us.

How can Americans battling disease and serious health issues be forced to stress over bills in a country as grand as ours? I urge you to encourage guideline reviews of the Social Security system and be an advocate for change.

If I wasn't married, I would've lost my health insurance and wouldn't be able to pay a mortgage, electric bills or even buy food. Even being married, we had to sell my car. We cannot share quality family time together if it costs money, due to our depleted budget. We were a two-income household, and now my husband had to get a second job just to help cover our normal bills.

There are many Americans suffering through these issues who are worse off than me. I choose to be their voice.

I had no idea how bad the Social Security system was until I needed it. I have been working over 35 years, sometimes at two jobs simultaneously, and contributing to Social Security the entire time. The attorney said if I had just filed in 2014 when first diagnosed, it probably would've been approved. It is crazy that I am being penalized for trying and fighting through the sickness to continue working.

Most Americans who haven't experienced health issues preventing employment may not realize these problems exist. I ask for you to please consider assisting, being another voice and advocating for change in our system that is desperately needed by those who have acquired disease and infirmity.

Tammy Summers
WICKSBURG, ALABAMA

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FIRSTLINE

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» DR. WENDY S. HARPHAM

PEOPLE POST

Two Decades Later, Woman Meets the Man Who Got Her Son's Heart

ELISABETH TILLY had the chance to meet 25-year-old Jon Hochstein and listen to his heart — the same heart that once beat in her son Christopher's chest. The heart saved Hochstein's life two decades ago.

Tilly's son, Christopher, died at age 8 in an accident while walking to school. A few rooms from Christopher in the hospital, 4-year-old Hochstein was in critical condition due to his own heart enlarging. At first, Tilly did not want to donate, but decided otherwise when she saw Christopher in critical condition.

After he received the heart, Hochstein nearly died again from Hodgkin lymphoma after drugs to keep his immune system from attacking his donated heart left him vulnerable to cancer. But he survived and went on to become a healthy Harvard University student who hopes to become a doctor someday.

"There's this massive special connection," Hochstein said after getting the chance to connect with Tilly. "She had to make this crazy decision amid this tragedy in her life to let someone else use her son's heart and other organs. I was really grateful that she got to listen to Christopher's heart in my chest. That was really powerful." — *Conor Killmurray*

» JON HOCHSTEIN, then 5, listens as Sen. DICK DURBIN speaks at a press conference about organ donation.

Dancing Pediatric Nurse Attracts Attention of Patients, Hospital Leaders and the Nation

AT ST. LUKE'S Children's Hospital in Boise, Idaho, one oncology nurse likes to brighten his patients' days through dance, and he has become so popular with the youngsters that he was featured in a commercial for the facility.

"It's kind of funny, because I think (people) thought it was an actor. I'm not an actor," Joe Ronquillo — or Nurse Joe, as he's known in the hospital — said in an interview. Ronquillo does hip-hop dance moves to cheer up his patients, some of whom have cancer, because he wants to improve their stays, which often last days or weeks. He has the children join in on the fun, which has led to some videos that went viral.

Along with Ronquillo, who is a first-generation American born to parents from El Salvador, his three siblings work in the hospital. He recently finished school to become a nurse practitioner, saying that he was inspired by his young patients to follow his dreams.

"The greatest joy for me is dancing for them here at the hospital," he said. "(We're) not just treating the disease, (we're) treating the entire patient, so I think those are the moments that I cherish the most." — *Conor Killmurray*

BOOKSHELF

Free E-Book Helps Patients Set Their Sights on Constructive, Attainable Goals

Dr. Wendy S. Harpham has long been committed to helping patients with cancer find hope that is realistic and achievable — or, as she describes it, healing hope.

Now, the physician, 30-year survivor of multiple recurrences of non-Hodgkin lymphoma and author has written an e-book, "Finding Hope That Heals," that is available for free on the website of the National Breast Cancer Foundation at tinyurl.com/FindHopeNBCF.

In the book, Harpham, who is also a member of *CURE*®'s advisory board, goes beyond the usual encouragement to "have hope" by offering practical guidance on how to find and nourish hopes that are constructive, which can help to improve quality of life.

"America's millions of breast-cancer survivors want and need hope. Not just any hope, but healing hope — namely hope that helps them live their best life," she said.

In "Finding Hope That Heals," Harpham encourages patients and their caregivers to think and talk about hope in ways that help them make wise deci-

HOCHSTEIN: TOM WILLIAMS/ROLL CALL/GETTY IMAGES; HARPHAM: JARED REY; E-BOOK FROM WWW.NATIONALBREASTCANCER.ORG

sions, take effective action and live with uncertainty. It presents a series of exercises that can help patients reflect on their hopes, let go of the ones that are leading them astray and find others that help them through and beyond breast cancer.

"Hope is central to getting good care and living as fully as possible," Harpham explains. "After decades of sharing insights and aphorisms in my lectures and one-on-one communications all over the world, I'm convinced that people are ready to think and talk about hope in new ways."

On its website, the foundation, which provides early detection, education and support services to those affected by breast cancer, explains its goal in sharing the book.

"The mission of NBCF revolves around hope. We want to change the conversation that often ends with a rallying cry to "Have hope!" Instead, we want that to start a new conversation about which hopes can help you today, how to nurture them, and how to let go of those that might harm," the website states. "We're honored that Dr. Harpham created this exciting e-book with us."

— Beth Fand Incollingo

HEALTH DISPARITIES

Rates of Cancer Are Higher in Transgender Men Than in Cisgender Men, a First-of-its-Kind Study Finds

Transgender men are twice as likely to have had cancer as cisgender men (who identify with their birth gender) , according to data published in *Cancer*.

In addition, transgender men and transgender women cancer survivors have higher rates of diabetes and heart disease than cisgender survivors. Researchers also found that nonbinary, or gender nonconforming, survivors of cancer have unusually high rates of depression and unhealthy lifestyle factors.

The survivors included in the study had reported diagnoses of any kind of cancer except skin cancer.

Data came from the 2014-2018 federal Behavior Risk Factor Surveillance System (BRFSS) for the 37 U.S. states and one territory (Guam) that ask gender identity questions in their surveys.

The study was the first to look at cancer prevalence in transgender people and examine the health of transgender survivors of cancer. Its authors, who embarked on the study because the needs of these populations "have received scarce attention", concluded that doctors must recognize these health disparities and step in to help.

"We hope these findings are a wake-up call for health care providers that transgender cancer survivors have complex medical needs," study lead author Dr. Ulrike Boehmer, associate professor of community health sciences at the Boston University School of Public Health, said in a press release. "Furthermore, in light of recent efforts to legalize discrimination against this population, any health care agency that is not publicly, visibly welcoming transgender individuals is worsening transgender survivors' health care experiences, and possibly augmenting their poor cancer survivorship."

Read more at curetoday.com/link/271.

— Beth Fand Incollingo

LEGISLATIVE REPORT

Clinical Trial Protocols Are Likely to Change During COVID-19 Pandemic

Clinical trials may slow, stop or change during the COVID-19 pandemic, according to the Food and Drug Administration (FDA), which issued official guidance March 18 for industry, investigators and any institutions conducting trials that are facing challenges like quarantines, travel restrictions, site closures and even self-isolation of researchers or trial participants that contract the virus.

Trial investigators are encouraged to consider whether self-administered drugs can be securely delivered to participants at home, and whether treatments usually given by health care professionals can be administered alternatively; for instance, by home nurses or other trained personnel. The guidance also calls for alternative methods of contacting participants, such as phone contacts or virtual visits, when possible or necessary, and extra safety monitoring for those who can no longer visit their trial site or get the investigational product and study-mandated tests they were previously taking.

Researchers will also need to consider whether delaying assessments, stopping recruitment or withdrawing participants will be necessary, and will be responsible for letting their review boards know about any changes, as well as for documenting any information that is missing due to the pandemic.

Finally, the FDA wants trial leaders to discuss with their review boards any modifications to the way study results will be collected and to document the reasons for any data that cannot be gathered.

"Efforts to minimize impacts on trial integrity, and to document the reasons for protocol deviations, will be important," the FDA wrote.

— Conor Killmurray

TRANSGENDER: VCHALUP / ADOBE STOCK; MASK: AA+W / ADOBE STOCK

Len Lichtenfeld, M.D., is deputy chief medical officer of the American Cancer Society.

Send House Call questions to **editor@curetoday.com**.

American Cancer Society®

HOUSE CALL

COVID-19 Concerns Interrupting Cancer Treatments For Some

COVID-19 — WHICH STANDS FOR coronavirus disease 2019 and is caused by a virus named SARS-CoV2 — is a serious illness for anyone, and especially so for patients with cancer. Cancer treatments, particularly those that specifically weaken the immune system, leave patients with cancer more susceptible to the ravaging effects of the coronavirus and can lead to death in a larger proportion of these patients who become infected compared with the general population.

That's one reason that measures to protect these patients from the virus are going beyond the handwashing and social distancing recommended for everyone and actually affecting treatments for the cancer itself.

Cancer care will be disrupted during this pandemic. In some parts of our country, cities will be severely affected, and the resources of health care teams and their supporting services such as labs, radiology departments and operating rooms will be diverted elsewhere to serve the needs of those in immediately life-threatening circumstances.

At the American Cancer Society call center, about 80% of the calls are now related to coronavirus questions. Patients are seeing their treatments disrupted with delays or are having surgeries and radiation therapy sessions canceled. Some are questioning the safety of their oncologists' offices, where patients and caregivers sit close together or may have to share a single bathroom. Cancer survivors are asking whether, as health care workers themselves, they can even go to work.

Cancer centers are literally reacting to the changes demanded by coronavirus on a day-to-day basis. This is truly uncharted territory, with no road map on how best to respond.

For some patients, such as those with a small, non-invasive and non-aggressive ductal carcinoma in situ breast cancer, surgery may be delayed while anti-hormonal treatment is started earlier. For others, such as patients with acute leukemia or advanced lymphoma, where time is of the essence, there is little doubt that their care will be prioritized.

Many centers are moving patients to virtual visits when the situation allows. Reconstructive surgery after breast cancer may be delayed, since operating suites are being closed and ventilators moved to acute care. And, unfortunately, we are hearing the difficult stories from patients whose treatment may not be considered lifesaving and therefore has been canceled for the immediate future.

Difficult decisions are going to be made, especially in communities where the virus is rampant. These aren't easy choices; however, they are necessary choices, since in some cases there are no other options. No health professional ever thought they would have to have these conversations; no patient or caregiver ever thought they would have to hear them.

We don't know today what the total impact of the COVID-19 pandemic will be on cancer care, clinical trials and outcomes. It will take years of study to figure out whether we were able to meet the challenge or suffered negative outcomes that would not have been dreamed of even a few short weeks ago.

As trite as it may sound, we are indeed all in this together — every one of us. If we stay focused and committed, we will get through this and continue back to our lives with some degree of routine and normalcy. That is our prayer and that is our hope.

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Improving the Journey

From advocacy to health risks, speakers at the 37th Annual Miami Breast Cancer Conference® touch on a variety of topics that are key to the well-being of patients.

For 37 years, the Miami Breast Cancer Conference® — run by *CURE*®'s parent company, MJH Life Sciences™ — has brought together a multidisciplinary faculty of surgical, medical and radiation oncologists, as well as geneticists, pathologists, radiologists and supportive-care specialists, to foster attendees' awareness of state-of-the-art treatments for all stages and subtypes of breast cancer. In parallel to this year's March 5-8 conference, for the second year in a row, CURE Media Group hosted a full-day meeting to help educate, inform and equip patients and their loved ones with resources and knowledge in the breast cancer space.

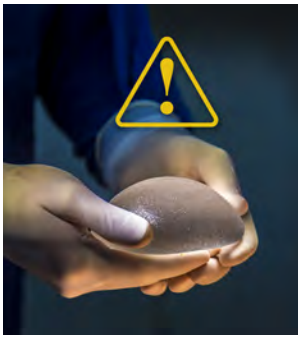
Here, we share some of the news that came out of sessions at the two conferences.

Patients Should be Educated About Cancer That's Associated With Breast Implants

People who have breast implants or are thinking of getting them should be aware of the signs and symptoms of a newly recognized rare cancer associated with use of the devices.

Plastic surgeon Dr. Valerie Lemaine, of Plastic Surgery Consultants at Minnesota Oncology, discussed the signs and symptoms of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), as well as how the disease is diagnosed and treated.

BIA-ALCL is a lymphoma, or blood cancer, that develops in T immune cells in the fluid and tissue adjacent to breast implants.



It has been linked to the use of textured, rather than smooth, implants. As of July 2019, the Food and Drug Administration (FDA) had received confirmation of 573 unique cases, including 481 that were linked to Allergan BioCell textured implants, that led to 33 deaths.

BIA-ALCL presents as a seroma, a collection of fluid that builds up under the skin around the breast implant, which occurs on average eight to 10 years after the placement of the device. Other symptoms can include a palpable mass, enlarged lymph nodes, skin rash, fevers and capsular contracture (the formation of a capsule of tissue that tightens around and squeezes the implant).

If BIA-ALCL is suspected, the first step is to undergo a breast ultrasound. If the ultrasound is indeterminate, a breast MRI should be performed. Any seroma, fluid collection or mass should be tested via fine needle aspiration.

If the disease has not spread, surgical removal of the cancer and the implant can be conducted. If the disease is stage 2 or higher, this may be followed by chemotherapy, and radiation is given if cancer cells remain after surgery or the cancer has invaded the chest wall.

A 2016 study showed that overall survival rates at three and five years were 94% and 91%, respectively.

"At this time, the FDA does not recommend removal of these or other types of breast implants in patients who have no symptoms due to the low risk of developing BIA-ALCL," Lemaine said. "(Health care providers) should inform patients about the risk of developing BIA-ALCL and what to look for." — *Kristie L. Kahl*

Learning Self Advocacy Is an Important Goal for Patients Who Have Breast Cancer

Patients with breast cancer must be their own best advocates, Stephanie Seban, a survivor of metastatic breast cancer, said in her keynote address at *CURE*®'s Educated Patient Breast Cancer Summit.

To explain why, Seban gave an example of the statistics she was told when diagnosed with metastatic breast cancer:

- One in five women with that diagnosis will live to see five years.
- A woman with metastatic breast cancer lives, on average, for 36 months.
- "We'll keep you alive as long as we can with the drugs that we have."

"I wasn't buying into the numbers or the death sentence that was staring me down," she said. "And I certainly wasn't going to take a back seat when it came to my cancer care. I made an oath to myself from the very start that I would be a very active participant on my healing journey, and I would do anything and everything in my power to defy the odds. That was over nine years ago, and last February, I celebrated my 40th birthday."

After receiving the wrong results in her original pathology report, Seban was treated for years with therapies that were not effective for her breast cancer subtype. As a result, her first piece of advice to others is to get familiar with their diagnosis, the appropriate options for treating it, the drugs they've been prescribed and what the medications do, as well as any promising new treatments being developed.

"The more you know, the more you will feel a bit more in control and, most importantly, empowered," Seban said.

She recommends that, to keep up to date, patients join online support communities, support groups and meetups and attend conferences or online courses.

Next, she reminded the audience that it is key to ask questions at medical appointments, bring a partner, take notes and/or record the conversation. Seban also urged the audience to get a second opinion when necessary.

"While having two options may seem even more confusing and overwhelming, having the choice to decide which feels right and which doctor's opinion and treatment plan resonates with you is so empowering and can be life-changing and, even in my case, lifesaving," she said.

Seban ended with a quote she considers relevant to this population of patients: "You are the CEO of your life. Hire and fire accordingly." — *Kristie L. Kahl*

MAILSON PIGNATA / ADOBE STOCK / ADAPTED BY RAY PELESKO

Survivorship Starts at Diagnosis and Moves Forward in Stages, a Doctor Asserts

While the meaning of the term "survivor" can vary for many patients with cancer, Dr. Don S. Dizon suggests that survivorship starts at diagnosis.

"A person becomes a survivor from the point they are diagnosed and for the balance of their lives," Dizon said in a presentation.

He broke cancer survivorship into four categories: acute, transitional, extended and permanent.

In acute survivorship, surgical issues are important to patients, as well as other medical therapies like fertility preservation and endocrine therapy.

"It's that time to retell patients how we're going to approach their treatment," said Dizon, who is the director of women's cancers at the Lifespan Cancer Institute, director of medical oncology at Rhode Island Hospital and an associate professor of medicine at Alpert Medical School of Brown University.

To shed light on that stage, a Brown University student conducted a Facebook survey of members of online "Go Flat" communities to find out how much they knew about their surgical options following a breast cancer diagnosis, and what their interactions with breast specialists and overall experiences were like.

"First off, they wanted (surgeons) to tell them that going flat is an option, not a mistake, not something that they're going to change their mind about," Dizon said. "They wanted to feel supported. They wanted pictures of what it is to go flat. They wanted this to be treated with the same seriousness as the reconstructive options themselves."

Transitional survivorship involves survivorship care planning. With this stage of survivorship also comes the fear of recurrence, which can be associated with younger age at diagnosis, having children, having limited support or having a higher stage of disease.

Extended survivorship includes a goal of three P's to strengthen quality of life: preserve, prevent and prolong.

Those in permanent survivorship are patients 10 years out from diagnosis or living with a relapse or secondary cancer. Oncologists recommend 360 minutes of physical activity per week for these survivors, which has been found to be prolong cancer-specific survival.

"We can make a difference in our patients' lives," Dizon concluded. "Survivorship, at the end of the day, is about meeting patients where they are." — *Kristie L. Kahl*

IN MEMORIAM

Remembering and Celebrating the Life of Patti Hennessy

DURING THIS YEAR'S Miami Breast Cancer Conference®, MJH Life Sciences™ remembered and celebrated the life of ***Patrice "Patti" Hennessy***, an interior designer, a patient advocate, a mother devoted to her four children and their spouses, and a grandmother who considered her nine grandchildren the loves of her life. On Jan. 28, she succumbed to the cancer she had lived with for nine years. She was 59 years old.

During her journey with ovarian and then breast cancer, Mrs. Hennessy watched her family grow, traveled with her husband and spent time with friends and in nature. She had recently celebrated the 36th anniversary of her marriage to Mike Hennessy Sr., chairman and founder of MJH Life Sciences™, parent company of *CURE*®; Physicians' Education Resource®, LLC (PER®); *OncLive*®; and more than 60 other medical media platforms.

PATTI HENNESSY with her husband, MIKE HENNESSY SR., chairman and founder of MJH Life Sciences™.

"Focusing on the cancer all the time defeats the purpose of the fight. I try to live and enjoy life," she said in 2018.

Mrs. Hennessy went out of her way to help others navigate the cancer experience. In 2018, she served as keynote speaker for PER®'s *35th Annual* Miami Breast Cancer Conference®, emphasizing the importance of testing for BRCA gene mutations in women with breast and ovarian cancers. She carried an inherited BRCA1 mutation, which predisposed her to both cancer types.

"I speak to so many people who are diagnosed with breast cancer, and when I ask if they have the gene, they know nothing about it," Mrs. Hennessy said in an interview prior to her talk. "This gene can impact your entire family and generations to come. There are also preventive things you can do, if you have it, to avoid both breast and ovarian cancer."

During her keynote address, she urged her audience of oncologists, nurses and other health professionals to take more detailed family histories, have their patients' tumors tested for genetic mutations and offer them personalized treatment based on the results. She credited her years of successful treatment to that kind of strategy and pointed out that advances in research will continue to expand the options for individualized therapy.

"I fight this fight so that I can be here with my family, and I won't give up — for myself and so many women like me, and for my family and their families," she said. "We're all counting on you to work hard toward a cure."

Mrs. Hennessy's determination in the face of her health challenges was recognized by Dr. Patrick I. Borgen, Miami Breast Cancer Conference® chair.

"Patti Hennessy can teach us two vitally important lessons in breast oncology," Borgen said. "She teaches us the depth of our ignorance about this complex disease and she teaches us to never give up, to maintain hope coupled with tenacity. Her message is clear — not to dwell on the uncertainties, but rather to revel in the distance yet to be traveled."

COURTESY OF THE HENNESSY FAMILY

Every day matters

Having more of them is possible with Verzenio + fulvestrant

~4
YEARS

Women lived longer on Verzenio + fulvestrant

In a clinical study, women taking Verzenio + fulvestrant lived for a median of 46.7 months vs 37.3 months on fulvestrant alone.

16.4
MONTHS

More time without disease progression

In the same study, Verzenio + fulvestrant delayed disease progression for a median of 16.4 months vs 9.3 months with fulvestrant alone.

Verzenio was studied in a clinical trial of 669 women with hormone receptor–positive (HR+), human epidermal growth factor receptor 2–negative (HER2–) metastatic breast cancer, whose disease had progressed after hormone treatment: 446 patients were treated with Verzenio + fulvestrant, and 223 were treated with fulvestrant alone.

everyday

Verzenio®

abemaciclib

50 | 100 | 150 | 200 mg tablets

twice a day

Learn more at verzenio.com

PURPOSE AND SAFETY SUMMARY

Important Facts About Verzenio® (ver-ZEN-ee-oh). It is also known as abemaciclib.

Verzenio is a prescription medicine used to treat a type of breast cancer. It is a medicine you can take if:

- You have a type of breast cancer called HR+/HER2– (hormone receptor positive/human epidermal growth factor receptor 2 negative) and the cancer has spread to other parts of the body (metastasized)
- Verzenio is given along with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women, along with fulvestrant in women whose disease has progressed after hormonal therapy, or by itself in adults whose disease has progressed after hormone therapy and prior chemotherapy

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

WARNINGS

Verzenio may cause serious side effects, including:

Diarrhea is common with Verzenio, may be severe and may cause dehydration or infection. The most common time to develop diarrhea is during the first month of Verzenio treatment. Your doctor may stop your treatment, lower your dose, or tell you to wait to begin your treatment cycle if you have diarrhea.

At the first sign of loose stools, tell your doctor. You may be advised to start taking an antidiarrheal medicine (such as loperamide) and drink more fluids.

Low white blood cell counts (neutropenia) are common with Verzenio and may cause serious infections that can lead to death. Your doctor should check your white blood cell counts before and during treatment. Tell your doctor right away if you have fever or chills.

Verzenio may cause severe or life-threatening inflammation (swelling) 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:

- Trouble breathing or shortness of breath
- Chest pain
- Cough with or without mucus

Verzenio can cause liver problems. Tell your doctor right away if you have any of the following signs or symptoms of liver problems:

- Feeling very tired
- Loss of appetite
- Pain on the upper right side of your stomach area (abdomen)
- Bleeding or bruising more easily than normal

Verzenio may cause blood clots in your veins or lungs. These may be serious and have led to death. Tell your doctor if you have the following signs and symptoms of a blood clot:

- Pain or swelling in your arms or legs
- Fast breathing
- Fast heart rate
- Shortness of breath
- Chest pain

Verzenio can harm your unborn baby. Use effective birth control during treatment and for at least 3 weeks after the last dose of Verzenio and do not breastfeed during treatment with Verzenio and for at least 3 weeks after your last dose. Verzenio may affect the ability of males to father a child.

COMMON SIDE EFFECTS

The most common side effects of Verzenio include:

- Nausea
- Infections
- Low red blood cell counts (anemia)
- Decreased appetite
- Headache
- Hair thinning or hair loss (alopecia)
- Abdominal pain
- Tiredness
- Low white blood cell counts (leukopenia)
- Vomiting
- Low platelet counts (thrombocytopenia)

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

Tell your doctor if you have any side effects. ***You can report side effects at 1-800-FDA-1088 or www.fda.gov/medwatch.***

BEFORE USING

Before you use Verzenio, tell your doctor:

- If you have fever, chills, or other signs of infection
- Have liver or kidney problems
- About all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your doctor if you take a medicine that contains ketoconazole. Avoid grapefruit products while taking Verzenio. Grapefruit may increase the amount of Verzenio in your blood

HOW TO TAKE

- Use Verzenio exactly as your doctor tells you
- Take your doses of Verzenio at about the same time every day
- If you vomit or miss a dose take your next dose at your regular time. Do not take 2 doses of Verzenio at the same time to make up for the missed dose
- If you take too much Verzenio, call your doctor or go to the nearest hospital emergency room right away

LEARN MORE

For more information, call 1-800-545-5979 or go to verzenio.com.

This summary provides basic information about Verzenio but does not include all information known about this medicine. Read the information that comes with your prescription each time your prescription is filled. This information does not take the place of talking with your doctor. Be sure to talk to your doctor or other healthcare provider about Verzenio and how to take it. Your doctor is the best person to help you decide if Verzenio is right for you.

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Lilly

Screen Time

Screening for lung cancer saves lives, but many aren't aware it's an option. Here's what people who face a high risk of the disease should know.

By BETH FAND INCOLLINGO

SCREENING FOR LUNG CANCER in high-risk individuals saves lives by detecting disease at an early stage when it's likely curable with surgery, without the need for drugs or radiation — or the side effects they can generate.

While 8 to 9 million people in America are eligible for screening via low-dose computed tomography (CT) due to their smoking history, nationwide, only 4% of them have participated, says Dr. Andrea McKee, a radiation oncologist who runs the lung cancer screening program at Lahey Hospital and Medical Center in Burlington, Massachusetts and volunteers as a spokesperson for the American Lung Association.

That level of participation pales in comparison to the screening rates for other cancers, McKee says: In Massachusetts, which holds the record for lung cancer screening with 12% of high-risk individuals participating, 75% of those eligible for colorectal screening get it, and an even higher percentage of eligible women get mammograms to check for breast cancer.

One reason for the low participation rate among people at risk for lung cancer is that the screening test for the disease is fairly new, and another is that awareness about it is low among patients and sometimes their doctors, McKee says.

ALA is determined to help change that.

On its website's homepage (lung.org), the ALA encourages visitors to consider screening. It offers a quick quiz that tells people whether they are eligible, as well as a list of conversation points for qualified patients to bring up with their doctors.

Furthermore, McKee says, "The ALA has recommended that organizations reach a goal of screening at least 20% of those eligible by 2025."

Her own institution has more than complied, having screened 65% of its eligible population, about 6,000 patients, since the test became available in 2011.

"It's doable, but it requires education, effort and outreach into the community and to primary-care doctors," she says.

(CONTINUED ON PAGE 23) »

СЕРГЕЙ УЛАНОВ / ADOBE STOCK

IN A CLINICAL TRIAL, PEOPLE TAKING IMFINZI LIVED LONGER THAN THOSE WHO TOOK NO MEDICINE AFTER CRT

For people with unresectable Stage 3 non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent chemoradiation therapy (CRT).

In a clinical trial, 66% of people taking IMFINZI were alive compared with 56% of people taking placebo (no medicine) at 2 years. IMFINZI may not work for everyone.

ASK YOUR DOCTOR ABOUT IMFINZI. VISIT IMFINZI.COM

IMFINZI was studied in a trial that included 713 patients with unresectable Stage 3 NSCLC who completed at least 2 cycles of chemotherapy that contained platinum given at the same time (concurrently) as radiation before starting the trial. Patients in the study had good Performance status (WHO grade 0 or 1).* This means they were able to carry on all pre-disease activities without restriction (0) or were restricted when engaging in physically strenuous activities but able to carry out light work (1). IMFINZI was tested against placebo (no medicine).

The main goal of the trial was to measure the length of time people remained progression-free (without cancer growing or spreading) and overall survival. This trial is still ongoing.

***WHO=World Health Organization.**

WHO IS IMFINZI FOR?

IMFINZI® (durvalumab) is a prescription medicine used to treat a type of lung cancer called non-small cell lung cancer (NSCLC). IMFINZI may be used when your NSCLC has not spread outside your chest, cannot be removed by surgery, **and** has responded or stabilized with initial treatment with chemotherapy that contains platinum, given at the same time as radiation therapy.

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

IMPORTANT SAFETY INFORMATION

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

IMFINZI is a medicine that may treat a type of lung cancer by working with your immune system.

IMFINZI can cause your immune system to attack normal organs and tissues and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead to death.

Call or see your healthcare provider right away if you develop any symptoms of the following problems or if these symptoms get worse:

Lung problems (pneumonitis). Signs and symptoms may include new or worsening cough, shortness of breath, and chest pain.

Liver problems (hepatitis). Signs and symptoms may include yellowing of your skin or the whites of your eyes, severe nausea or vomiting, pain on the right side of your stomach area (abdomen), drowsiness, dark urine (tea colored), bleeding or bruising more easily than normal, and feeling less hungry than usual.

Intestinal problems (colitis). Signs and symptoms may include diarrhea or more bowel movements than usual; stools that are black, tarry, sticky, or have blood or mucus; and severe stomach-area (abdomen) pain or tenderness.

Hormone gland problems (especially the thyroid, adrenals, pituitary, and pancreas). Signs and symptoms that your hormone glands are not working properly may include headaches that will not go away or unusual headaches; extreme tiredness; weight gain or weight loss; dizziness or fainting; feeling more hungry or thirsty than usual; hair loss; feeling cold; constipation; your voice gets deeper; urinating more often than usual; nausea or vomiting; stomach-area (abdomen) pain; and changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness.

Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include decrease in the amount of urine, blood in your urine, swelling of your ankles, and loss of appetite.

Skin problems. Signs may include rash, itching, and skin blistering.

Problems in other organs. Signs and symptoms may include neck stiffness; headache; confusion; fever; chest pain, shortness of breath, or irregular heartbeat (myocarditis); changes in mood or behavior; low red blood cells (anemia); excessive bleeding or bruising; muscle weakness or muscle pain; blurry vision, double vision, or other vision problems; and eye pain or redness.

Severe infections. Signs and symptoms may include fever, cough, frequent urination, pain when urinating, and flu-like symptoms.

Severe infusion reactions. Signs and symptoms may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, fever, feeling like passing out, back or neck pain, and facial swelling.

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 IMFINZI. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may delay or completely stop treatment with IMFINZI if you have severe side effects.

Before you receive IMFINZI, 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 had an organ transplant; have lung or breathing problems; have liver problems; or are being treated for an infection.

If you are pregnant or plan to become pregnant, tell your healthcare provider. IMFINZI can harm your unborn baby. If you are able to become pregnant, you should use an effective method of birth control during your treatment and for at least 3 months after the last dose of IMFINZI. Talk to your healthcare provider about which birth control methods to use. Tell your healthcare provider right away if you become pregnant during treatment with IMFINZI.

If you are breastfeeding or plan to breastfeed, tell your healthcare provider. It is not known if IMFINZI passes into breast milk. Do not breastfeed during treatment with IMFINZI and for at least 3 months after the last dose of IMFINZI.

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

What are the possible side effects of IMFINZI?

IMFINZI can cause serious side effects (see earlier).

The most common side effects in people with non-small cell lung cancer (NSCLC) include cough, feeling tired, inflammation in the lungs (pneumonitis), upper respiratory tract infections, shortness of breath, and rash.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of IMFINZI. Ask your healthcare provider or pharmacist for more information.

Call your healthcare 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 see Brief Summary of complete Prescribing Information on adjacent page.

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

IMFINZI®
durvalumab
Injection for Intravenous Use 50 mg/mL

AstraZeneca

IMPORTANT INFORMATION ABOUT IMFINZI® (im-FIN-zee) (durvalumab) INJECTION

IMFINZI™ durvalumab Injection for Intravenous Use 50 mg/mL

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT IMFINZI?

IMFINZI is a medicine that may treat a type of lung cancer by working with your immune system.

IMFINZI can cause your immune system to attack normal organs and tissues and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead to death.

Call or see your healthcare provider right away if you develop any symptoms of the following problems or these symptoms get worse:

Lung problems (pneumonitis). Signs and symptoms of pneumonitis may include:

- new or worsening cough
- shortness of breath
- chest pain

Liver problems (hepatitis). Signs and symptoms of hepatitis may include:

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

Intestinal problems (colitis). Signs and symptoms of colitis may include:

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

Hormone gland problems (especially the thyroid, adrenals, pituitary and pancreas). Signs and symptoms that your hormone glands are not working properly may include:

- headaches that will not go away or unusual headaches
- extreme tiredness
- weight gain or weight loss
- dizziness or fainting
- feeling more hungry or thirsty than usual
- hair loss
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness
- feeling cold
- constipation
- your voice gets deeper
- urinating more often than usual
- nausea or vomiting
- stomach area (abdomen) pain

Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include:

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

Skin problems. Signs of these problems may include:

- rash
- itching
- skin blistering

(continued)

Problems in other organs. Signs and symptoms may include:

- neck stiffness
- headache
- confusion
- fever
- chest pain, shortness of breath, or irregular heartbeat (myocarditis)
- changes in mood or behavior
- low red blood cells (anemia)
- excessive bleeding or bruising
- muscle weakness or muscle pain
- blurry vision, double vision, or other vision problems
- eye pain or redness

Severe infections. Signs and symptoms may include:

- fever
- cough
- frequent urination
- pain when urinating
- flu-like symptoms

Severe infusion reactions. Signs and symptoms of severe infusion reactions may include:

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- fever
- feel like passing out
- back or neck pain
- facial swelling

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 IMFINZI. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may delay or completely stop treatment with IMFINZI, if you have severe side effects.

WHAT IS IMFINZI?

IMFINZI is a prescription medicine used to treat:

- a type of lung cancer called non-small cell lung cancer (NSCLC). IMFINZI may be used when your NSCLC:
  - has not spread outside your chest
  - cannot be removed by surgery, **and**
  - has responded or stabilized with initial treatment with chemotherapy that contains platinum, given at the same time as radiation therapy.

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

Before you receive IMFINZI, 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 had an organ transplant
- have lung or breathing problems
- have liver problems
- are being treated for an infection
- are pregnant or plan to become pregnant. IMFINZI can harm your unborn baby. If you are able to become pregnant, you should use an effective method of birth control during your treatment and for at least 3 months after the last dose of IMFINZI. 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 during treatment with IMFINZI.
- are breastfeeding or plan to breastfeed. It is not known if IMFINZI passes into your breast milk. Do not breastfeed during treatment and for at least 3 months after the last dose of IMFINZI.

(continued)

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 IMFINZI?

- Your healthcare provider will give you IMFINZI into your vein through an intravenous (IV) line over 60 minutes.
- IMFINZI is usually given every 2 weeks.
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will test your blood to check you for certain 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 IMFINZI?

IMFINZI CAN CAUSE SERIOUS SIDE EFFECTS, INCLUDING:

SEE "WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT IMFINZI?"

The most common side effects of IMFINZI in people with NSCLC include:

- cough
- feeling tired
- inflammation in the lungs (pneumonitis)
- upper respiratory tract infections
- shortness of breath
- rash

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

These are not all the possible side effects of IMFINZI. Ask your healthcare provider or pharmacist for more information. 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 IMFINZI.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about IMFINZI, talk with your healthcare provider. You can ask your healthcare provider for information about IMFINZI that is written for health professionals.

AstraZeneca

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(CONTINUED FROM PAGE 20)

EVIDENCE SUPPORTS SCREENING

Low-dose CT screening combines X-ray and computer components to image the inside of the chest. It employs less ionizing radiation, which can damage cells and cause them to malfunction, than a conventional CT scan.

The technique "has been proven to significantly reduce mortality due to lung cancer and is one of the greatest advances we've been able to achieve in the fight against an otherwise very deadly disease," McKee says.

Clinical trials of the test found a mortality benefit — or reduction in the rate of death — between 20% and 60%, which McKee described as "huge."

The National Lung Screening Trial, concluded in 2011, gave one group of patients an annual low-dose CT of the chest while another got an annual chest X-ray in three rounds of screening over two years. After six years, the researchers followed up and found that there had been 20% more deaths in the chest X-ray group compared with the CT group. There were 247 deaths from lung cancer per 100,000 person-years in the low-dose CT group and 309 deaths per 100,000 person-years in the radiography group. A person year is a measurement that takes into account the number of people in a study and the amount of time each one participates. These results show "that low-dose CT saves lives," McKee says.

In Europe, the Nelson study compared low-dose CT of the chest against no intervention. Four screens were conducted over 5 1/2 years, and in a follow-up 10 years later, the CT group was found to enjoy a 25% mortality benefit across the board (2.5 deaths per 1,000 person-years in the CT group versus 3.3 deaths per 1,000 person-years in the no-intervention group); when only the study's women were looked at, the CT group was determined to have experienced a 60% mortality benefit.

And the MILD trial, which compared the effectiveness of a pulmonary function test with or without CT, found a 40% mortality benefit for those who got CT scans. That broke down to 247 deaths per 100,000 person-years in those who received CT scans versus 309 deaths per 100,000 person-years in the chest radiography arm.

> **"Low-dose CT scanning has been proven to significantly reduce mortality due to lung cancer and is one of the greatest advances we've been able to achieve in the fight against an otherwise very deadly disease."**
>
> *— DR. ANDREA MCKEE, radiation oncologist and volunteer spokesperson for the American Lung Association*

McKee explained the results she's seen in her own experience screening patients.

When screening for the first time, she's found that cancers show up in 2% to 3% of patients, 70% early stage and 30% later stage. After that, these patients develop lung cancers at a rate of 1% to 2% per year, and with continued annual screening, 90% of them are caught in an early stage.

This is important because "stage 1 lung cancer has an 88% chance of cure," McKee says. "Compare that with stages 3 or 4, whose five-year survival rates are less than 35% and 5%, respectively."

The experience of being treated for an early-stage cancer is also less grueling, she noted. While treatment for stage 1 or 2 lung cancer typically consists of surgery alone, treatments for stage 3 or 4 disease may include radiation, chemotherapy, targeted drugs and/or immunotherapy.

DETERMINING ELIGIBILITY

Those eligible for screening have histories of heavy smoking.

"Almost all guidelines support screening of patients over age 55 with a 30 pack-year history of smoking who currently smoke or quit within the past 15 years," McKee says. Pack years are measured by multiplying the average number of packs a person smoked per day by the number of years they smoked.

"What is argued over is whether the screening should stop at age 77 or 80," she says. "The United States Preventive Services Task Force recommends screening until age 80, while the Centers for Medicare & Medicaid Services recommend screening until age 77. The National Comprehensive Cancer Network takes a broader approach, recommending screening for patients 50 and over with a 20 pack-year history of smoking and no upper age limit, but patients must have one other risk factor for lung cancer, such as first-degree family history or personal history of lung cancer, history of a tobacco-related cancer, non-carcinogenic exposure or a history of COPD or interstitial lung disease."

It's possible that guidelines could change, McKee says: The USPSTF is considering whether there's value in screening another high-risk population based on data from two randomized controlled trials published since its last review. The studies included people age 50 and older with somewhat lighter smoking histories compared with those enrolled in previous trials.

Under the Affordable Care Act, annual lung cancer screening is free to high-risk individuals through health insurance, but insurers may use varying guidelines to determine who is eligible.

"The issue is if there's additional testing recommended as a result of the screening test," McKee says. "If it shows a finding that requires a three- or six-month follow-up scan, that might be subjected to a deductible." »

She adds that some screening programs are free for the uninsured or underinsured, although not widely available.

"If we were to discover lung cancer," she says, "most hospitals can work with a patient to get emergency coverage in place."

REASONS FOR UNDERUSE

With screening available, why do so few take advantage of it? "The Centers for Disease Control just reported that nine out of 10 eligible people are not aware of the recommendations for testing," McKee says.

One reason is that the test is so new. Although the study that established the benefit of screening was published in 2011, "until 2015 there was almost no way of being able to charge for the test — there was no billing code for insurance companies to use," she says. During that period, most of the scans conducted were done for free or at a reduced charge by hospitals, including Lahey.

"We did it as a mitigating effort to level the playing field, because if you were a patient at high risk and wanted the test, it could cost $1,000 out of pocket," McKee says.

She added that a stigma, or blame, associated with lung cancer because many cases are linked with smoking could be another a reason there isn't more enthusiasm around the idea of CT screening to detect the disease.

"If we were to find a tool that reduced the mortality benefit 20% to 60% in breast cancer or other cancers that perhaps aren't as stigmatized as lung cancer," McKee says, "we may not be seeing some of the challenges we've been seeing. We need to deal with the stigma associated with this diagnosis to help drive this forward."

SAFETY AND EFFECTIVENESS

In addition to being simple — patients are asked to hold their breath for 10 seconds and don't even need to change into a gown — low-dose CT screening is quite safe, McKee says.

"The test uses about as much radiation as a mammogram, and we've been treating with that for many decades with no proven increased risk to that population, which is similar in age to the group at risk of lung cancer," she says.

She adds that patients don't need to worry about a high rate of false-positive results (positive scans that lead to normal biopsies or no subsequent lung cancer development)associated with CT screening for lung cancer. Despite widely misreported numbers in 2011, the rate is reasonable, she says.

"The actual rate is 9% to 10% in the first year of screening, because we have nothing to compare the results against, and 5% after that, and that's very comparable to what we see with mammography," she says. "This, too, may have to do with bias about screening in this patient population. It's been reported wrongly, and we've been working to get it corrected."

TORWAIPHOTO / ADOBE STOCK / ADAPTED BY RAY PELESKO

GETTING THE TEST

Those interested in getting screened should know that most hospitals have or are developing lung cancer screening programs, and that there are centers in every state conducting the tests, some of which are listed on the ALA's website. There are even mobile CT units in some underserved states.

"Patients should check out ALA site, take the quiz, find out if they meet the high-risk criteria and arm themselves with information so they can have a conversation with their physician," McKee says. "They shouldn't be surprised if the doctor is not fully informed of the new data, so being proactive and advocating for themselves is a good thing."

LC HEROES™

Nominate a hero today!

Do you know an individual going above and beyond to make a difference in the lives of those affected by lung cancer, and who deserves to be honored as a part of our inaugural **2020 Class of Lung Cancer Heroes™**?

CURE® is proud to host our inaugural

Lung Cancer Heroes™

recognition event!

Nominations are now being collected from colleagues, patients, friends, and family of outstanding individuals from across the globe.

Visit **curetoday.com** to nominate your hero!

Selected essayists and the individuals they nominated will be flown to the event destination to be our honored guests at a reception ceremony. Event date and location will be announced when those details become available. We're very much looking forward to celebrating with everyone for our inaugural event!

cure®

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Support for Lung Cancer Heroes™ is made possible by Takeda.

American Lung Association. LUNG FORCE

GO2 FOUNDATION FOR LUNG CANCER

LUNGEVITY Find it. Treat it. Live.

LCFA Lung Cancer Foundation of America

LUNG CANCER RESEARCH FOUNDATION Living. Breathing. Science.™

Proud partners of the Lung Cancer Heroes™ celebration.

Navigating a Pandemic

Experts around the country offer advice about how patients with cancer should handle medical care during the COVID-19 pandemic. By RYAN MCDONALD

PEOPLE WHO HAVE RECENTLY received a cancer diagnosis and are preparing to undergo the necessary treatments, as well as those who have been in remission for any amount of time, constantly face an uphill battle. Whether it's difficult treatments and their side effects or concerns of the disease returning or spreading, the anxiety likely never goes away.

The ever-changing developments during the past couple of months as the coronavirus disease 2019 — a respiratory illness — has spread across the world have surely added to that anxiety.

However, Dr. Harold Burstein, a senior physician at Dana-Farber Cancer Institute in Boston, noted that there are still a lot of unknowns in terms of how the coronavirus, also known as COVID-19, affects individuals with cancer.

"Patients with hematological malignancies, or those getting chemotherapy, bone marrow transplantation, or taking other medicines that lower the white blood count or otherwise depress the immune system should be considered more vulnerable to infection in general," Burstein told *CURE*®. "We don't really know how that affects COVID-19, but it is reasonable to assume that such patients are more susceptible to serious infection. They should take special care to isolate themselves and reduce infection risk."

Dr. Steven Pergam, medical director of the infection prevention program at Seattle Cancer Care Alliance, agrees and says that, although he doesn't want to be alarmist, he wants to be truthful.

"All patients with cancer should be concerned about COVID-19 because they are at higher risk," Pergam says. "I also consider any cancer patient in active treatment — this includes surgery, radiation, chemotherapy and/or immunotherapy — at risk, particularly those who are told by their doctors that they are immunosuppressed because of their treatment. Many patients with cancer also have additional complications, such as diabetes, lung complications or heart disease that might put them at increased risk. The combination of immunosuppression, other health problems and age makes COVID-19 a major concern for many individuals."

CORONAVIRUS GUIDELINES

Patients should abide by all the guidelines being widely distributed through public health channels, which include meticulous handwashing, steering clear of those who are sick, staying home if fever or respiratory symptoms develop and disinfecting high-touch areas, Pergam says. Additionally, he recommended having a few extra months' worth of prescription medications on hand just in case.

MARIDAV & DOTTEDYETI / ADOBE STOCK / ADAPTED BY RAY PELESKO

"Basically, my advice is to take seriously all the precautions advised for everyone but be even more vigilant," says Pergam.

Both Pergam and Burstein heavily stress the importance of adhering to social distancing.

"Given the risk of infection from close contact, it seems prudent that most people should avoid large gatherings, airports and air travel," Burstein says. "There are growing restrictions around the world on air travel. Cruise ships are canceling their voyages. There are going to be more cases. First, we want patients to take care of themselves."

If a patient with cancer starts feeling sick, Pergam recommends that they call their provider team, describe their symptoms and ask whether they should come into the clinic and be seen right away or instead stay home and monitor their symptoms.

"Those who have severe symptoms and are struggling to breathe should call ahead before they go to the ER (emergency room) or clinic and let them know about their symptoms," he says. "As a matter of caution, patients should always call the clinic ahead of time if they develop a cough or experience shortness of breath. It's important to ensure that the care team is prepared to handle the situation with a separate room to avoid placing other patients at risk."

COVID-19'S IMPACT ON CARE

Institutions across the country have implemented precautionary measures. For instance, Dana-Farber has modified its chemotherapy programs where appropriate or is using growth factor support to prevent neutropenia (a deficiency of neutrophils in the blood that can raise the risk of infection) as much as possible in patients, Burstein explains.

"Many patients with cancer are probably at average risk, the same as the general public," Burstein says. "Patients with histories of early-stage colon, breast or prostate cancer; patients who have had surgery and/or radiation but not chemotherapy; or patients who are many years out from treatment and doing well are likely at more or less the typical risk profile. There is no reason to think that the hormonal treatments used in breast and prostate cancer would put patients at jeopardy."

In addition, Dana-Farber has opened discussions as to how to best reduce the number of procedures and tests being done to try and preserve health care resources.

"We are encouraging patients to push off routine follow-up appointments," Burstein says. "We have stopped performing screening mammograms in asymptomatic patients. We expect that there will be staffing challenges in the weeks and months ahead and are planning for that." One way that's happening is through telemedicine. "Health care systems are being stretched to the max," he says. "Hopefully, we can marshal the resources to give good care to everyone still, even if the care looks a bit different."

As for operations at Seattle Cancer Care Alliance, Pergam says there has been constant coordination across its various departments and partner institutions, including Fred Hutchinson Cancer Research Center, University of Washington Medicine and Seattle Children's, on best practices to support the community.

Pergam, who spoke with *CURE*® in mid-March when Seattle was one of the U.S. communities hit hardest by COVID-19, says Seattle Cancer Care Alliance had "a head start in formulating and communicating guidelines and recommendations to our patients." That includes an extensive list of frequently asked questions that are regularly updated, he says.

At that time, Seattle Cancer Care Alliance was operating under normal business hours and continuing to provide care to patients, but asking patients experiencing symptoms such as fever, cough, congestion, sore throat, runny nose or shortness of breath to call a newly established nurse triage line before arriving at the clinic.

"We are not turning away any patients, but we are taking different precautions if they are symptomatic," Pergam says. "We've also made the difficult decision to reschedule non-essential patient visits for the time being out of concern for our patients' health and to make sure that we are well-positioned to care for our patients in active treatment and prepare as the number of COVID-19 cases in our area continues to grow."

> **"We've made the difficult decision to reschedule non-essential patient visits for the time being out of concern for our patients' health."**
>
> — DR. STEVEN PERGAM

Pergam and Burstein agree that patients must be in constant and close communication with their care teams, nurses and oncologists if they are concerned about potential exposure to the virus as well as with questions about what care is essential and what may be safely postponed.

"Having cancer and being concerned about the coronavirus can feel overwhelming," Pergam says. "Patients should be vigilant about their health and not hesitate to reach out to their providers if they're experiencing any symptoms or need support. Finally, patients should turn to reliable sources such as CDC.gov and their local health departments to get up-to-date information on COVID-19, while avoiding websites that promise a quick fix or treatment to protect them from the virus."

For Burstein and his institution, plans are changing daily as the pandemic evolves. He says he hopes that society can learn how to best test, treat and care for those with COVID-19 infections, but in the meantime, he advises patients to "do what you can to keep yourself and your family healthy."

Reversing Course

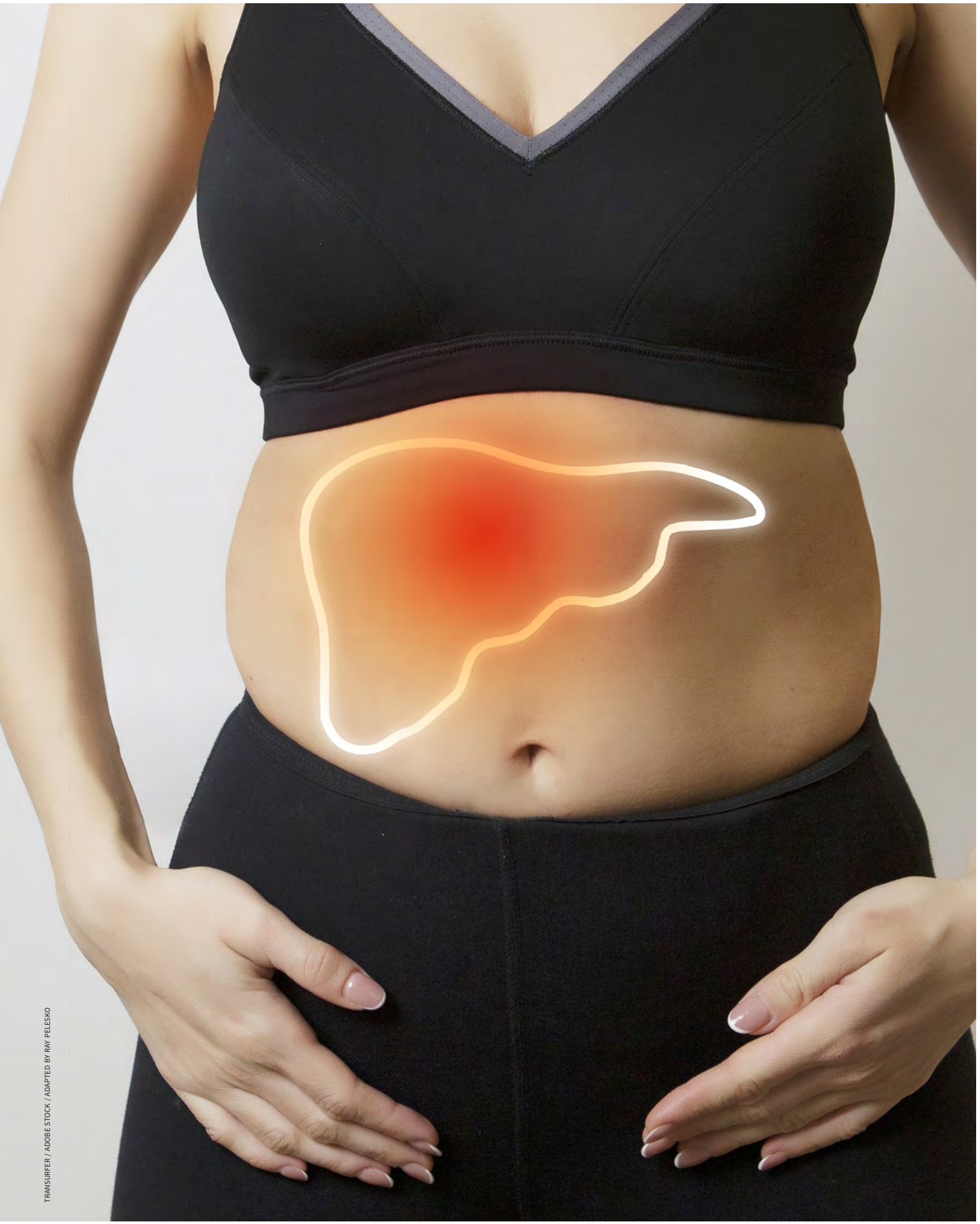
Nonalcoholic fatty liver disease can lead to cancer. Patients can reverse the damage through diet and exercise, but how can they know if they have the common condition?

By HEATHER STRINGER

After giving blood in 1998, Terri Milton received a call from the donor organization alerting her that her liver enzymes were elevated. She saw her doctor, and results from a CT scan and an ultrasound showed that her liver was storing excess fat, which can be a symptom of drinking too much alcohol. But Milton, a Houston resident who was 37 at the time, never imbibed. Her doctor explained that she had nonalcoholic fatty liver disease (NAFLD), a condition that affects about 25% of the U.S. population.

The doctor described the disease as very common and nothing to worry about, and Milton experienced no symptoms at the time. Eight years later, she received a diagnosis of type 2 diabetes. Then, in 2016, she felt pain in her upper right torso and underwent surgery to remove her gallbladder. During the procedure, her surgeon discovered that Milton's liver had a rough texture. He ordered three biopsies, which revealed advanced cirrhosis, or late-stage scarring of the liver. Eight days after the surgery, she was hospitalized because fluid was accumulating in her abdomen, leading to a 40-pound weight gain. She was experiencing ascites, a symptom of cirrhosis and impaired liver function.

Over the years, Milton's untreated liver disease had progressed to nonalcoholic steatohepatitis (NASH), an aggressive form of fatty liver disease that leads to liver inflammation and increases the risk of cirrhosis. In 2018, likely as a result of her progressive liver disease, Milton received the devastating news that she had liver cancer, or hepatocellular carcinoma. To treat the cancer, her hepatologist suggested transarterial chemoembolization, which blocks the blood supply to the tumor and infuses it with chemotherapy. Now her liver shows no signs of cancer, but she still experiences fatigue and frequent infections as a result of cirrhosis. Eventually, she will need a transplant, which is possible in a small minority of patients whose cancer has not spread beyond the liver or only affects certain portions of the organ. »



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"I wish my doctor had explained 20 years ago that NAFLD is reversible," says Milton, 56. "Just losing 10% to 15% of my body weight could have made a significant difference in reversing my fatty liver disease."

The urgent need to spread this message is gaining momentum nationwide because NAFLD is the fastest-rising cause of liver cancer in Western countries.

More than 42,000 people will receive a liver cancer diagnosis this year in the United States, and data suggests that more than 14% of cases will be associated with NAFLD. Alcohol-related cirrhosis is another major risk factor for liver cancer, but a third is becoming less of a threat: hepatitis B and C infections are causing fewer cases of liver cancer due to advances in antiviral therapies that reduced the progression of these conditions to cirrhosis. The risk factors for NAFLD include obesity, type 2 diabetes and high cholesterol, and researchers are still trying to understand why certain people with this disease progress to NASH, cirrhosis and cancer and others do not.

Findings from a new study also showed a 91% higher risk of developing several forms of cancer in people with NAFLD compared with those without the disease, with the highest risk associated with liver, pancreatic, stomach, colon and uterine cancers. The researchers were interested in understanding whether the combination of obesity and NAFLD influenced cancer risk, and they found that people with a high body mass index (BMI) and NAFLD faced double the risk of cancer compared with people who were obese only. "This raises questions about the impact of fatty liver," says study author Dr. Alina Allen, a gastroenterologist at Mayo Clinic in Rochester, Minnesota. "It could be a biomarker for cancer."

Cancer risk may increase in part because excess fat in the liver, known as steatosis, can stimulate inflammatory cytokines, which are proteins important in cell signaling, says Dr. Arthur McCullough, a hepatologist at Cleveland Clinic. "This inflammation creates oxidative stress, which can cause alterations in cell growth and tumor suppressor genes," he explains.

Studies also suggest that the gut microbiome may be linked to NAFLD and NASH. "We know that the nature of the gut bacteria in the intestines can have profound effects on liver function," says Dr. Scott Friedman, dean for therapeutic discovery and chief of the division of liver diseases at Icahn School of Medicine at Mount Sinai in New York City. "Bacteria can produce different products that activate inflammation in the liver, and we are still trying to understand which bacteria and products produce liver injury."

> **"I wish my doctor had explained 20 years ago that NAFLD is reversible. Just losing 10% to 15% of my body weight could have made a significant difference in reversing my fatty liver disease."**
>
> *— TERRI MILTON, patient*

EARLY DETECTION EFFORTS

Although the evidence linking NAFLD to cancer is sobering, researchers like Allen make it clear to the people they treat that fat and even scar tissue in the liver can disappear if patients lose weight, limit sugar and exercise more.

"I think the reversibility of many forms of fatty liver disease needs greater attention in primary care settings, and we will make the biggest gains by educating the public," says Dr. Julia Wattacheril, director of the NAFLD program at NewYork-Presbyterian/Columbia University Irving Medical Center in New York City. "I've found that a significant number of patients lose weight when they are told that they have earlier stages of fatty liver disease that are most likely reversible."

She gathers details about a patient's nutrition and exercise habits and discusses any barriers to implementing lifestyle changes. "Some patients may not have a safe place to walk or experience food insecurity, which is why it's so important to get a good history first," Wattacheril says. If needed, she can refer them to a nutritionist who provides education and guidance in developing a plan to make changes.

Early intervention is also the goal of a project led by Dr. Jessica Hwang, a professor of general internal medicine at The University of Texas MD Anderson Cancer Center in Houston. In August 2019, her team received $2.4 million in funding from the Cancer Prevention & Research Institute of Texas to screen 1,000 patients for liver cancer risk factors including hepatitis B, hepatitis C and alcohol use and metabolic conditions such as obesity and diabetes. The participants are patients at Hope Clinic in Houston, a health center for low-income, uninsured and underinsured people.

The patients will undergo a FibroScan with the ultrasound imaging machine that detects fat, stiffening (fibrosis) and hardening (cirrhosis) of the liver. The researchers will analyze the data to determine which risk factors predict fibrosis and then develop a risk tool to help primary care providers and specialists determine which patients have a high likelihood of developing NAFLD and NASH.

"The future of fatty liver disease hinges upon diagnosis, but right now there are no clear screening recommendations for physicians," Hwang says. "We hope to change that problem with the risk tool that would be developed in our study."

» TONY VILLIOTTI is trying to raise awareness about the silent disease because his NAFLD progressed to NASH, cirrhosis and then, ultimately, liver cancer.

JOE APPEL

A STEALTHY CONDITION

One of the challenges in the effort to reduce liver cancer is the fact that patients with underlying liver disease that can lead to cancer typically experience no symptoms until the disease has progressed. "The earlier stages of liver disease usually get detected only if patients are having a liver blood test or an abdominal imaging test for some other health issue," Friedman says.

Tony Villiotti, 73, is trying to raise awareness about the silent disease because his NAFLD progressed to NASH, cirrhosis and ultimately liver cancer. In 2018, he founded NASH Knowledge, a nonprofit organization that provides information and resources related to liver disease, including a link to a documentary Villiotti produced to share his story. He got a diagnosis of NAFLD in 2005 at the age of 59, but his doctor didn't raise any concerns. "He encouraged me to lose some weight, but I had been told that many times in my life," says Villiotti, who also has type 2 diabetes. "I didn't realize high BMI could increase my risk of developing NASH."

After a routine blood test nine years later, Villiotti was told that his liver enzymes were highly elevated, and an MRI showed that his condition had progressed to cirrhosis. "My first reaction was that cirrhosis was a drinker's disease, so I thought they had the wrong person," says Villiotti, who lives in Pittsburgh. "I felt fine, and my diabetes was under control." He started seeing a hepatologist, who suggested that he consider getting a transplant, but Villiotti resisted the idea because he had heard that people with diabetes had difficulty tolerating the anti-rejection drugs.

In 2017, he was told he had liver cancer. He also started experiencing cirrhosis symptoms, including hepatic encephalopathy, or mental confusion caused by excess toxins in his blood. "I had a foggy brain, so I couldn't drive or read a book, and sometimes I wandered around in the middle of the night," Villiotti says. He was ready to join the national transplant waiting list but unsure whether he would get a donor liver before it was too late. In March 2018, his doctor called with the good news that a liver was available. Villiotti was weak for the first few months after the transplant, but now he has more energy than he had in 15 years.

"I wish I had known more about this disease earlier," he says. "Now I'm trying to help others understand that they need to talk to their doctors about NAFLD."

(CONTINUED ON PAGE 35) »

Jakafi®
ruxolitinib (tablets)

FOR ADULTS WITH INTERMEDIATE OR HIGH-RISK MYELOFIBROSIS

Discover Your Path to Possible

Move your journey in the direction that's right for you

When you're living with a rare disease like intermediate or high-risk myelofibrosis (MF), the path you take to move your treatment journey forward depends on your individual condition as well as the decisions you make with your Healthcare Professional.

Discover what's possible with Jakafi®—the *first prescription medicine approved by the FDA* for adults with intermediate or high-risk MF.

Clinical studies showed that Jakafi helped some patients:

- Reduce spleen size
- Improve the core symptoms of MF, including: night sweats, itching, bone/muscle pain, abdominal discomfort, pain under the left ribs and an early feeling of fullness

Two clinical studies have been conducted with Jakafi and patients with MF. In an additional analysis of one of the trials, **some patients taking Jakafi experienced improvement in their fatigue-related MF symptoms** and in the associated impacts of fatigue on their daily activities (i.e., work, self-care, and exercise).

Fatigue-related MF symptoms included:

Tiredness | Exhaustion | Mental tiredness | Lack of energy

How your MF progresses and how you may respond to Jakafi depends on your specific circumstances. Your individual results may vary. **Please read the Important Safety Information for Jakafi to the right and discuss any questions you have with your Healthcare Professional. Only your Healthcare Professional can determine if Jakafi is right for you.**

Discover what's possible for you.
Talk with your Healthcare Professional about Jakafi today.

If you and your Healthcare Professional decide that Jakafi is right for you, the oncology certified nurses of **IncyteCARES** can help eligible patients* understand their insurance coverage and financial assistance options, as well as provide ongoing education and support resources. **Learn more at IncyteCARES.com**.

Incyte**CARES**: **C**onnecting to **A**ccess, **R**eimbursement, **E**ducation and **S**upport

*Terms and conditions apply.

Important Safety Information

Jakafi can cause serious side effects, including:

Low blood counts: Jakafi® (ruxolitinib) may cause your platelet, red blood cell, or white blood cell counts to be lowered. If you develop bleeding, stop taking Jakafi and call your healthcare provider. Your healthcare provider will perform blood tests to check your blood counts before you start Jakafi and regularly during your treatment. Your healthcare provider may change your dose of Jakafi or stop your treatment based on the results of your blood tests. Tell your healthcare provider right away if you develop or have worsening symptoms such as unusual bleeding, bruising, tiredness, shortness of breath, or a fever.

Infection: You may be at risk for developing a serious infection during treatment with Jakafi. Tell your healthcare provider if you develop any of the following symptoms of infection: chills, nausea, vomiting, aches, weakness, fever, painful skin rash or blisters.

Skin cancers: Some people who take Jakafi have developed certain types of non-melanoma skin cancers. Tell your healthcare provider if you develop any new or changing skin lesions.

Increases in cholesterol: You may have changes in your blood cholesterol levels. Your healthcare provider will do blood tests to check your cholesterol levels during your treatment with Jakafi.

The most common side effects of Jakafi include: for certain types of MF and PV – low platelet or red blood cell counts, bruising, dizziness, and headache; and for acute GVHD – low platelet, red or white blood cell counts, infections, and fluid retention.

These are not all the possible side effects of Jakafi. Ask your pharmacist or healthcare provider for more information. Tell your healthcare provider about any side effect that bothers you or that does not go away.

Before taking Jakafi, tell your healthcare provider about: all the medications, vitamins, and herbal supplements you are taking and all your medical conditions, including if you have an infection, have or had tuberculosis (TB) or have been in close contact with someone who has TB, have or had hepatitis B, have or had liver or kidney problems, are on dialysis, have high cholesterol or triglycerides, had skin cancer, or have any other medical condition. Take Jakafi exactly as your healthcare provider tells you. Do not change your dose or stop taking Jakafi without first talking to your healthcare provider.

Women should not take Jakafi while pregnant or planning to become pregnant. Do not breastfeed during treatment with Jakafi and for 2 weeks after the final dose.

Please see the summary of important information on the next page, which includes a more complete discussion of the risks associated with Jakafi.

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**.

You may also report side effects to Incyte Medical Information at 1-855-463-3463.

Jakafi®
ruxolitinib (tablets)

Summary of Important Information About Jakafi®

Please read this summary carefully and then talk with your healthcare provider about Jakafi (JAK-ah-fye).

No advertisement can provide all the information needed to determine if a drug is right for you or take the place of careful discussions with your healthcare provider. Only your healthcare provider has the training to weigh the risks and benefits of a prescription drug.

What is Jakafi?

Jakafi is a prescription medicine used to treat:

- adults with certain types of myelofibrosis (MF).
- adults with polycythemia vera (PV) who have already taken a medicine called hydroxyurea and it did not work well enough or they could not tolerate it.
- adults and children 12 years of age and older with acute graft versus host disease (GVHD) who have taken corticosteroids and they did not work well enough.

It is not known if Jakafi is safe or effective in children for treatment of myelofibrosis or polycythemia vera.

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

- have an infection.
- have or had tuberculosis (TB), or have been in close contact with someone who has TB.
- have or had hepatitis B.
- have or have had liver problems.
- have or have had kidney problems or are on dialysis. If you are on dialysis, Jakafi should be taken after your dialysis.
- have a high level of fat in your blood (high blood cholesterol or triglycerides).
- have had skin cancer in the past.
- are pregnant or plan to become pregnant. It is not known if Jakafi will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Jakafi passes into your breast milk. Do not breastfeed during treatment with Jakafi and for 2 weeks after the final dose.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Taking Jakafi with certain other medicines may affect how Jakafi works. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take Jakafi?

- Take Jakafi exactly as your healthcare provider tells you.
- Do not change your dose or stop taking Jakafi without first talking to your healthcare provider.
- You can take Jakafi with or without food.
- Jakafi may also be given through certain nasogastric tubes.
  - Tell your healthcare provider if you cannot take Jakafi by mouth. Your healthcare provider will decide if you can take Jakafi through a nasogastric tube.
  - Ask your healthcare provider to give you specific instruction on how to properly take Jakafi through a nasogastric tube.
- If you miss a dose of Jakafi, take your next dose at your regular time. Do not take 2 doses at the same time.
- If you take too much Jakafi call your healthcare provider or go to the nearest hospital emergency room right away.
- You will have regular blood tests during your treatment with Jakafi. Your healthcare provider may change your dose of Jakafi or stop your treatment based on the results of your blood tests.

What are the possible side effects of Jakafi?

Jakafi can cause serious side effects including:

Low blood cell counts. Jakafi may cause low platelet counts (thrombocytopenia), low red blood cell counts (anemia), and low white blood cell counts (neutropenia). If you develop bleeding, stop Jakafi and call your healthcare provider. Your healthcare provider will do a blood test to check your blood cell counts before you start Jakafi and regularly during your treatment with Jakafi. Tell your healthcare provider right away if you develop or have worsening of any of these symptoms:

- unusual bleeding
- bruising
- tiredness
- shortness of breath
- fever

Infection. You may be at risk for developing a serious infection during treatment with Jakafi. Tell your healthcare provider if you develop any of the following symptoms of infection:

- chills
- aches
- fever
- nausea
- vomiting
- weakness
- painful skin rash or blisters

Skin cancers. Some people who take Jakafi have developed certain types of non-melanoma skin cancers. Tell your healthcare provider if you develop any new or changing skin lesions during treatment with Jakafi.

Cholesterol increases. You may have changes in your blood cholesterol levels. Your healthcare provider will do blood tests to check your cholesterol levels during treatment with Jakafi.

The most common side effects of Jakafi in adults with certain types of MF and PV include:

- low platelet counts (thrombocytopenia)
- low red blood cell counts (anemia)
- bruising
- dizziness
- headache

The most common side effects of Jakafi in people with acute graft versus host disease (GVHD) include:

- low red blood cell counts (anemia)
- low platelet counts (thrombocytopenia)
- low white blood cell counts (neutropenia)
- infections
- fluid retention

These are not all the possible side effects of Jakafi.

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 Incyte Corporation at 1-855-463-3463.

The risk information provided here is not comprehensive. To learn more, talk about Jakafi with your healthcare provider or pharmacist. The FDA-approved product labeling can be found at www.jakafi.com.

Manufactured for:
Incyte Corporation, 1801 Augustine Cut-off, Wilmington, DE 19803

Revised: May 2019 PLR-JAK-00021

Incyte

> **"I think the reversibility of many forms of fatty liver disease needs greater attention in primary care settings, and we will make the biggest gains by educating the public. I've found that a significant number of patients lose weight when they are told that they have earlier stages of fatty liver disease that are most likely reversible."**
>
> *— DR. JULIA WATTACHERIL, NewYork-Presbyterian/Columbia University Irving Medical Center*

(CONTINUED FROM PAGE 31)

EMERGING TREATMENTS FOR LIVER DISEASE

Research also suggests that, along with obesity, diabetes and high cholesterol, certain gene variations can increase the chances of developing fatty liver disease. One of the earliest studies that revealed a genetic risk was the 2008 Dallas Heart Study, which included 6,000 residents of Dallas County ages 18 to 65. The researchers found that the PNPLA3 variant was associated with steatosis, inflammation, fibrosis, cirrhosis and even liver cancer. Forty-nine percent of Hispanics in the study had the gene compared with 17% of African Americans and 23% of European Americans, and these findings prompted researchers to explore drugs that target this variant.

"It's important to understand that there may be other ancestry groups with undetected variants that have not yet been studied," Wattacheril says. "Patients who are thin, seemingly fit and do not have diabetes may still be at risk of NAFLD." For example, South Asians and East Asians tend to accumulate fat in the liver at a lower BMI, yet these groups have not been studied systematically, according to Wattacheril. "The need for longitudinal studies in diverse populations is critical," she says.

Standard treatments for liver cancer include surgery, transplant, embolization, radiation and medications such as chemotherapy or targeted drugs.

Doctors may also have a new option for treating patients who have NASH. Recent phase 3 clinical trial results were encouraging for participants who took Ocaliva (obeticholic acid), a drug that reduces inflammation in the liver. Participants took either a placebo or 10 or 25 milligrams of the medication daily for 18 months, and fibrosis improved more frequently in the groups that took the drug. "I'm excited about these results because many trials of other drugs targeting the liver have not worked," McCullough says.

Even patients who progress to liver cancer have more treatment options than ever, says Dr. Ghassan Abou-Alfa, a medical oncologist specializing in liver cancer at Memorial Sloan Kettering Cancer Center in New York City. Tyrosine kinase inhibitors, for example, block proteins that help tumor cells grow or form new blood vessels, and the Food and Drug Administration approved three of these medications to treat liver cancer within the past few years, and another in 2007. In 2017, the agency approved the first immunotherapy treatment for liver cancer, Opdivo (nivolumab); Keytruda (pembrolizumab) got the OK a year later. "Now we are finding that if you combine two forms of treatment, such as immunotherapy with a biologic or two immunotherapies, patients are having good outcomes," Abou-Alfa says.

Although the number of treatments is rising, hepatologists like Dr. Sonali Paul, of The University of Chicago Medicine, are eager to, when possible, prevent liver cancer from developing. That's why education should start early, she says. NAFLD has become the most common cause of chronic liver disease among children and adolescents, which comes as no surprise to Paul, because the obesity epidemic also affects youth. "For now, there is no pill to treat fatty liver, and it is best to talk to patients about the risks before scarring takes effect," she says. "If we explain to kids and adults that their livers are sick, they have a chance to change their eating and exercise habits for the long run."

People with specific health backgrounds should ask their doctors about blood tests to check for elevated liver enzymes, which could indicate nonalcoholic fatty liver disease (NAFLD). This includes individuals with:

- Excess body weight.
- Type 2 diabetes.
- High cholesterol.
- A family history of NAFLD or liver cancer.

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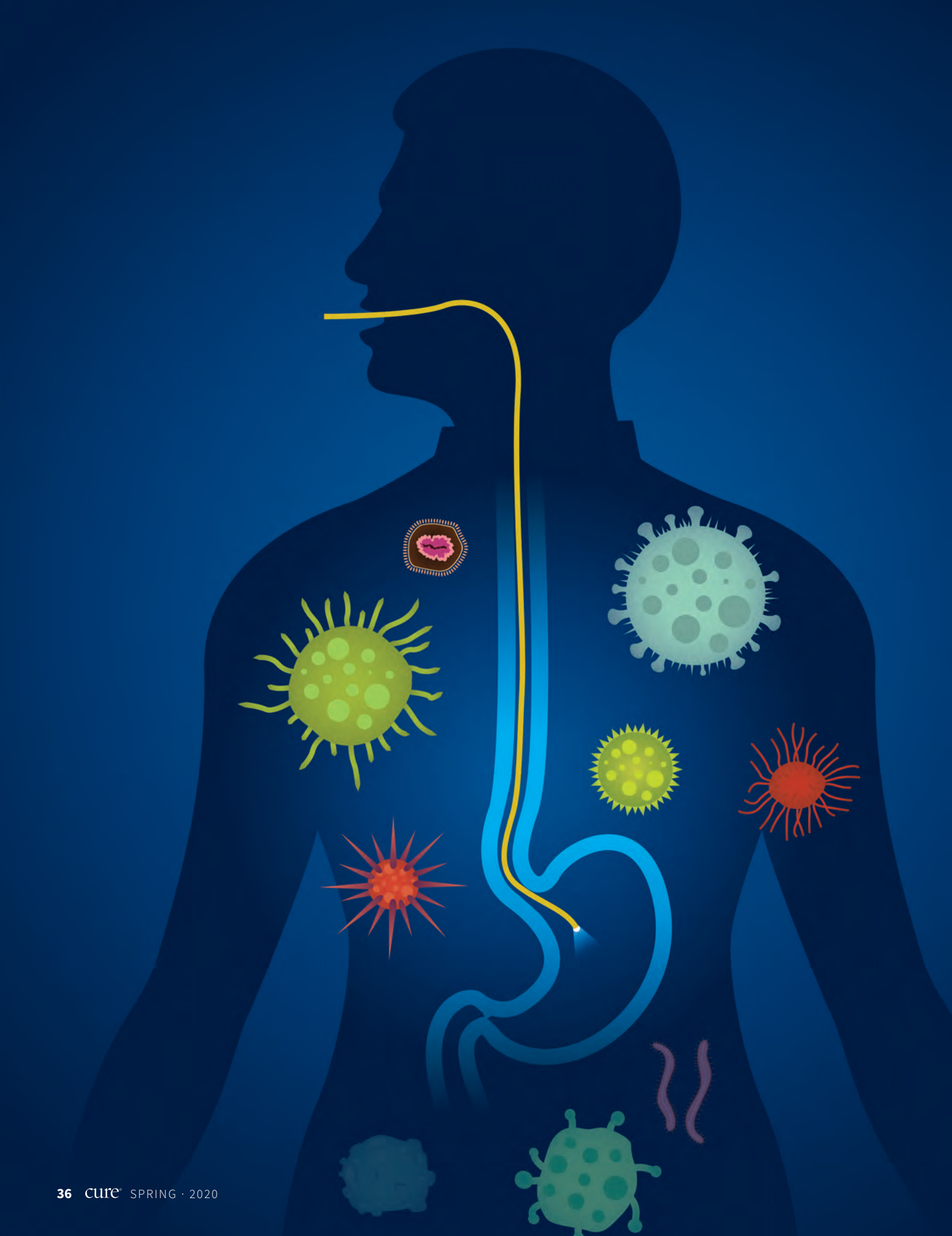

Coming Clean

Bacteria lingering on endoscopes can lead to drug-resistant infections. Before getting scoped, patients should ask how they will be protected.

By DEBORAH ABRAMS KAPLAN

When Bill Warner received a diagnosis of a possible bile duct tumor in December 2012, he underwent an endoscopic retrograde cholangiopancreatography (ERCP). This procedure uses a duodenoscope, a tubular, flexible endoscope with a light, camera and biopsy tools. Doctors were unable to biopsy during several ERCP procedures, and after additional testing, he had surgery in February 2013 to remove and test part of the tumor in his liver. He and his wife, Carla Warner, breathed a sigh of relief when the results were benign. Their relief was short-lived.

Within a few weeks, Bill had a low-grade fever and didn't feel well. Blood tests revealed carbapenem-resistant Enterobacteriaceae (CRE) bacteria. "As the infection became stronger and stronger, he became weaker," Carla says. The former concrete mixer driver lost 60 pounds over the next eight months and experienced weakness, delusions and "unbelievable pain," she says. The only antibiotics that could treat the infection either caused kidney damage or made him vomit. Bill died from the infection in November 2013 at age 55.

CRE are, by definition, bacteria resistant to the carbapenem class of antibiotics, the last-resort treatment for severe infections. Mortality rates for those infected with CRE and related superbugs are up to 50%.

At the time, Carla and her husband's doctors did not know how Bill had acquired the infection. Then, in spring 2015, while getting ready for work, she caught a morning television news segment that linked a child's CRE infection to a duodenoscope used during ERCP. "His story was almost identical to ours. It was deja vu," she says. Friends and family started texting: "Are you watching the news? Isn't this what Bill had?" »

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» CARLA WARNER's husband died from infection after a duodenoscopy. Still, "I will never advocate for someone to go against what their physician recommends they need in treatment," she says.

IMAGEN PORTANOVA SCARBORO

Carla requested her husband's medical records and found the duodenoscope maker and model. According to testimony before the Food and Drug Administration (FDA) and a 2015 *Los Angeles Times* story, the model used, an Olympus TJF-Q180V, was later associated with similar infections. It turned out that duodenoscopes from several manufacturers had designs that did not allow complete cleaning and disinfecting of tiny crevices in the movable elevator mechanism, even when medical centers followed manufacturers' cleaning recommendations.

The FDA, researchers and device manufacturers are looking at updated disinfection or sterilization guidelines to minimize risks going forward, as well as design changes, such as manufacturers making disposable parts or instruments. The strategies vary in popularity and acceptance, with associated cost concerns.

Although CRE infections from duodenoscopes made the biggest news splash, other endoscopes have been associated with infection transmission, too, though to a lesser extent. Recent research in the journal *Chest* showed that bronchoscopes, inserted through the nose or mouth to inspect the lungs, may have a higher risk of transmitting superbugs like CRE or other multidrug-resistant organisms than previously thought. This seems to be connected to procedures used for reprocessing — disinfecting or sterilizing — the scopes. In certain circumstances, current reprocessing guidelines and instructions may not be enough to eliminate the low risk of transmission.

A handful of cases in 2016 linked gastroscopes, which are used to inspect the stomach, to superbug infections, and a few reports suggest that, although also a low risk, improperly reprocessed colonoscopes could expose patients to CRE infections, said Lawrence Muscarella, a consultant in quality improvement and health care safety who holds a doctorate in bioengineering and works with health care organizations and device manufacturers on causes of infection and prevention.

All of this poses a concern for those who have or had cancer and require repeated scoping. It also affects people predisposed to cancer who need ongoing surveillance, patients with unexplained gastrointestinal symptoms and those who simply get routine screening colonoscopies.

About half a million ERCPs are performed in the U.S. each year, and that's just a fraction of 56 million upper

endoscopies. In addition, 19 million colonoscopies are performed, according to an analysis conducted by iData Research.

UNDERSTANDING INFECTION

"Any time there's an invasive procedure, regardless of the type, there's always a risk of bacterial translocation," says Dr. Elizabeth Robilotti, an infectious disease specialist at Memorial Sloan Kettering Cancer Center. There are two ways to get an infection. The first, translocation, occurs when normally present bacteria move from their regular environment to another part of the body. Bacteria could travel from, say, the colon to the prostate during a transrectal prostate biopsy procedure or from the gut or skin into the blood, where there is no barrier to the development of infection. Although the risk exists, it's exceedingly rare in healthy people, she says, and even rare in immunocompromised individuals. The other way to be infected is by acquiring someone else's bacteria from an improperly reprocessed endoscope.

Remaining CRE bacteria are not inherently resistant to endoscopic cleaning, Robilotti says; rather, the cleaning process does not always allow full access to the instrument. "Cleaning of the duodenoscope is a recognized challenge," she says.

The bronchoscope's design is less complex, but if the device is not properly serviced, it can pose a risk of transmitting CRE even when cleaned according to manufacturers' instructions, Muscarella says. A study he co-authored found that damage and inadequate maintenance were risk factors for bronchoscopes exposing patients to bacteria. Bacteria can be deposited in tiny cracks and tears, out of reach of cleaning processes, and grow in a resistant biofilm. The risk is low, and exposure does not guarantee infection, Muscarella adds.

The bacteria causing the CRE outbreaks were likely present in health care facilities before becoming drug-resistant, so infected patients received successful antibiotic treatment or recovered on their own. As recently as 20 years ago, bacteria like Klebsiella and E. coli, which today may be considered CRE, were susceptible to several types of antibiotics, according to Muscarella. "Transmissions may have been happening, but in the past, they were eradicated by the antibiotics or the patient's own immune system," he says.

The wide use of antibiotics and the constant development of new ones to address resistance has led to a long list of "superbugs."

Improving Safety

The FDA, researchers and device manufacturers are looking at updated disinfection or sterilization guidelines to minimize risks going forward, as well as design changes, such as manufacturers making disposable parts or instruments.

REDUCING THE RATE

The chances of passing along bacteria on endoscopes can be reduced in several ways: repeating the disinfection, implementing sterilization or using partially or completely disposable endoscopes.

Disinfection: Flexible endoscopes are considered semicritical devices that normally come in contact with mucous membranes but not blood or otherwise sterile tissue. Although the FDA prefers that they be sterilized, it requires only disinfection. However, in spite of health care facilities following manufacturers' directions for disinfecting flexible endoscopes, including duodenoscopes, the FDA reported in a 2018 study that up to 3% of duodenoscopes tested were considered reprocessing failures after being found positive for high-concern organisms, and up to 3% tested positive for low-concern organisms. The agency had expected a total failure rate of less than 0.4%. After cleaning with brushes and a detergent, high-level disinfection includes immersing an instrument in a liquid chemical germicide for the FDA-recommended amount of time, at the right concentration and temperature. The agency suggests repeating the process to ensure that it is done properly.

Sterilization: Some health care organizations are switching their protocol to sterilizing, instead of disinfecting, flexible endoscopes. When it comes to duodenoscopes, the FDA recommends sterilization over high-level disinfection when possible and practical, though availability of this method is limited.

Sterilization can be difficult because the heat can damage components. One technique uses pressurized steam, but for more delicate instruments, organizations can use a low-temperature liquid chemical processing system, a sporicidal technology. Ethylene oxide gas is another sterilization option.

In 2018, North Dakota's Altru Health System was the first to sterilize the duodenoscope. "I'm encouraged to know that there are some hospitals out there that are using sterilization (for these instruments)," Carla Warner says. "If tested, these should not grow any type of bacteria or show any signs of leftover biomatter."

Some hospitals may be reluctant to sterilize bronchoscopes or rigid endoscopes, Muscarella says, especially if the central reprocessing area is in the basement, requiring more careful tracking and monitoring of the instruments. When scopes are reprocessed closer to procedure rooms, they spend less time out of commission for cleaning, so the hospital can keep a lower inventory of them, he says. »

Using sterilized equipment, even if not mandated by the FDA, can still be cost-effective, according to Carla. If hospitals realize that sterilization is a deciding factor for patients, they can highlight the practice in their advertising, she says.

Disposable Parts: To give duodenoscopes a safety update, the FDA recommends that health care systems transition to instruments with disposable components, such as end caps, or to fully disposable devices, allowing for more effective reprocessing or eliminating the need for it. Currently, five manufacturers offer disposable end caps, and single-use duodenoscopes are entering the market. The FDA approved a Boston Scientific model in December 2019. Disposable bronchoscopes are available, Muscarella says, but not widely used in the U.S.

One problem with disposable devices is cost and who pays it. The Boston Scientific single-use duodenoscope is expected to cost $3,000, and insurance coverage is not yet guaranteed, according to *The New York Times*. Hospitals already own reusable scopes at upward of $40,000 each. "(If insurance doesn't cover a disposable scope,) the burden could shift onto the patient to decide whether to purchase it themselves, and that doesn't typically happen in medicine," Muscarella says. If hospitals can't negotiate the price, disposable instruments could be too expensive, he says.

Other concerns with disposable scopes include reuse for economic reasons. Inexpensive disposable equipment is discarded, Muscarella says, but there could be a financial incentive to reuse costly single-use devices, which is counter to their purpose. Also, disposable scopes would not prevent infections caused by bacteria's movement from one part of the body to another. "The infection rate is not entirely eliminated by single-use endoscopes, but clearly, it would prevent patient-to-patient transmission," Muscarella says.

3 QUESTIONS TO ASK YOUR DOCTOR

- ❑ WHAT IS THE RATE of infection after endoscopy (or duodenoscopy, colonoscopy, gastroscopy or bronchoscopy) at this facility and, specifically, in your patients?
- ❑ HOW DOES THIS FACILITY clean its duodenoscopes or endoscopes, by disinfection or sterilization?
- ❑ DOES THIS FACILITY USE disposable endoscopes or parts, and, if so, can I be assured that these are never reused?

ASSESSING THE RISK

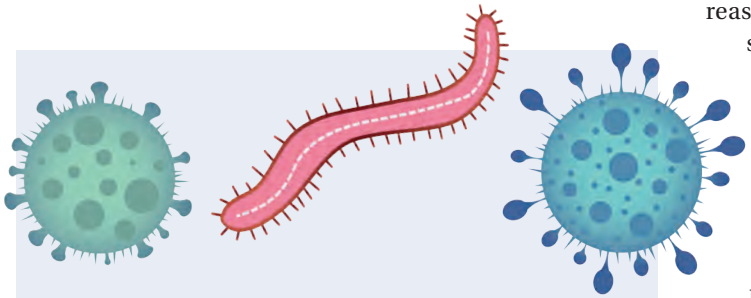
Patients don't always know what to ask their doctors regarding recommended endoscopies.

When Carla had to schedule a spinal fusion after her husband died, she asked the doctor to explain each step from beginning to end, telling her how every item in the operating room would be reprocessed, which ones would have been sterilized, and which would be new or unused. "He was a little taken aback by the question, and it was something he had not discussed with a lot of patients," she says. She also asked why he chose to work at that hospital. When he said it was because of lower infection rates, she was satisfied. After she shared her reasons for asking such detailed questions, the doctor said, "I should be having this discussion with all my patients."

Carla recommends also asking about the equipment and model numbers, steps taken to clean the endoscopes, whether the scopes are sterilized or disinfected, and whether they are inspected with a borescope, a small instrument that helps detect tears and defects that can harbor bacteria. Not all physicians understand how reprocessing works because they are involved only with the procedure, but Carla encourages physicians to visit the central reprocessing area to learn. "The first red flag for me is if a physician can't tell me the steps they take to make sure the patient is safe," she says. If the medical staff, including the receptionist, do not take concerns seriously and provide answers, patients should find a new doctor or facility, she says.

Muscarella agrees that patients have some control and power because they can decide where to have procedures done. They can tell doctors or clinics that they plan to call

(CONTINUED ON PAGE 43) »



ANANALINE / ADOBE STOCK

Two ways to get an infection

Translocation occurs when bacteria that are normally present move from their regular environment to another part of the body. Bacteria could travel from the colon to the prostate during a transrectal prostate biopsy or from the gut or skin into the blood, causing an infection. Although the risk exists, it's rare in both healthy and immunocompromised people. Alternatively, a patient can get infected by acquiring someone else's bacteria from an improperly reprocessed endoscope.

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 trouble breathing or shortness of breath, cough with or without mucus, and chest pain.

Before you take IBRANCE, tell your doctor if you:

- have fever, chills, or any other signs or symptoms of infection.
- have liver or kidney problems.
- have any other medical conditions.
- 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.
  - **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.

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

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 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 if you have any side effect that bothers you or does not go away.

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.

IBRANCE® palbociclib 125 mg capsules

IBRANCE®
palbociclib | 125 mg capsules

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 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:

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

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 you take IBRANCE, tell your healthcare provider if you:

- have fever, chills, or any other signs or symptoms of infection.
- have liver or kidney problems.
- have any other medical conditions.
- 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.
  - **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.

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

How should I take IBRANCE?

- Take IBRANCE exactly as your healthcare provider tells you.
- Take IBRANCE with food.
- IBRANCE should be taken at about the same time each day.
- Swallow IBRANCE capsules whole. Do not chew, crush or open IBRANCE capsules before swallowing them.
- Do not take any IBRANCE capsules 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?"

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.

Tell your healthcare 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 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-0723-8.0, Rev. 9/2019.

(CONTINUED FROM PAGE 40)

several facilities and choose the one that best meets their requirements. For instance, patients could look for a facility with a robust safety program, which could include using a certain type of endoscope or sterilizing instruments instead of disinfecting them.

These conversations are one positive result of the infection outbreaks, says Andrea Dwyer, director of the Colorado Colorectal Screening Program and adviser to the patient advocacy group Fight Colorectal Cancer. In addition to asking about procedure risk, "it's OK to ask how many procedures the doctor does per year, the volume — and, if something happens, how to follow up and who to follow up with," she says.

DENELLE SURANSKI undergoes a colonoscopy and endoscopy each year to check for Barrett's esophagus, a change in the lining of the organ that can lead to cancer. She advises that patients talking with their doctors about these procedures bring a loved one along to advocate, take notes and even record the conversation.

JOE APPEL

RECOGNIZING THE SIGNS

Infection following an endoscopic procedure could occur within 24 hours or longer, says Robilotti. During diagnosis, doctors consider the severity of the illness and may test for infection in multiple sites, such as blood, urine and possibly bile, if a bile drain is involved. "We have to put the whole clinical picture together to establish if certain signs or symptoms are from an infection," he says, and, if so, where it arose.

Determining causality is important. If a patient develops an infection but does not inform the doctor who performed the endoscopy or tell the doctor treating the infection about prior procedures, the doctors may not connect the dots. One remedy is for the doctor's office or clinic to contact patients after the procedure and ask if they have any infection symptoms. "The FDA is reporting reduced infection rates," Muscarella says, "but if the medical facility doesn't track all infections, then the risk could be underreported."

The risk of getting an infection from a diagnostic procedure is real. But when a doctor recommends an endoscopy, it's important to consider the risk versus benefit, Dwyer says. Colonoscopies, for example, carry a small risk of complications but a high rate of effectiveness for identifying potentially cancerous polyps.

In spite of her husband's death from the CRE infection, "I will never advocate for someone to go against what their physician recommends they need in treatment," Carla says. What if her own doctor recommended an ERCP? "I wouldn't say I would not do the procedure," she says. "I'd have to do my research really well. If I couldn't find a satisfactory local provider, I'd go somewhere else that has technologies available for true sterilization."

Transforming Reality

More cancer centers are introducing virtual reality headsets, which can help relieve anxiety and pain and educate patients about their treatments.

By KATHERINE MALMO

Given the choice of being on a beach or in an oncology ward, most people would choose the beach. So, if there was a technology that allowed you to take a mini-vacation while you waited for your appointment or received your treatment, you'd want to use it, right?

There is, and you can. Heather Bucalos of upstate New York learned the value of virtual reality in January 2020 when she resided in a hospital room at Roswell Park Cancer Institute in Buffalo for four weeks after a stem cell transplant to treat her recurrence of Hodgkin lymphoma.

"I felt closed in, kind of like a zoo animal," Bucalos says. "My room was small and only had one window and the only interesting thing I could see was a multicolored house between the buildings in the distance. When I felt well enough, I used the headset and chose an application that is like going to a beach. I could see the sunshine and it was like being outside."

With virtual reality, users look into a headset that includes a computer providing real-time animation which, in some cases, moves or changes based on the position of the head. Cynthia Waddington, a nurse navigator and clinical director of the cancer program at Christiana Care — which serves all of Delaware and parts of Pennsylvania, Maryland and New Jersey — defines it as "a visual and auditory immersion into an environment that looks and feels real." »

HEATHER ESPOSITO

« HEATHER BUCALOS used virtual reality to take a simulated trip to the beach while she was quarantined after a stem cell transplant to treat Hodgkin lymphoma.

Kim Vernick of Philadelphia describes her virtual reality experience at the Roberts Proton Therapy Center at Penn Medicine, in Philadelphia, as "Zen." Vernick, who received a diagnosis of pancreatic cancer in 2010 and esophageal cancer in 2019, says that it transported her to "a happy place where I was sitting in an Adirondack chair by the lake watching the sunrise with geese flying over."

Other patients have benefited from the technology, too. An aggregate analysis of studies that examined virtual reality use for symptom management in cancer care found statistically significant effects on reducing anxiety, depression and pain.

Virtual reality's value isn't limited to acute patient care. It can help with education — showing patients where their tumor is located and how treatment will work, as well as training medical practitioners how to treat certain conditions and operate equipment.

IMPROVING PATIENT COMFORT

Sitting in a waiting room and counting the long minutes until an appointment can be stressful enough for people with cancer and their families.

"Add on TV, chatter and overhead announcements and it can become even more stressful," says Dr. William Levin, an associate professor of clinical radiation oncology at Penn Medicine in Philadelphia. "Utilizing this kind of immersive experience can take you out of that reality and give you time to regroup. It can make you feel better than you did when you walked in."

Over the years, Levin has taught many patients about mindfulness meditation and seen it help slow their minds and calm their breathing. Still, some have trouble getting their brains to stop racing. He says technology can help patients over that hurdle, which is why Penn now offers a virtual reality mindfulness experience in its radiation oncology waiting area.

"The goal of using virtual reality is to combine deep breathing and being in the moment with an immersive experience," Levin says. "Rather than closing your eyes and telling someone to think of nothing, we created a placid lake scene at sunrise. And we have the voice of a mindfulness practitioner pointing out some of the salient features of the scene."

Matthew Stoudt, the CEO and cofounder of AppliedVR, a Los Angeles company that develops therapeutic virtual reality content, agrees that some people find it hard to meditate. "A lot of people say, 'Yeah, I understand the benefits of meditation, but I can't do it.' But you put them in a virtual reality headset that blocks everything else out and they can't help but do it."

Waddington, who oversees Christiana Care's cancer center and infusion sites, says those facilities offer six videos that provide a "positive distraction" without taxing the patient's energy.

A pilot study of the program found that all the participants enjoyed the experience and would do it again — with 98% saying it was relaxing and 64% saying it reduced their anxiety and boredom.

"Every patient comes in highly anxious because they just don't know what to expect," Waddington says. "When we're anxious, it's hard to focus and it's hard to retain information."

COURTESY OF KIM VERNICK

> **"My room was small and only had one window and the only interesting thing I could see was a multicolored house between the buildings in the distance. When I felt well enough, I used the headset and chose an application that is like going to a beach. I could see the sunshine and it was like being outside."**
>
> *— HEATHER BUCALOS, cancer survivor*

COURTESY OF HEATHER BUCALOS

HEATHER BUCALOS used a virtual reality headset in her hospital room for a positive distraction as she recovered from a stem cell transplant.

Pain is just as serious a problem for many patients with cancer, and virtual reality may be able to help with that, too, not only by making patients more comfortable but also by reducing their reliance on opioids at a time when use of those drugs has reached epidemic proportions in the United States.

Ten years ago, Diane Jooris saw the technology's potential while working at The University of Texas MD Anderson Cancer Center in Houston. Back then, Jooris sat with patients during breast cancer surgeries and provided clinical hypnosis, a psychological intervention that took the place of IV sedation.

These procedures were successful, but Jooris was limited by the number of therapists and the languages they spoke. She decided to start a company, Oncomfort, which would use virtual reality to make clinical hypnosis more accessible. Now, patients can choose from three sessions that last from two to 60 minutes and are offered in 12 languages. The aim is to reduce both anxiety and pain.

"Through these sessions, we bring the patient to a dissociated state," Jooris says. "We have some patients who are snoring on the table during surgery. They're in a state of modified consciousness, which allows them to be more comfortable while less aware of what is happening in the room and with their body. Often, they are so relaxed they don't even feel when the doctor injects the local anesthesia."

It's proven to work. One 2019 study found that breast cancer patients randomized to receive a virtual reality experience in addition to morphine reported significant reduction in pain and anxiety compared with those who got morphine alone.

Additional studies have shown that virtual reality technology can help with other side effects of therapy.

Some treatments leave patients with low vision, an impairment that can't be corrected medically, surgically or with conventional glasses, and virtual reality may be a way for them to see more clearly. In a study conducted at Johns Hopkins University and published in February 2019 in T*ranslational Vision Science Technology,* virtual reality devices improved vision in patients with macular degeneration, boosting it, on average, from 20/400 to 20/30 while the headsets were in use. Virtual reality is already in use at more than 100 U.S. ophthalmology and optometry centers, according to a 2019 article in the *ASCO Post.*

There is also evidence that virtual reality can help improve the symptoms of fatigue, another common side effect of cancer treatment.

PROVIDING VIRTUAL EDUCATION

Once Penn Medicine started working with virtual reality, Levin said, leaders there realized the technology could help solve another problem — communicating complicated information.

Stressed-out patients have a hard time understanding and remembering material that is conveyed verbally, so Levin's team created an application to explain particular disease processes and treatments.

"For instance, if I'm speaking to someone with lung cancer," Levin says, "they'll be able to visualize the lungs and the location of the tumor and how it impacts normal functioning. The other thing we'll be able to do is provide a visual of how the radiation treats that tumor and the potential side effects from the treatment itself."

The team at Christiana Care saw the opportunity for patient education about a different part of the treatment »

process. Waddington says team members decided to address a common question: "Why do I have to wait so long?"

"We filmed what happens in the pharmacy," Waddington says. "It showed how the pharmacists are gowned and gloved and how they take orders, double check what we've already double checked, and make the medication in a sterile environment."

Education via virtual reality is available to children, too. Oncomfort offers four applications for youngsters, including an interactive game that allows players to shoot and destroy cancer cells. It helps doctors explain what chemotherapy does in words that don't create scary images or more fears.

"We use metaphors, specific verbiage and narrative to teach the kids about their treatment," Jooris says. "It gives them the feeling they play an active part in their therapy while using techniques that completely dissociate them from the perception of the body so the nurse can connect the port and get chemotherapy running."

At Penn Medicine, Fern Nibauer-Cohen, director of patient engagement in the department of radiation oncology, says that virtual reality technology is part of the facility's global training and education program for radiation oncologists, therapists and medical physicists.

When Penn decided to build a proton therapy center, its radiation therapists, oncologists, physicists and dosimetrists came for two- to four-week in-person training programs. The curriculum was supplemented with virtual reality modules covering everything from how to position a patient on the table through delivery of treatment.

Levin points out that this technology also helps students understand human anatomy. "It's important for trainees to learn three-dimensional thinking," Levin says. "This can take a decade or more to develop, and we think that we can reduce the learning curve."

> **"The goal of using virtual reality is to combine deep breathing and being in the moment with an immersive experience. Rather than closing your eyes and telling someone to think of nothing, we created a placid lake scene at sunrise. And we have the voice of a mindfulness practitioner pointing out some of the salient features of the scene."**
>
> *— DR. WILLIAM LEVIN, associate professor of clinical radiation oncology, Penn Medicine, Philadelphia*

VIRTUAL REALITY IN PRACTICE

Since her treatment, Bucalos has become an advocate for virtual reality and often tells her doctors about it. She hopes more patients will be able to realize the benefits soon.

Vernick is just as enthusiastic and now volunteers at Penn Medicine, where she offers a headset to anyone in the waiting room. "It should really be offered to all patients and caregivers," she says, "because it takes away anxiety and angst and really puts you at ease."

Levin envisions virtual reality headsets being used all over the medical center. "In the exam or consult room, it could be set up by anyone from a nurse to a volunteer to a nurse navigator or a student or a res-ident. It shouldn't be labor-intensive or complicated," he says.

But virtual reality isn't right for everyone. Waddington says it isn't recommended for patients who struggle with vertigo, dizziness or motion sickness.

Jooris says it isn't appropriate for people who suffer from acute psychiatric disorders such as schizophrenia or have a fragmented vision of reality. It's also not good for people who are very anxious and want to know everything that's happening at all times, which Jooris says applies to about 2% to 3% of patients.

Levin says the devices themselves do not emit radiation, and that the only worry is that the headsets may be damaged by scattered radiation in certain treatment rooms.

"The nice thing is that there are no irreversible side effects or significant toxicities," Levin says. "If someone says they aren't comfortable, it's easy to just take off the headset."

So how can the health care system get more virtual reality headsets to patients?

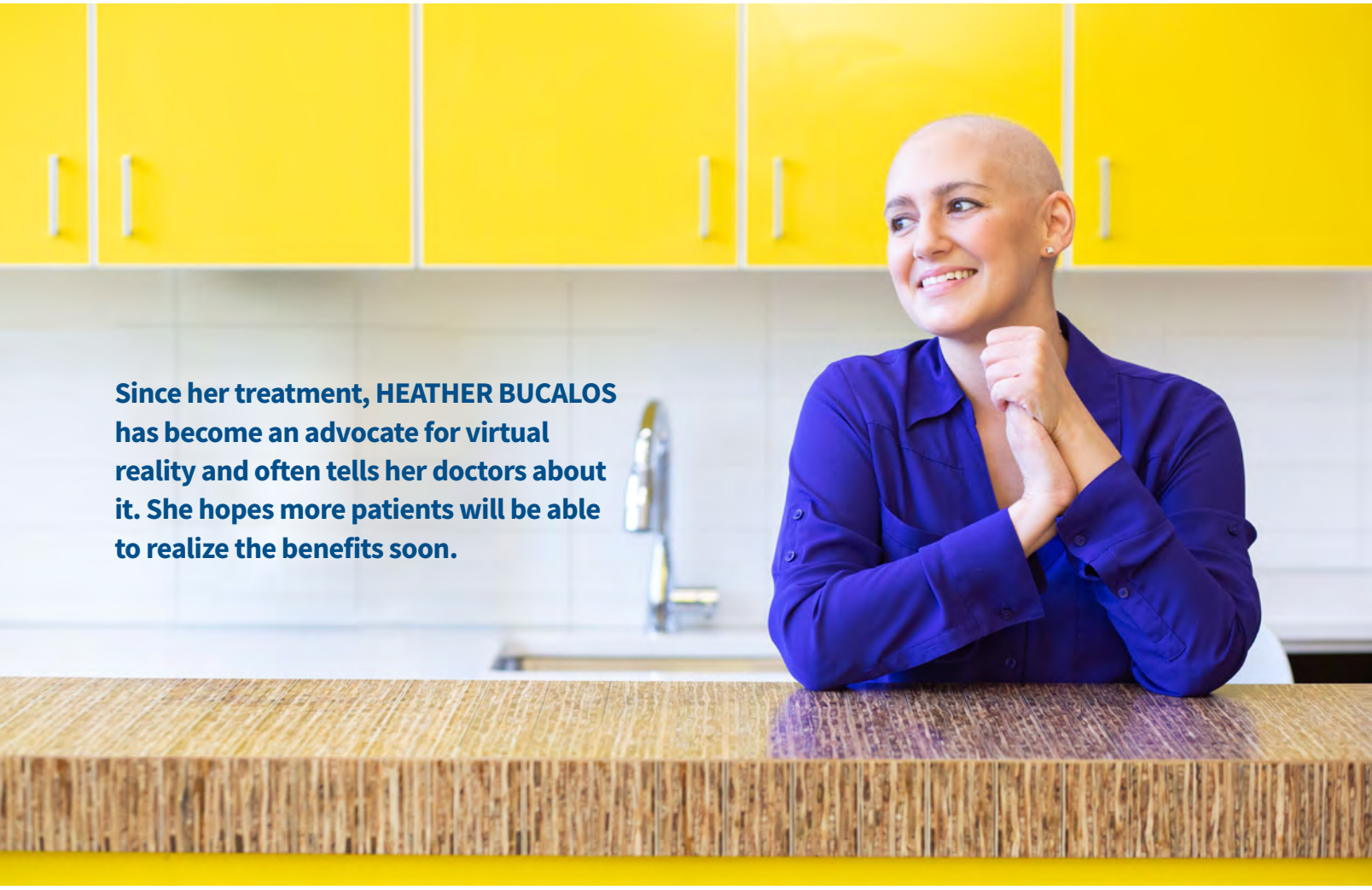
Stoudt says that his company's systems are used in over 100 medical and hospital systems, including Northwestern Medicine in Chicago, Cedars Sinai in Los Angeles and Boston Children's Hospital, as well as in people's homes. Right now, the hospitals are focused on conducting studies that demonstrate the technology's value — not only to drive adoption, but also to validate requests for FDA approval for certain therapeutic uses.

In most cases, the hospitals pay for the headsets, which cost between $500 and $2,000 apiece, Stoudt says. A 2018 survey of hospitals showed that those that invested in the technology saved $5.39 per patient across their entire treatment population due to factors including shorter stays and less opioid use. That broke down to a savings of $98.49 per patient eligible and willing to use virtual reality therapy (20%) and a loss of $16.90 for every patient not eligible or not willing to try it (80%).

LOOKING AHEAD

Stoudt would like to see clinical standards of care change to include virtual reality headsets as a part of routine treatment for patients with cancer.

To help build a body of evidence, AppliedVR has partnered with the National Cancer Institute to launch a feasibility



Since her treatment, HEATHER BUCALOS has become an advocate for virtual reality and often tells her doctors about it. She hopes more patients will be able to realize the benefits soon.

HEATHER ESPOSITO

study to investigate the efficacy of using virtual reality to treat anxiety patients with cancer.

About 2,000 patients are enrolled in various clinical trials testing virtual reality around the world, according to Jooris.

She describes one study: "One group had prostate resection surgery under intravenous sedation plus local anesthesia. The other had digital sedation, which is clinical hypnosis with virtual reality, and spinal-block anesthesia. Digital sedation was superior to IV sedation." Both the patients and the anesthesiologists rated virtual reality higher than IV sedation because it avoided the respiratory side effects of the drug midazolam.

Stoudt believes the future of virtual reality ultimately will involve reaching America's 50 million individuals with chronic pain. He envisions the technology being covered by public and private health insurers and the headsets being found in every home, allowing physicians to prescribe a variety of therapies delivered through the devices.

"Then it's not simply a one-off intervention patients use in a moment of crisis or pain, but a tool to help them learn to live with their pain on a daily basis," Stoudt says. "It's about improving the quality of patients' lives by addressing the pain, but also by teaching them coping skills so they can apply those skills in their daily lives outside of the headset."

Stoudt is also excited about the possibility of using biofeedback to deliver more precise virtual reality content. AppliedVR has developed a system that can capture the patient's breath and use that information to drive the virtual reality experience.

As wearable biofeedback devices that monitor factors such as heart rate variability and alpha and beta brain waves get smaller, they can be incorporated into the headsets to create all-in-one devices.

"As you get this data back, you can see the impact the content is making on the patient," Stoudt says. "Then the challenge becomes how we optimize the content on the fly. How do we deliver the right piece of content to the right patient at the right time? Then you can adjust content in real time, and that gets super exciting."

Finding Meaning

One survivor makes the most of time in the infusion chair, creating beaded jewelry and helping herself and others to heal. By BETH FAND INCOLLINGO

WHEN LINDA DZIOBEK WAS lost in chemotherapy-induced brain fog and facing neuropathy that made every movement of her hands a struggle, her love of beading helped heal her. Now the jewelry she makes while sitting in the infusion chair does the same for those around her.

After every treatment at Women & Infants Hospital in Providence, Rhode Island, the 15-year survivor of ovarian cancer adds sparkling creations to an "earring tree" placed there by volunteers. Patients are free to choose from and keep the jewelry that hangs there.

Dziobek also gives away jewelry when she's treated at Dana-Farber Cancer Institute in Boston. She has made rings for patients whose swollen fingers are too large for standard sizes and instructed others in bracelet-making techniques.

"It makes people feel good, and doing something productive while I'm here gives me purpose," Dziobek, a retired nurse, says. "A couple of months ago, a woman told me that my blue earrings were the only ones she could find that matched her dress for her daughter's wedding. She was in the middle of her treatment and had no hair, but she had a beautiful scarf with the earrings to match her dress. It really helped, and she couldn't thank me enough. I had tears in my eyes; it was like a connection was made. You don't realize the impact you have when you do something like this."

LINDA DZIOBEK poses with jewelry she made, including the dragonfly bracelet that helped her through chemotherapy.

IMAGES COURTESY OF LINDA DZIOBEK

Dziobek picked up her hobby in 2010 and was taking classes at a bead store when she experienced a recurrence of her cancer, first diagnosed in 2004. After radiation, she joined a clinical trial of intraperitoneal chemotherapy plus

What's in Your Chemotherapy Travel Kit?

We asked *CURE*® readers what they bring to chemotherapy infusions to make the experience more comfortable. Here's what they told us.

"After I finished all my treatments, I started making cancer care goody bags for all those at the infusion center. In the bags were bandannas, lip balm, hard candy, hand sanitizer, hand lotion, a notepad and pen, and other items. Many of my friends wanted to help, so the cost to me was minimal. I make up the bags twice a year and take them to a local infusion center."

"Books, my prescribed Ativan (lorazepam), slip-on socks, a water bottle and snacks."

"A blanket, water, cheese crackers, goldfish crackers, a neck pillow and my bag of good juju."

"My own pillows."

"A journal."

the targeted drug Velcade (bortezomib), but complications arose after one treatment, and she needed surgery. That was followed by six months of intravenous chemotherapy.

While recovering, Dziobek periodically reflected on a cuff bracelet she'd begun before treatment. Although she was not sure if she would be able to follow the directions or do the intricate beading work due to her brain fog and neuropathy, she returned to her project. It took her three months to finish.

"It helped me to focus, and I started to come out of the fog of chemo brain and my hands felt better," she recalls. "I felt like I was creating new pathways in my brain by focusing and figuring out color palette, placement of beads and measurements."

Dziobek was still part of the beading group, and her fellow members decided to help other patients enjoy a similar experience. They developed the Plum Blossom Project, bringing beaders to cancer centers to instruct patients in making bracelets. After completing a piece, each patient was gifted a beaded necklace made by volunteers. Dziobek's husband, Joe, helped raise funds for the project by selling CDs of two songs he wrote and performed, one about Plum Blossom and the other about the caregiver's journey (youtube.com/watch?v=cd3DotLtwrE).

The group recently stopped working with patients who have cancer, but a few years ago Dziobek invited members to give a class for the gynecologic cancers support group at Women & Infants, where she goes twice a week for magnesium infusions to treat a long-term side effect of chemotherapy.

Dziobek beads on a small tabletop during infusions.

It made a difference for participants, especially one woman and her daughter.

"The mom, who had been in treatment all day, wanted to take the class, but the daughter was burnt out and wanted to get home," Dziobek recalls. "In the 15 to 20 minutes that they were selecting beads and putting their bracelets together, we could see the daughter's shoulders and facial muscles relax, and the conversation changed. By the time they left, rather than a stressed-out caregiver taking care of a relative, it was now a mother-daughter relationship. They were excited about the bracelets they'd made, and their whole demeanor changed."

Their story is a reminder, Dziobek says, of the importance of finding something enjoyable to do during cancer treatment, an idea she keeps front of mind as she prepares to enter a clinical trial at Dana-Farber.

"Treatment really wears you down and the toll is cumulative, but if there's something you can do to help yourself at least feel a little better, do it," suggests Dziobek, who also finds meaning by volunteering with the Partnership to Reduce Cancer in Rhode Island, a community advisory group that works with the state health department's comprehensive cancer control program. The partnership holds an annual June cancer summit, for which Dziobek is planning a survivor-led presentation to show participants how to make meditation bracelets and emphasize the health benefits of beading.

"I firmly believe that we have to have some purpose each day and something to look forward to, no matter how we feel," she says. "It continues to give you hope and keeps you moving forward."

"I'm going to start bringing a comfy throw. I find myself getting colder and colder. I also bring hard candy."

"Beanie for the naked head! Ice socks and gloves for the neuropathy. IPad with lots of reading and music and headphones, as well as my telephone."

"My best friend! I also bring a bag of various goodies packed by my daughter after she researched what I might need."

"Prayer shawl, comfy warm hat and warm blanket."

"Since my clinic provided the things I needed, all I brought was a positive attitude to share with my health care team and other patients. I try to be a ray of hope to my caretakers, because they say they like to see positive people who give hope to others. I've tried to do nice things for others every day since I was diagnosed."

An Off-the-Shelf Solution

CAR-NK cell immunotherapy elicits good responses but no serious side effects in patients with CD19-positive blood cancers. By KRISTIE L. KAHL

PATIENTS WITH RECURRENT OR treatment-resistant blood cancers driven by the protein CD19 experienced responses when given an immunotherapy made from umbilical cord blood — and did not develop major side effects, according to findings from a small, phase 1/2 trial published in the *New England Journal of Medicine*.

The treatment, which demonstrated effectiveness in two kinds of lymphoid malignancies, is known as chimeric antigen receptor (CAR)-natural killer (NK) cell therapy, which homes in on the CD19 protein expressed on the surface of B cell lymphocytes. CAR-NK cells, which are a type of immune cell, are taken from an unrelated healthy donor, manufactured as part of a medicine and stored for off-the-shelf use. The appeal of this treatment option is that it is ready for immediate use, whereas other CAR therapies involve a patient's own genetically modified T cells and take much longer to prepare, according to a press release issued by The University of Texas MD Anderson Cancer Center in Houston. The multiweek process involves collecting T cells from a patient, engineering them to fight cancer, multiplying the cells and then infusing them back into the patient.

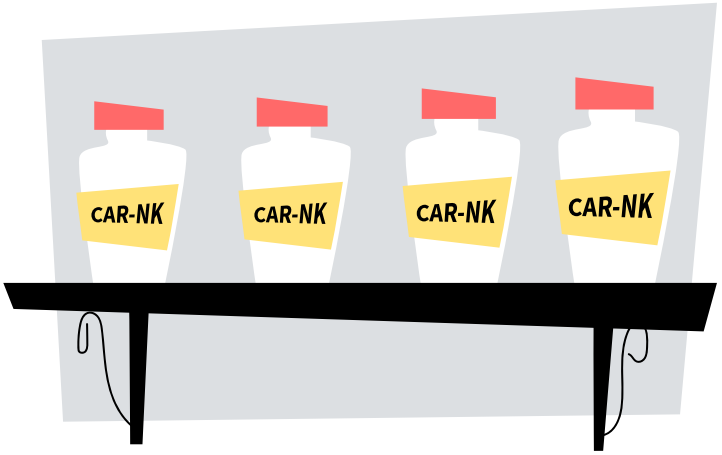
"We have shown that it is possible to produce more than 100 doses of CAR-NK cells from a single cord-blood unit," the researchers wrote. "This capability, together with the apparently minimal HLA (human leukocyte antigen)-matching requirements between the donor of CAR-NK cells and the patient, may pave the way for a truly off-the-shelf product that could increase treatment accessibility for many more patients."

At the university, the NK cells are isolated from donated umbilical cord blood. The researchers genetically engineer the cells to recognize and kill CD19 and reinforce them with an immune signaling molecule, interleukin-15, that enhances the multiplication and survival of the NK cells.

In their study, the researchers administered a single dose of the CAR-NK cell therapy at one of three dose levels to 11 patients; five had chronic lymphocytic leukemia (CLL) and six had non-Hodgkin lymphoma.

At a median follow-up of 13.8 months, eight patients (73%) had responded to therapy, seven of whom achieved a complete response and no longer showed evidence of disease. One patient experienced remission of Richter's transformation, which turns CLL into a more aggressive lymphoma, but had persistent CLL.

"Responses were rapid and seen within 30 days after infusion at all dose levels," the researchers wrote. "The infused CAR-NK cells expanded and persisted at low levels for at least 12 months."



Five of the responding patients received post-remission therapy.

"We are encouraged by the results of the clinical trial, which will launch further clinical studies to investigate allogeneic cord blood-derived CAR-NK cells as a potential treatment option for patients in need," corresponding author Dr. Katy Rezvani, a professor in the department of stem cell transplantation and cellular therapy at MD Anderson, said in a press release.

No patients experienced the serious side effects that can be associated with CAR therapy: cytokine release syndrome, a systemic inflammatory response; neurotoxicity, an alteration in the activity of the nervous system; or graft-versus-host disease, in which donor immune cells attack the patient's tissues. The participants' side effects were primarily related to the conditioning chemotherapy given before cell infusion to deplete the number of lymphocytes and resolved within one to two weeks, Rezvani said in the release. Moreover, no patient required admission to an intensive care unit for management of treatment side effects.

Finally, the maximum tolerated dose was not reached, meaning that no doses tried were too toxic for use.

"Due to the nature of the therapy, we've actually been able to administer it in an outpatient setting," Rezvani said. "We look forward to building upon these results in larger multi-center trials as we work with Takeda to make this therapy available more broadly."

IRYNA / ADOBE STOCK / ADAPTED BY RAY PELESKO

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Learn more at CALQUENCE.com

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

Select Safety Information

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

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

Please see Brief Summary of Prescribing Information on adjacent pages.

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(acalabrutinib) 100 mg capsules

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

CALQUENCE®
(acalabrutinib) 100 mg capsules

What is CALQUENCE?

CALQUENCE is a prescription medicine used to treat adults with:

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

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

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

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

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

How should I take CALQUENCE?

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

(continued)

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

What are the possible side effects of CALQUENCE?

CALQUENCE may cause serious side effects, including:

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

(continued)

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

The most common side effects of CALQUENCE include:

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

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

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

How should I store CALQUENCE?

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

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

General information about the safe and effective use of CALQUENCE.

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

What are the ingredients in CALQUENCE?

Active ingredient: acalabrutinib

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

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

AstraZeneca

For more information, go to www.CALQUENCE.com or call 1-800-236-9933.

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US-34063 11/19

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

Having a Say

The EndBrainCancer Initiative wants patient concerns reflected in national treatment guidelines. By DELLANN ELLIOTT MYDLAND

DID YOU KNOW THAT patients, caregivers, family members and advocacy organizations can help shape the clinical practice recommendations that guide doctors in treating brain cancer, as well as treatment guidelines aimed at patients?

The EndBrainCancer Initiative (EBCI) has an ongoing opportunity to provide input about clinical practice guidelines as well as patient guidelines released by the National Comprehensive Cancer Network (NCCN), and we want to incorporate insights from the brain cancer community in the next update. We are also asking patients with metastatic disease to the brain to tell us what would make their journey better.

ASKING PATIENTS FOR HELP

The NCCN issues guidelines for physicians that set forth standard treatment protocols for specific cancer types and stages. The aim is to provide standards of care for clinical practice and ensure that all patients have equal access to the most appropriate diagnostic testing and treatments, no matter where they receive care, to ensure the best possible outcome.

It's important that patients are familiar with these protocols, as well, so they're able to ask for appropriate diagnostic testing and treatment if they aren't receiving it. That's why the NCCN also issues patient versions of its guidelines.

NCCN's patient guidelines are reviewed and updated periodically to reflect advances in diagnostic testing and treatment of brain cancer and other solid tumors, so it's imperative that the patient voice be an integral part of these updates, last done in 2016. That's why we're asking those in the brain cancer community to tell us what's meaningful to them when it comes to treatment options and quality of life. We ask that patients email us their suggestions, stories and pictures to WeCare@EndBrainCancer.org.

In addition to using these insights to educate the public and pharmaceutical companies about what's meaningful to those with brain cancer, we'll share the feedback with the NCCN for possible inclusion in its patient guidelines on treatments for central nervous system (CNS) cancers — including gliomas and other brain cancers. We'll also share some of these patient experiences and suggestions in a white paper we plan to submit to the advisory panel responsible for updating NCCN's clinical treatment guideline for CNS cancers.

ENSURING APPROPRIATE CARE

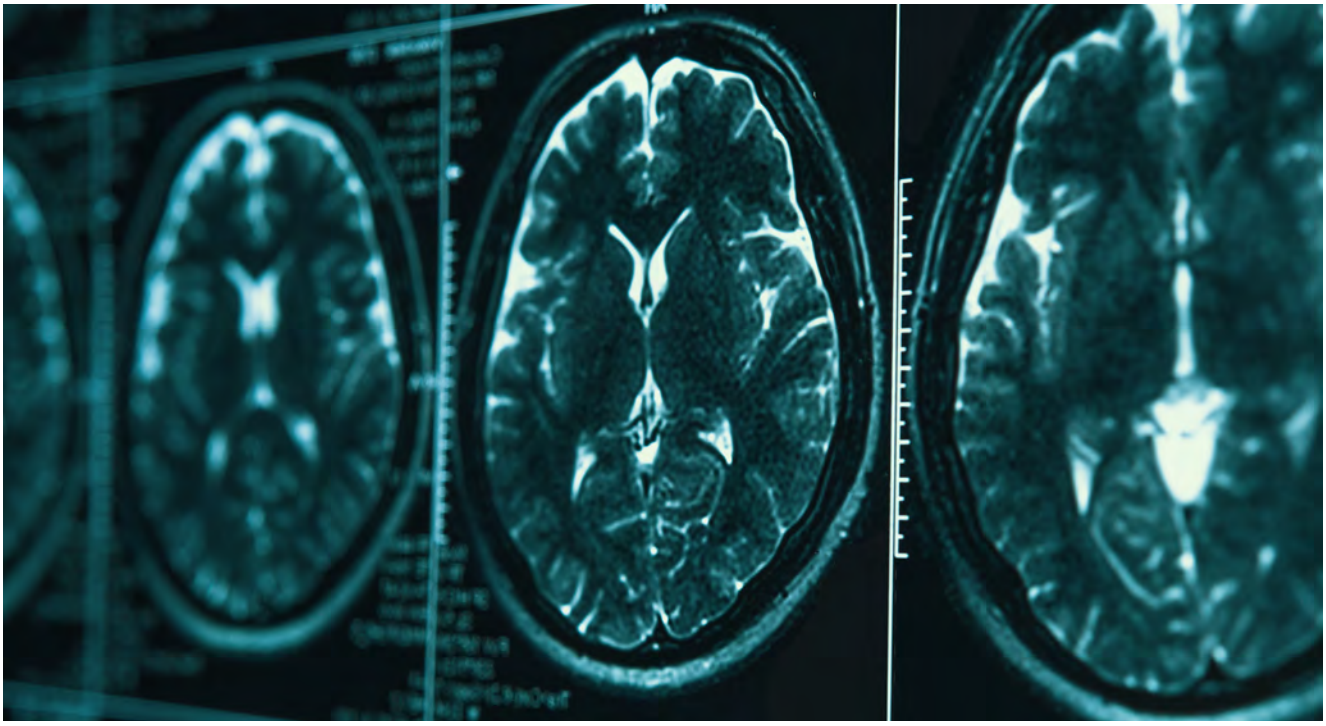
The main thrust of our paper will be to communicate our desired guideline updates, along with supporting data. EBCI is seeking grant funding and donations to support this work. Please contact Dellann@EndBrainCancer.org if you or your company can help fund this effort.

We want the guidelines to state that patients with brain cancer should, upon diagnosis, have all their treatment options presented to them: clinical trials, surgery, radiation, chemotherapy and Optune (a wearable device that delivers low-intensity electronic fields, known as tumor treating fields, that help to stop the growth and division of glioblastoma cells). Furthermore, patients should be advised to take time before surgery to arrange to save their tumor tissue and have genomic testing done on it, with assurance that the tissue will remain available if the patient ever needs it to create a personalized vaccine or for testing to allow enrollment in a clinical trial.

Not every hospital saves patients' tumor tissue or has genomic testing done on it if patients don't ask. And even when they do, hospitals often check for just a few genetic mutations/biomarkers that can help doctors accurately diagnose and categorize a brain tumor and brain cancer. Patients should know that it's much better if tumor tissue undergoes next-generation sequencing, which tests for about 500 mutations that could be linked to brain cancer. Scientists »

COURTESY OF DELLANN ELLIOTT MYDLAND

DELLANN ELLIOTT MYDLAND started the Chris Elliott Fund in May 2002 in honor of her late husband, Christopher Stewart Elliott, in response to the difficulty he faced after a brain cancer diagnosis in being referred to specialists and finding advanced treatments. The 501 (c)3 nonprofit organization became the EndBrainCancer Initiative, EndBrainCancer.org, in 2015. Under both names, the organization's goal has always been to provide patients with immediate access to brain tumor specialists, advanced treatments and clinical trials and to drastically increase quality of life and survivorship for all patients with brain tumors or brain cancer.



are testing drugs that target a variety of mutations, but to enter these clinical trials or get the drugs that target these specific mutations/biomarkers through the FDA's compassionate use program, patients need to know their tumor's mutational status.

CONTRIBUTING TO A FINAL DOCUMENT

The most recent NCCN CNS clinical treatment guidelines were published in November 2019, and we're happy that some of the updates we've been advocating for were included. The guideline encourages genetic testing of brain tumor tissue but does not demand it; however, it does tell physicians to test the tissue for expression of the proteins IDH1 or IDH2, and for methylation of the enzyme MGMT, meaning it has undergone chemical changes. The MGMT information is critical in informing the treatment decision since these characteristics mean the tumor is more likely to respond well to alkylating chemotherapy, such as Temodar (temozolomide).

In March 2020, the NCCN updated the documents with preferred practices that will probably be finalized as recommendations in the November 2020 publication. In that document, we are hopeful that the NCCN will state that the standard of care for gliomas must include the saving of tumor tissue, patient access to it, next-generation sequencing and the use of that data to stratify patients into appropriate clinical trials, whether at the patient's treating facility or somewhere else. In our white paper, we'll argue that this is not only important from a patient perspective, but also in the research world. Think about how much research data is being lost in this patient population, and how that's stifling research and clinical trial enrollment!

KEEPING PATIENTS INFORMED

To further be a part of the NCCN's process, EBCI has entered into a permissions agreement to distribute the patient version of the CNS guideline. We'll offer it online and will seek grants and donations to distribute this information in hard copy as we feel it's incredibly important to get this into everyone's hands.

Finally, we will soon be listed in the NCCN patient guidelines for CNS tumors as an endorser, which will help patients with brain cancer find us and seek our help. EBCI can then connect these patients to a brain tumor center that routinely performs next-generation sequencing and offers a wide variety of treatment options.

Our mission every day is to introduce patients and their caregivers to brain tumor specialists and/or clinical trials and advanced care. Through our national Direct Connect program, we provide education and help patients to manage distress, create action plans, find second opinions, work with health insurers, search for clinical trials, seek compassionate use of drugs and fill the role of patient navigator to guide them through the process.

To use Direct Connect, contact clinical research nurse and patient navigator Delores Kannas, M.S.N., M.H.A., RN, by filling out EBCI's patient/caregiver inquiry form at endbraincancer.org/inquiry-form/, emailing Delores@EndBrainCancer.org or calling her directly at 424-444-2215 Monday through Thursday, 10 a.m. through 4 p.m. PT.

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12:30PM - 4:30PM

Bellevue Club

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Questions & Planning

425.444.2215

Join us to support and uplift brain cancer patients and their caregivers. All brain cancer patients welcome! A unique opportunity to meet other brain tumor patients as well as provide your unique perspective as a patient or caregiver.

This year's event will feature breakout sessions where patients and caregivers will be able to provide their perspective on topics such as:

- Meaningful treatment options
- Clinical trial design…the "patient voice" on what's needed
- Quality of Life…what really matters to patients in survivorship

12:30p: Check-in/Networking - Light lunch provided
1:30-3:30p Programs & Break Out Sessions
3:30-4:30p Appetizers & Networking

Register: endbraincancer.org/patient day

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A Rising Concern

As risk of colorectal cancer grows among those under 50, younger adults should know more about signs and screening. By BETH FAND INCOLLINGO

HISTORICALLY, COLORECTAL CANCER (CRC) primarily affected older people. But in the 1990s, a puzzling new trend began: As the disease rate dropped in people over age 50, it rose fairly rapidly in younger adults.

The trend continues today with no signs of abating, and researchers are working to determine whether factors such as diet and a sedentary lifestyle play a role or if a unique new subtype of the disease is striking younger adults. Questions are also arising about how best to diagnose and treat CRC in this younger population.

Dr. Zsofia K. Stadler, an oncologist with Memorial Sloan Kettering Cancer Center in New York City and co-director of the annual Early Age Onset Colorectal Cancer Summit hosted by the Colon Cancer Foundation, a patient advocacy group, sat down with CURE® to delve into those issues.

***CURE*®: Please tell us about the rise of CRC in younger adults.**

Stadler: Since the 1990s, we've had guidelines for colonoscopy screening for patients over the age of 50. And in fact, we have seen a slow but steady decrease in colon cancer risk in the over-50 population. This is because colonoscopy detects and removes premalignant polyps, thus preventing cancers. But what has become quite striking is that, since the 1990s, the incidence of colon cancer in the under-50 population, which doesn't usually get colonoscopies, has been increasing annually by about one to two percentage points, which is quite a large increase. And that increase is even more profound in very young patients. In those 20 to 29, the increase is approximately 4% annually — wow!

Another trend involves younger adults receiving diagnoses at later stages. Why is that?

We don't exactly know the answer. One hypothesis is that maybe the biology of some of these cancers is more aggressive, but most of the data that has been presented does not demonstrate that. Later diagnosis may also just be due to patients presenting at later stages because they're not undergoing routine screening.

Some interesting research suggests that the later diagnosis is due to actions by both the provider and the patient. For example, it's known that patients with early-onset colon cancer wait up to a year after presenting with symptoms to seek medical attention. In addition, the average number of providers that an early-onset colon cancer patient sees prior to diagnosis is three, and the reason is that, often, the symptoms are dismissed as hemorrhoids or hemorrhoidal bleeding, which is quite common.

TERAVECTOR / ADOBE STOCK

What are other possible signs of CRC?

Other symptoms can include rectal bleeding, changes in bowel habits — either diarrhea or constipation — and abdominal pain. Any of these can be symptoms if they occur over time or are progressively getting worse.

Are there differences between young-adult CRC and the disease in older adults?

We know that, in younger adults, more of the colon cancer is genetic, meaning that an inherited genetic mutation is causing a predisposition to it. The most common hereditary cause is Lynch syndrome, which overall accounts for about 3% of CRC cases. But in the young patients under 50, it accounts for about 10% of all colon cancer diagnoses.

About 80% to 85% of younger-adult colon cancers are not linked to heredity, and that leaves the rest unexplained. A lot of research has looked into epidemiological factors that may be associated with the increased risk, but, interestingly, although we know of many risk factors that increase average-onset colorectal cancer — Western diet, obesity, diabetes, smoking, excessive alcohol consumption — those don't seem to account for the rise. So, we are still very much investigating the causes of this dramatic shift.

Due to the rise of the disease in younger adults, the American Cancer Society now recommends earlier screening for CRC. What are its recommendations?

The American Cancer Society did a modeling study that demonstrated that perhaps we should lower the average age at which we begin screening from 50 to 45. In fact, in African Americans, for example, this has been a recommendation for quite a while now. The studies seem to suggest that we'll pick up more cases by expanding screening this way, but because the most dramatic increase in colon cancer in young patients is actually in the age group of 20 to 29, we won't necessarily be targeting the group where the increase in risk is the most dramatic.

If we're not screening the younger adults who are most at risk, how can we stem the rising tide of disease?

Many families also have polyps that increase the risk of colorectal cancer. And there is a lack of knowledge in many families about how many polyps an individual had, at what age and what the pathology of the polyps was, which can be very important for determining the risk a certain patient faces.

One of the most important predictive aspects is that, in 15% to 25% of patients, there's a family history of the disease, which raises risk. That's why the United States Preventive Services Task Force put out recommendations that anyone with a first-degree relative who got colon cancer at age 60 or under should get colonoscopy screening starting at age 40. However, I don't think we always follow those guidelines, and patients may not be aware that earlier-age screening is recommended for them.

Sometimes primary care physicians don't even start to talk about colon cancer risk until age 50, at which time they usually start colonoscopy screening, but in some individuals, a primary care physician who was aware of the family history might have initiated colonoscopies sooner. So, patients need to know that, if there's a new diagnosis in the family, they should inform their primary care physicians. But at the same time, the primary care physicians should be asking the patients every once in a while: "Is there anything new going on in your family? Has anyone been diagnosed with cancer?" Because sometimes, these family histories change, and you could uncover a genetic predisposition syndrome.

When someone does develop colorectal cancer, it's now routine for doctors to check the tumor for mutations, some of which can indicate the presence of a syndrome that predisposes patients to colorectal and other cancers. Having this information allows healthy relatives to undergo careful screening for cancer over time, so that any disease is caught and treated early.

> **"I think it would help a great deal if everyone realized that, if even one first-degree relative got colon cancer at the age of 60 or under, all the other first-degree relatives need colonoscopies starting at age 40."**
>
> *— DR. ZSOFIA K. STADLER*

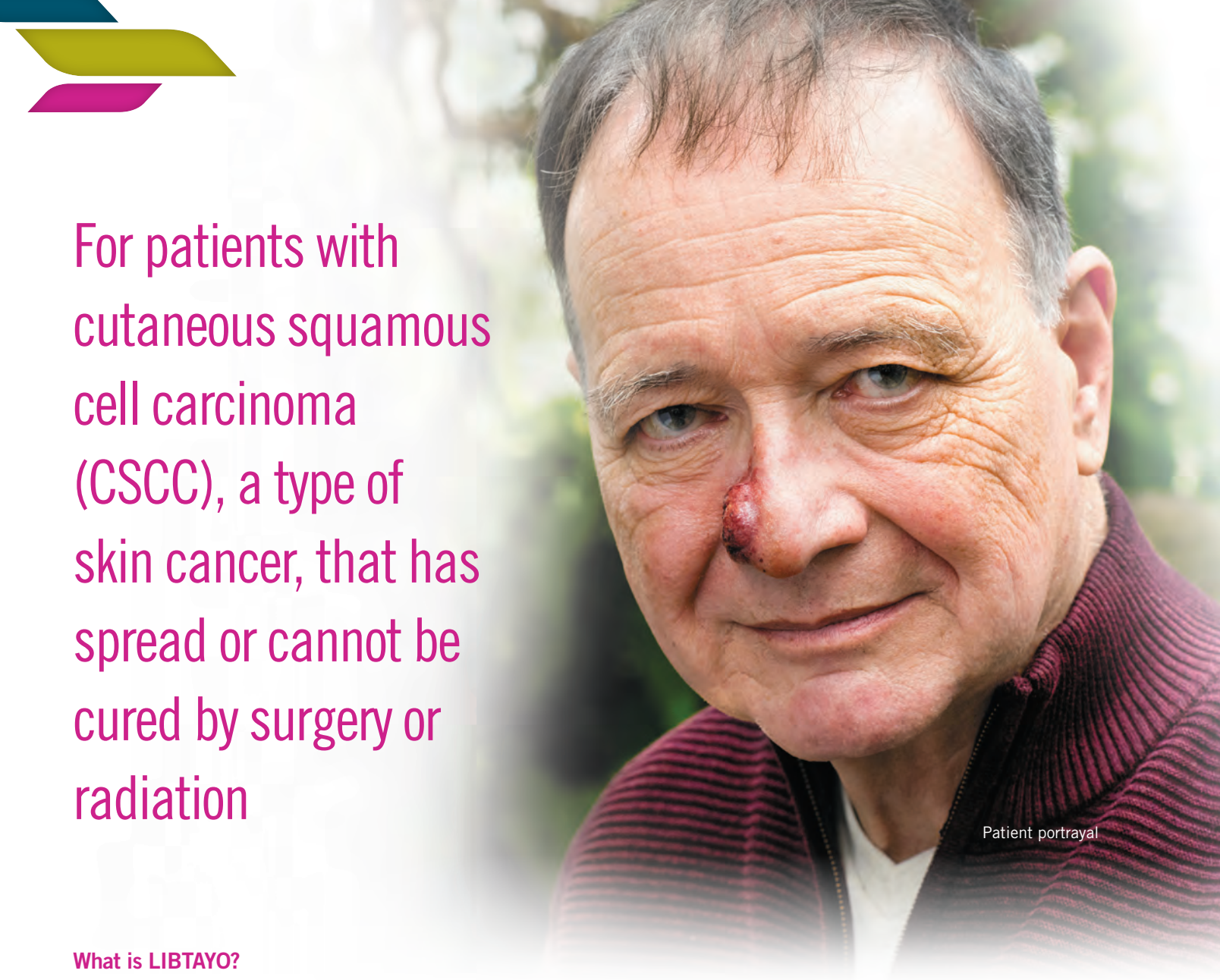
You mentioned colonoscopy. Are there any other screening types that would be appropriate for younger adults?

There are other types of screening, but none are as good as colonoscopy. There is sigmoidoscopy, but that screens only the left side of the colon, missing the entire right side. Hemoccult or guaiac tests that look for blood in the stool are better than nothing, but if someone has symptoms of rectal bleeding, our recommendation is really solid to get a colonoscopy.

What's your most important advice for a young adult who's facing a CRC diagnosis?

They should know that they're not alone as patients and they're not alone in the field that's trying to study this. Gastroenterologists, primary care physicians, medical oncologists and surgeons are more and more aware of the rise in early-onset colon cancer. In fact, many larger cancer centers have set up early-onset colon cancer centers where these patients can go to address their unique issues, including social and psychological concerns, fertility and genetics. There are resources for these patients.

For patients with cutaneous squamous cell carcinoma (CSCC), a type of skin cancer, that has spread or cannot be cured by surgery or radiation


Patient portrayal

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 type of skin cancer by working with y our 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. These problems may happen anytime during treatment or even after your treatment has ended.

Always talk with your doctor if you have any questions about your treatment or any side effects.

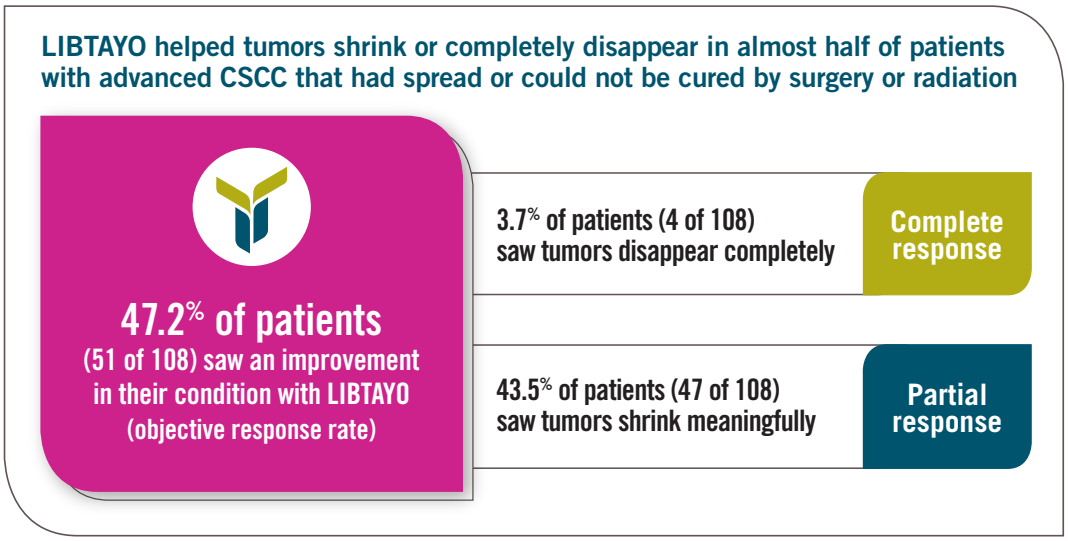
Please see additional Important Safety Information throughout, including brief summary of Prescribing Information on the following pages.

In patients with CSCC that had spread or could not be cured by surgery or radiation

LIBTAYO helped tumors shrink or completely disappear in almost half of clinical trial patients

LIBTAYO was studied in clinical trials

LIBTAYO has been studied in 108 patients in 2 ongoing clinical trials of patients with CSCC that had spread or could not be cured by surgery or radiation.



In 80% (41 of 51) of patients who saw an improvement with LIBTAYO, the effect was still ongoing at the time of last follow-up.

Responses lasted 6 months or longer in 61% (31 of 51) of patients who responded to LIBTAYO.

Responses lasted between 1 month and 15.2+ months (still ongoing at time of last follow-up).

Important Safety Information

Call or see your healthcare provider right away if you develop any symptoms of the following problems or these symptoms get worse:

- **Lung problems (pneumonitis).** Signs and symptoms of pneumonitis may include new or worsening cough, shortness of breath, and chest pain.
- **Intestinal problems (colitis) that can lead to tears or holes in your intestine.** Signs and symptoms of colitis may include diarrhea (loose stools) or more frequent bowel movements than usual; stools that are black, tarry, sticky or that have blood or mucus; and severe stomach-area (abdomen) pain or tenderness.

LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg

Important Safety Information (continued)

Call or see your healthcare provider right away if you develop any symptoms of the following problems or these symptoms get worse (continued):

- **Liver problems (hepatitis).** Signs and symptoms of hepatitis may include yellowing of your skin or the whites of your eyes, severe nausea or vomiting, pain on the right side of your stomach area (abdomen), drowsiness, dark urine (tea colored), bleeding or bruising more easily than normal, and feeling less hungry than usual.
- **Hormone gland problems** (especially the adrenal glands, pituitary, thyroid and pancreas). Signs and symptoms that your hormone glands are not working properly may include headaches that will not go away or unusual headaches, rapid heartbeat, increased sweating, extreme tiredness, weight gain or weight loss, dizziness or fainting, feeling more hungry or thirsty than usual, hair loss, feeling cold, constipation, deeper voice, very low blood pressure, urinating more often than usual, nausea or vomiting, stomach-area (abdomen) pain, and changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness.
- **Kidney problems,** including nephritis and kidney failure. Signs of these problems may include decrease in your amount of urine, blood in your urine, swelling in your ankles, and loss of appetite.
- **Skin problems.** Signs of these problems may include rash, itching, skin blistering, and painful sores or ulcers in the mouth, nose, throat, or genital area.
- **Problems in other organs.** Signs of these problems may include headache, tiredness or weakness, sleepiness, changes in heartbeat (such as beating fast, seeming to skip a beat, or a pounding sensation), confusion, fever, muscle weakness, balance problems, nausea, vomiting, stiff neck, memory problems, seizures (encephalitis), swollen lymph nodes, rash or tender lumps on skin, cough, shortness of breath, vision changes, or eye pain (sarcoidosis), seeing or hearing things that are not there (hallucinations), severe muscle weakness, low red blood cells (anemia), bruises on the skin or bleeding, and changes in eyesight.
- **Rejection of a transplanted organ.** Your doctor should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.
- **Infusion (IV) reactions that can sometimes be severe and life-threatening.** Signs of these problems may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, fever, feeling of passing out, back or neck pain, and facial swelling.

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 delay or completely stop treatment if you have severe side effects.

Please see additional Important Safety Information throughout, including brief summary of Prescribing Information on the following pages.

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 had an organ transplant;
- have lung or breathing problems;
- have liver or kidney problems;
- have diabetes;
- 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.


Patient portrayal

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, and diarrhea. These are not all the possible side effects of LIBTAYO. 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.** You may also report s ide effects to Regeneron Pharmaceuticals and Sanofi at 1-877-542-8296.

REGENERON | SANOFI GENZYME

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

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 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. 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 symptoms of the following problems or these symptoms get worse:

Call or see your healthcare provider right away if you develop any symptoms of the following problems or these symptoms get worse:
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- new or worsening cough
- chest pain
- shortness of breath

Lung problems (pneumonitis). Signs and symptoms of colitis may include:
- diarrhea (loose stools) or more frequent bowel movements than usual
- severe stomach-area (abdomen) pain or tenderness
- stools that are black, tarry, sticky, or have blood or mucu

Liver problems (hepatitis). Signs and symptoms of colitis may include:
- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting
- pain on the right side of your stomach area (abdomen)
- feeling less hungry than usual
- drowsiness
- dark urine (tea colored)
- bleeding or bruising more easily than normal

Hormone gland problems (especially the adrenal glands, pituitary, thyroid, and pancreas). Signs and symptoms that your hormone glands are not working properly may include:
- headache that will not go away or unusual headaches
- rapid heart beat
- increased sweating
- extreme tiredness
- weight gain or weight loss
- dizziness or fainting
- feeling more hungry or thirsty than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- very low blood pressure
- urinating more often than usual
- nausea or vomiting
- stomach-area (abdomen) pain
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Kidney problems, including nephritis and kidney failure. Signs of these problems may include:
- decrease in your amount of urine
- swelling in your ankles
- blood in your urine
- loss of appetite

Skin problems. Signs of these problems may include:
- rash
- skin blistering
- itching
- painful sores or ulcers in mouth or nose, throat, or genital area

Problems in other organs. Signs of these problems may include:
- headache
- tiredness or weakness
- sleepiness
- changes in heartbeat, such as beating fast, or seeming to skip a beat, or pounding sensation
- seeing or hearing things that are not there (hallucinations)
- severe muscle weakness
- low red blood cells (anemia)
- bruises on the skin or bleeding
- changes in eyesight
- confusion, fever, muscle weakness, balance problems, nausea, vomiting, stiff neck, memory problems, or seizures (encephalitis)
- swollen lymph nodes, rash or tender lumps on skin, cough, shortness of breath, vision changes, or eye pain (sarcoidosis)

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

Infusion (IV) reactions that can sometimes be severe and life-threatening. Signs of these problems may include:
- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- fever
- feel like passing out
- back or neck pain
- facial swelling

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 delay or completely stop treatment with LIBTAYO if you have severe side effects.

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.

Before you receive LIBTAYO, tell your healthcare provider about all your medical conditions, including if you: can sometimes be severe and life-threatening. Signs of these problems may include:
- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have had an organ transplant
- have lung or breathing problems
- have liver or kidney problems
- have diabetes
- 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 leas 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.

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:
- **Your healthcare provider will give you LIBTAYO into your vein through an intravenous (IV) line over 30 minutes.**

The most common side effects of LIBTAYO include tiredness, rash and diarrhea. These are not all the possible side effects of LIBTAYO. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
General information about the safe and effective use of LIBTAYO. Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about LIBTAYO, talk with your healthcare provider. You can ask your healthcare provider for information about LIBTAYO that is written for health professionals.

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

REGENERON | SANOFI GENZYME

Heeding the Forecast

Liquid biopsy can predict relapse in patients with stage 3 melanoma, making early treatment or prevention possible. By CONOR KILLMURRAY

CIRCULATING TUMOR CELLS (CTCS) in the blood are associated with early relapse in patients with stage 3 melanoma and could help reveal risk of disease recurrence, according to research published in the journal *Clinical Cancer Research*.

CTCs are shed from a primary tumor into vessels, where they are picked up by blood as it circulates and carried throughout the body. They can then be detected with a blood test known as a liquid biopsy, which helps determine a patient's prognosis. Although researchers knew it was possible to detect CTCs in the blood of patients with melanoma, they weren't sure of the significance for prognosis until recently.

Three-quarters of skin cancer-related deaths are caused by melanoma, and five-year survival rates vary greatly for patients with stage 3 disease. "Our findings are significant, given that there is a need for blood-based biomarkers to guide clinical decision-making for patients with stage 3 melanoma," lead author Dr. Anthony Lucci stated in a press release from The University of Texas MD Anderson Cancer Center in Houston, the institution behind the study. "There currently are no blood tests available to help doctors accurately tell which patients are likely to relapse and should be given therapy and which are low risk and could be observed."

In the study, blood was drawn from 243 patients who, between February 2012 and June 2017, received a diagnosis of cutaneous melanoma that had spread to lymph nodes but not beyond. Researchers assessed whether CTCs were present, and then compared relapse-free survival in the patients who had at least one CTC per 7.5-milliliter tube of blood compared with those who had no detectable CTCs.

Over half the patients were given adjuvant therapy — additional therapy after initial treatment of early-stage cancer — but no particular adjuvant treatment was significantly associated with the discovery of CTCs.

In 37% of the patients, at least one CTC per tube of blood was detected, which researchers found was significantly associated with a greater likelihood of relapse within six months. Having at least one CTC was also linked with a higher risk of relapse at 54 months.

"A blood-based biomarker that identifies those at high risk for disease relapse can potentially add important prognostic information that simply cannot be accessed with the advent of the new, limited node-dissection protocols," the researchers wrote. That refers to testing for potential relapse by removing and dissecting lymph nodes near the original cancer site.

IVECTOR / ADOBE STOCK / ADAPTED BY RAY PELESKO

Within six months, 21 of the 90 patients with at least one CTC relapsed compared with 12 of the 153 who did not present CTCs. At the full follow-up period of 54 months, 43 of the 90 patients with CTCs had relapsed compared with 56 of those who showed no CTCs.

Understanding this link will make it more possible for doctors to treat likely relapses in high-risk patients with stage 3 melanoma. Moreover, incorporating CTCs as a biomarker for relapse could allow for more customized therapy, such as using more aggressive adjuvant therapies in those who need them while sparing low-risk patients from these treatments and their side effects.

The liquid biopsy would be easy to assimilate into practice, the researchers added.

They believe their findings will provide the basis for future clinical trials of adjuvant treatments in this patient population, and also for enhanced imaging in those who face the highest risk of relapse.

FOR POSTMENOPAUSAL WOMEN WITH HR+, HER2- METASTATIC BREAST CANCER (MBC)

LIVING LONGER IS POSSIBLE & PROVEN

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

Please see Summary of Important Information on the following page.

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

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

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

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

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

KISQALI + fulvestrant can help you live longer with mBC.

In a clinical trial, KISQALI + fulvestrant extended the length of time women were alive from the start of treatment—also called overall survival (OS). Median OS is the length of time when half of the women were still alive. Median OS was not reached for KISQALI + fulvestrant vs 40 months for those taking fulvestrant alone. Median progression-free survival (PFS) is the length of time when half of the women had not yet progressed. 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.

KISQALI®
ribociclib 200 mg tablets

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

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:

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- 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

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

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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:

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- chest pain

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.

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- 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.

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- 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.
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  - Talk to your health care provider about birth control methods that may be right for you during this time.
  - If you become pregnant or think you are pregnant, tell your health care provider right away.
- are breastfeeding or plan to breastfeed. It is not known if KISQALI passes into your breast milk. Do not breastfeed during treatment with KISQALI and for at least 3 weeks after the last dose of KISQALI

What other medications might interact with KISQALI?

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

What should I avoid while taking KISQALI?

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

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

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

The most common side effects of KISQALI include:

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

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

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

These are not all of the possible side effects of KISQALI. For more information, ask your health care provider or pharmacist. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

General information about the safe and effective use of KISQALI

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

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

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PIXEL-SHOT / ADOBE STOCK

Doing the Heart Good

For those with breast cancer, exercise improves cardiovascular health.

By BRITTANY LOVELY

REDUCING THE RISK OF cardiovascular disease should be a priority of long-term care for patients with breast cancer, and doctors can help by prescribing exercise programs, according to Dr. Jean-Bernard Durand.

"The mortality for breast cancer continues to go down, but what women are going to be faced with if they do not have a recurrence (is that) their No. 1 cause of death is cardiovascular disease," Durand said in a presentation at the 37th Annual Miami Breast Cancer Conference in early March. "We have to do a much better job of managing their modifiable risk factors and comorbid conditions."

Durand, medical director of cardiomyopathy services and director of cardiovascular genetics research and the cardiology fellowship program at The University of Texas MD Anderson Cancer Center, explained how, by looking at a patient's cardiorespiratory fitness level, physicians can craft a personalized exercise program to curb side effects from disease and treatment.

He said a study of 248 patients with breast cancer found that, despite normal cardiac function, participants demonstrated a peak oxygen consumption one-third lower, on average, than that of age-matched sedentary but otherwise healthy women without a history of breast cancer.

A separate analysis of six studies involving 571 adult patients with cancer found that supervised exercise training versus non-exercise improved peak oxygen consumption by a statistically significant 15%.

Durand noted that MD Anderson's Healthy Heart Program offers patients a screening exam and a treadmill test to determine their maximal oxygen consumption.

"This will allow us to assess cardiopulmonary safety and determine the exercise dose, as well as compare fitness level relative to age and sex," he explained. Also assessed are the impact of prior cancer treatment on heart health, cholesterol levels, risk of high blood pressure or diabetes, body weight and waist measurements, family history of heart health and, if needed, smoking cessation efforts.

In a separate study highlighted in Durand's presentation, exercise programs that consisted of nine or more MET hours per week were associated with a 23% reduction in the risk of cardiovascular events regardless of age, cardiovascular disease risk factors at diagnosis, menopausal status and type of anticancer therapy. METs are metabolic equivalents, defined as the ratio at which a person expends energy relative to their mass.

It's important to ease patient concerns about exercise, Durand said. "The patient bias is that you are expecting them to get to a gym, get a personal trainer and do exercise every single day, and that could not be further from the truth," he said. "I like to recommend the buddy program — finding a neighbor or friend who will walk with you at a brisk pace — and set up a schedule so you can do this as a team."

Supplement or Detriment?

Vitamins, herbal medicines and other nutritional products may be more harmful than helpful to individuals with cancer. Check with an expert before taking them.

By CHRISTINE A. ADAMO

CHRISTINE A. ADAMO is a board-certified integrative medical physician who specializes in the field of oncology. She holds a master's degree and a doctorate in traditional Asian medicine and practices functional medicine, herbal medicine, natural supplementation and acupuncture. Although her office is in San Diego, she sees patients around the country via virtual appointment to provide care for those going through chemotherapy, immunotherapy, radiation and/or surgery.

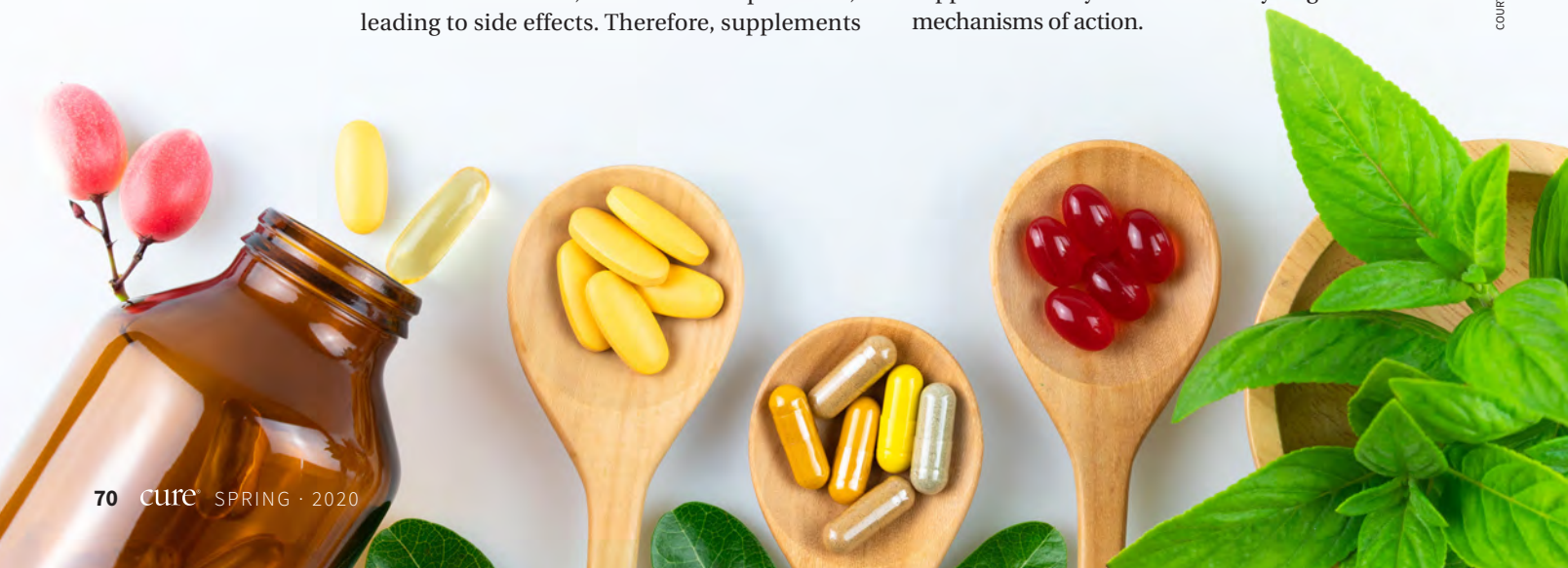
AS AN INTEGRATIVE MEDICAL physician who specializes in cancer, I see many patients who are extremely ill. In addition to recognizing the health benefits of proper nutrition, many suspect that supplements may help but don't know how to safely or effectively administer them on their own. It is not uncommon for patients to come into my office with a shopping bag full of vitamins and other supplements they've purchased via infomercials, online or at local drugstores. Seeing this happen over and over again concerns me, as many products aren't what they claim to be. Because vitamins, herbs and natural supplements aren't completely regulated by the Food and Drug Administration (FDA), many available over the counter (OTC) are of poor quality and, in some cases, more harmful than helpful.

When considering supplements to support health, a number of factors must be taken into account. First, just because a product is labeled "natural" doesn't mean it's safe or that the recommended dose is right for everyone. The recommended daily intake of most vitamins and supplements is based on the needs of average healthy individuals in specific age and gender groups. Good health is a game of balance. Someone with nutrient deficiencies can experience signs and symptoms of fatigue; weakened immunity; changes in hair, nails and skin; poor cognition; or even bone loss. Excessive intake of nutrients, such as vitamin D, vitamin B6 and iron, can also cause problems, leading to side effects. Therefore, supplements should be dosed according to therapeutic intention and an individual's specific needs found in bloodwork.

Second, mixing vitamins, supplements, medications and even foods, without knowledge about how they will react or interact, can be dangerous. Remember mixing baking soda and vinegar in science class, then waiting for the reaction? That scenario shows that even the most benign substances, when mixed, can create a strong chemical reaction. For example, substances known as furanocoumarins in grapefruit and some other citrus fruits inhibit an enzyme called cytochrome p450 3A4, which is responsible for the metabolization of certain drugs. If taken within 24 hours of certain medications, including some chemotherapies and other cancer treatments, grapefruit juice can cause elevated blood levels of those drugs, making them much more potent than intended.

Next, timing of consumption should be considered. All vitamins, supplements and herbs have a mechanism of action, a describable manner in which they work. For example, some supplements are anabolic. They have a buildup effect in cells to allow activities such as creating muscle or bone, which uses up energy. Other supplements are catabolic. They have a breakdown effect, which releases energy to be used for body functions such as digestion. As a clinician, I find that patients get the most effective results when the supplements they combine have synergistic mechanisms of action.

COURTESY OF CHRISTINE A. ADAMO



> **“It is not uncommon for patients to come into my office with a shopping bag full of vitamins and other supplements they’ve purchased via infomercials or at online or local drug stores. Seeing this happen over and over again concerns me as many products aren’t what they claim to be.”**
>
> *—CHRISTINE A. ADAMO*

Also, despite appealing product labels and clever marketing tactics, many products do not contain the high-quality ingredients they claim to. Although a regulatory standard called the Current Good Manufacturing Practice guides manufacturers on processing and labeling, the FDA does not review the safety or effectiveness of vitamins or supplements before they go to market. A number of labs can measure quality, efficacy and safety, but many OTC supplements do not go undergo quality-control measures outside the companies that make and sell them. In addition to poor-quality ingredients, OTC products can contain various contaminants, artificial fillers, preservatives, heavy metals or other toxic agents.

Finally, it’s extremely important to use the best quality products available. Products made according to United States Pharmacopeia guidelines and labeled as such go through stringent quality-control measures to check their processing procedures and purity. An agency other than the manufacturer must verify that all ingredients are at least 99% pure. Random samples are tested throughout the year to ensure that quality control and purity are maintained over time. Some of these products are available OTC, and some can be purchased at the offices of health care providers.

It’s easy to get overwhelmed when it comes to choosing supplements that are safe, effective and of high quality. I strongly recommend that anyone taking more than one multivitamin and one medication per day consult a natural medical provider who has extensive knowledge about vitamins, supplements and interactions in patients with cancer, as well as an oncologist, an oncology nurse or a cancer center pharmacist. Don’t let products that are supposed to optimize health cause more harm than good.

SUPPLEMENTS: PHOTOBYTAWAT / ADOBE STOCK

Guiding Light

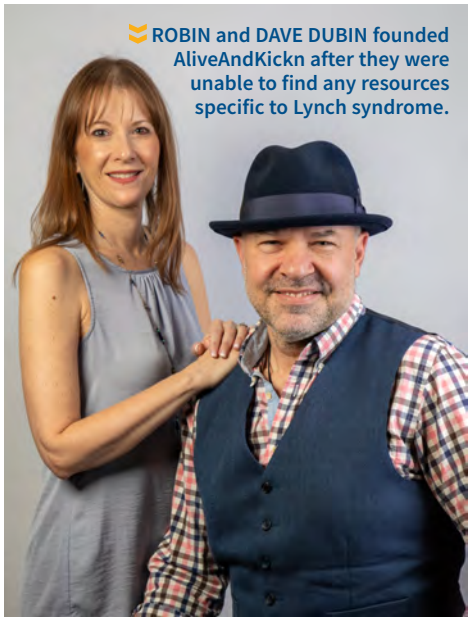
Most people are in the dark about Lynch syndrome, a condition that predisposes individuals to cancer. Patient advocacy group AliveAndKickn works to illuminate the issue. By BETH FAND INCOLLINGO

MANY HAVE HEARD OF the BRCA gene mutation, which predisposes one in 400 people to cancers including breast, ovarian and prostate.

Less familiar but more common is Lynch syndrome, which occurs with an inherited mutation in any of about half a dozen genes that play a role in DNA repair. Individuals with Lynch syndrome are especially susceptible to developing colorectal and endometrial cancers and also face an increased risk of stomach, breast, ovarian, small bowel, pancreatic, prostate, urinary tract, liver, kidney and bile duct cancers.

"The most recent studies show that one in 279 individuals has the Lynch mutation. Over 95% of them don't know it," says Robin Dubin, who co-founded AliveAndKickn (aliveandkickn.org), a Lynch syndrome patient advocacy group, with her husband, Dave Dubin, who has the condition and is a two-time survivor of colon and kidney cancers.

The couple sat down with *CURE*® to discuss Lynch syndrome and what people should know about diagnosing it and treating associated cancers.



ROBIN and DAVE DUBIN founded AliveAndKickn after they were unable to find any resources specific to Lynch syndrome.

CURE®: What prompted you to form AliveAndKickn?

Robin Dubin: We started AliveAndKickn in 2012. Dave got a colon cancer diagnosis in 1997 at age 29, and we knew there was a family history, but genetic testing for Lynch syndrome wasn't routinely available yet. It wasn't until 2007, when he received a second diagnosis, that he got genetic testing done and found out about Lynch syndrome, which we had never heard of.

That's when Dave started getting involved with advocacy and quickly realized that there were no patient resources or awareness efforts completely focused on Lynch. With his voice and storytelling abilities, we felt it would make sense for us to focus on Lynch syndrome. We've been working hard ever since to provide ways for patients with Lynch syndrome to connect with researchers, as well as to partner with other organizations to provide resources and support and build awareness and education.

Dave Dubin: Before we founded the organization, our first effort was a backyard barbecue that we held four years in a row, and the name of the event was Dave's Not Dead Yet. Robin didn't like that name. I was always a soccer player and, as I've gotten older, I have become more of a coach than a player. I felt that the name AliveAndKickn was appropriate, considering the number of surgeries and diagnostic tests I'd been through while continuing to play and coach the game I loved.

How is your organization raising awareness about Lynch syndrome?

Robin: We held an event in fall 2019 that brought together a dozen patients with Lynch syndrome at The University of Texas MD Anderson Cancer Center in Houston for roundtable discussions with researchers and clinicians. We educated the patients, did advocacy training and captured their stories on camera. We'll enable them to use that content on social media as they talk about their personal and family stories.

We did that project with one of our national partners, the Colon Cancer Coalition, and with them we're working on a co-branded microwebsite, livingwithlynch.org, where we'll post all the video content. A lot of it will be set up as educational pieces. For example, one will talk about genetic testing and another about risk-reducing surgeries.

We also recently launched a podcast. Dave has been spending some time doing interviews with various patients who have Lynch syndrome, doctors, clinicians and researchers in the field, and we'll continue to add episodes.

We also have an annual spring fundraising cocktail reception in New York City, the Blue Genes Bash.

Finally, we have a patient registry that collects medical and genomic data for researchers to use in studies, and we expect to expand the type of information collected soon.

Who should be tested for Lynch syndrome and when?

Robin: Currently, the majority of people get tested for Lynch syndrome and other hereditary cancer genes

IMAGE COURTESY OF ROBIN AND DAVE DUBIN / ALIVEANDKICKN

after a cancer diagnosis, and then the rest of their family members hear about it and get tested, too. We need to figure out how to get more people tested at the primary care level based on family history alone, before they get cancer. That's because most Lynch syndrome cancers are early onset, with people getting colon or endometrial cancer in their 20s, 30s or 40s, and to change the outcomes and improve their care, they need to know about this before they get cancer.

In an ideal world, everybody who walks into a primary care doctor's office for an annual physical should be filling out a family history questionnaire and having a doctor determine if they meet the criteria to be referred to a genetic counselor. That's not happening, for the most part.

How do prevention and treatment strategies change when patients know they have Lynch syndrome?

Robin: When someone has Lynch syndrome, they're dealing with a chronic condition that needs to be monitored, screened and scanned every year.

If someone knows they have Lynch syndrome and they get a diagnosis of colon cancer, often doctors recommend total versus partial colectomy (surgical removal of the colon) because these patients are at higher risk of getting colon cancer again. But most of the time, Lynch syndrome testing is done after surgery, so patients don't have the option of making that decision.

Dave is a perfect example. In 2007, he had colon cancer for the second time. He had surgery and they removed another section of colon, but he still has 18 inches left. It was only after the surgery that he got genetic testing done and found out about Lynch syndrome. If we'd known, they probably would have recommended removing all of his colon.

When it comes to treatment, it's also crucial for patients to know that nearly all tumors associated with Lynch syndrome are microsatellite instability (MSI) high. This means that the cancers have trouble repairing their own DNA after it's damaged, and it makes them good candidates for treatment with immunotherapy.

Some immunotherapies are approved by the Food and Drug Administration for MSI-high tumors regardless of their location in the body, for use after chemotherapy has stopped working. But studies now suggest that platinum-based chemotherapies don't work for patients with Lynch syndrome and can actually be detrimental. At academic cancer centers that are doing lot of immunotherapy clinical trials, patients with Lynch syndrome are now getting these drugs as earlier lines of treatment.

What kind of testing do patients need to determine whether they have Lynch syndrome?

Robin: Germline testing, which looks for inherited cancer-causing mutations in the patient's DNA, usually involves a blood or saliva sample test for Lynch syndrome genes or a panel that can identify 30 to 40 hereditary cancer genes, including Lynch and BRCA mutations.

MSI status and other mutations that are specific to the cancer, not the person, are found by doing a different kind of test on the tumor itself. Often, what happens first is that someone's tumor is tested and found to be MSI high, and then doctors say that this indicates a potential Lynch mutation, so they'll order germline testing for Lynch syndrome.

All tumors should be tested for MSI-high status, but, unfortunately, that isn't always done. Especially when care is given outside a major cancer center in a community hospital setting, someone could be diagnosed with early age-onset colon cancer and be prescribed standard chemotherapy and surgery without ever being tested for MSI status or Lynch syndrome.

Dave: Very frequently, people have their cancer treated and still don't know they have Lynch syndrome. Even in the most obvious cases, many young adults with colon cancer don't get genetic testing. When you ask someone if they've had it, they often say "I think so" or "maybe." It's easily confused with a standard complete blood (cell) count or tumor testing.

Robin: A lot of people are told by their doctors that their tumor was tested, but they aren't told what kind of tests were done, and they assume that means they're OK and there's nothing further to look at. If they want to be sure, they can check their pathology report, which should specifically state whether the tumor was tested for mismatch repair.

How can patients protect themselves?

Robin: Patients with cancer, survivors and their relatives need to have conversations with their doctors about family history, and they can even mention that evidence of Lynch syndrome is sometimes not as obvious as you'd think. It could be that a patient's grandmother had endometrial cancer and great-grandfather had colon cancer or the patient's mother had ovarian cancer and grandfather had colon cancer. It's important to talk to doctors and ask if that warrants a referral to genetic counseling.

In what ways can people support AliveAndKickn's work?

Robin: We have opportunities for patients to tell their stories through our podcast and a share-your-story forum on our site, and we'll go forward with more Living With Lynch patient gatherings like the one at MD Anderson — hopefully, annually.

We offer a lot of opportunities to get involved through the Colon Cancer Coalition, which runs Get Your Rear in Gear 5K races around the country. People can sign up on our site to be Lynch syndrome patient advocates at local races. They can man a table where they talk about Lynch syndrome and genetics with members of the colon cancer crowd. C

In Predicting Risk, Size Matters

Childhood body mass index plays a role in adult kidney cancer risk, a study finds.

By CONOR KILMURRAY

BIRTH WEIGHT, HEIGHT AND childhood body mass index (BMI) are associated with adult kidney cancer, also known as renal cell carcinoma (RCC), meaning they could be valuable predictors of a person's risk of developing the disease, according to new research findings published in the *European Journal of Epidemiology*.

Having a high BMI as an adult is an established risk factor for RCC, but the researchers wanted to see if this characteristic early in life is also associated with the eventual development of the disease. They suggested that understanding risk early in life could lead to more effective prevention of kidney cancer, which accounts for about 2% of all newly diagnosed tumors and 90% of malignant kidney tumors.

The researchers examined data from 301,418 children from the Copenhagen School Health Records Register born between 1930 and 1985 and looked at their birth weight, along with their heights and weights at ages 7-13. Rare cases of childhood RCC were excluded from the data. They followed the data of these patients through their dates of RCC diagnosis, death, emigration, dropout from study follow-up or the end of the study. After some individuals were eliminated from participation, nearly 230,000 were eligible for inclusion in the analysis.

The follow-up period began in 1968 or at 30 years of age, whichever was most recent.

In total, 1,010 cases of renal cell carcinoma were identified. The median age of diagnosis was 62, and, in both men and women, childhood height and BMI were positively and linearly associated with adult RCC.

"Among men and women, positive associations were generally observed between childhood BMI and RCC, with a tendency towards a stronger association with increasing childhood age," the researchers wrote. "Compared with children with a normal BMI at both ages 7 and 13 years, children with normal BMI at age 7 and overweight at age 13 years had a 1.7-fold increased risk of RCC later in life."

Children with a normal BMI at age 7 and overweight at age 13 also had a higher risk of RCC than children who were overweight at ages 7 and 13.

The researchers observed that children whose BMI changed from above average at age 7 to average by age 13 had a lower risk of RCC than children with an average BMI change between 7 and 13, according to the researchers. However, children consistently overweight between the ages of 7 and 13 did not have an increased risk for RCC.

"Adjustment for birth weight had little influence on the results, thus suggesting that the observed associations were not due to an effect of children with a high BMI also having a high birth weight," the researchers explained.

The researchers found that children who were persistently taller between 7 and 13 had a higher risk of RCC in adulthood compared with those of average height in that same age range. Those who grew significantly taller between 7 and 13 also had a higher risk of RCC in adulthood compared with children who remained an average height in this age range.

Researchers found no significant difference between boys and girls, even when adjusted for BMI and birth weight.

"We found that children with a high birth weight, a high BMI, gain in BMI or a tall height, respectively, had higher risk of developing RCC later in life," the researchers concluded. "Our findings indicate that RCC may originate earlier in life than previously thought and suggest that new explorations into the mechanisms underlying these associations should be undertaken."

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Seeking Clarity

Many experience brain fog during or after treatment for cancer, but strategies can help survivors manage the problem.

By MICHELLE FERRETTI, LCSW, OSW-C; TYLER PUDLEINER M.S.; AND REBECCA BABB, M.S.N., APRN, CPNP-AC

"A WORD WILL BE at the tip of my tongue, but that's where it stays."

"I recognize the face and I know I know the name, but I just can't find it."

"I still feel like things are more jumbled up in my head than they used to be, and it's so much harder to clear them."

"I'm just not as sharp as I used to be."

Sound familiar?

Those are quotes from participants in the Life With Cancer program at Inova Schar Cancer Institute in northern Virginia. The program offers free education and services designed to help patients, survivors and their families cope with cancer, its treatments and survivorship. This includes a course designed to educate patients on handling cognition changes often called brain fog or chemo brain.

Although many patients receiving chemotherapy, surgery, radiation or other cancer treatments experience changes in attention, memory or thinking during the course of therapy, the vast majority recover within a year after treatment is completed. However, for some patients, symptoms persist.

Genetics, age, hormonal changes and other medical conditions also can contribute to this fog, known in the medical community as cancer-related cognitive impairment (CRCI). Other contributors include poor sleep and nutrition, lack of movement, long-term emotional imbalance, and use of alcohol or other substances.

Symptoms may include the following:

- Trouble focusing, making it hard to complete tasks or follow instructions or conversations.
- Difficulty with short-term memory.
- Struggling to find words or remember names.
- Disorganization leading to problems with multistep tasks.
- Emotional changes, including loss of motivation, increased isolation or changes in perspective.

Members of the Inova Life With Cancer Program co-facilitate a brain fog program for survivors of cancer.

COURTESY OF LIFE WITH CANCER

A FOUNDATION FOR SUCCESS

Many factors that play a role in CRCI cannot be controlled, such as genetics and necessary cancer treatments. However, factors that can be controlled include response to strong emotion and management of stress, sleep, exercise and nutrition. All can affect the body's internal environment by changing hormones and other biochemicals that affect brain function. The following strategies can help counteract this:

Address strong emotions. Emotions themselves do not cause CRCI but over time can further symptoms, particularly when depression or anxiety arises. Meeting with a therapist familiar with cancer is one way to get support and learn coping techniques. Connecting with others, engaging in exercise and

eating well are also ways to manage strong emotion.

Sleep. Sleep disturbances can lead to a lack of mental clarity, mood changes, decreased pain tolerance and an increase in the inflammatory response that can exacerbate CRCI. Practice good sleeping habits and consider cognitive behavioral therapy for insomnia, which is the first-line treatment for chronic insomnia, according to the American Academy of Sleep Medicine.

Get moving. Exercise and movement, especially outdoors, can decrease stress. Done at adequate intensity, exercise can improve cognitive function in as little as a month. Physical activity can also ease emotional symptoms and sleep problems. Exercise can be done formally, such as in a gym, or informally, such as walking or climbing stairs.

Learn ways to cope and build emotional resilience. Mind-body interventions, including meditation, medical qi gong and mindfulness-based cancer recovery, have proved effective for CRCI. Practicing these strategies can lead to better understanding of, and the ability to alter, seemingly automatic reactions to challenging events.

NAVIGATING BRAIN FOG

CRCI presents many challenges when it comes to managing roles, responsibilities and relationships. The following strategies can be helpful in coping with these obstacles:

Use external aids. Smartphones, computers, tablets, Post-it notes, pillboxes, calendars and centralized noticeboards can keep track of information such as appointments, finances, medications, lists, diet and exercise.

Establish a set routine. When tasks become habits, the brain starts to implement them with less cognitive effort.

Engage in challenging activities. Solving crossword puzzles, visiting museums, reading, playing a musical instrument, creating art or taking a course challenges the brain and helps create new neuronal connections.

Say the steps out loud when performing a complicated task. This script can help with preparation, staying on track and evaluating progress. Eventually, the brain may not need the support of the script.

Request workplace accommodations if needed. Individualized adjustments can include extended time to complete assignments, relocation or redesign of the workspace, a modified schedule or the use of leave. Speak with a manager and a human resources representative to make such arrangements.

Seek support from trusted friends and family members. Being socially engaged can help regulate the nervous system, make the brain more receptive to learning, and be emotionally and logistically helpful.

Practicing these strategies will help you better manage brain fog's impact on your life. CRCI is real.

FRANCESCO CHIESA / ADOBE STOCK

Life With Cancer therapists Drucilla Brethwaite, LCSW; Michelle Ferretti, LCSW, OSW-C; Tyler Pudleiner, M.S., a nurse practitioner; Rebecca Babb, M.S.N., APRN, CPNP-AC; and Dr. Sermsak Lolak, M.D., a psychiatrist, co-facilitate a brain fog program at Inova Life With Cancer in the Washington, D.C., area. Over four weeks, clinicians provide an overview of cancer-related cognitive impairment and evidence-based strategies to help participants develop personalized brain fog plans. To learn more about the program, visit lifewithcancer.org.

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IOVANCE BIOTHERAPEUTICS

Making the Most of Life

At 101, one survivor of cancer makes the most of every minute, whether climbing a mountain or piloting a glider. By ART VINALL

MY LIFE HAS ALWAYS been an active one. I was born and raised on a farm in Iowa and have participated in sports regularly, and in my later life I have walked at least 2 miles most days. Since age 43, I have been an avid downhill skier.

In 2011, I moved to Bend, Oregon, where there is, in the city limits, a butte that is 500 feet high. I saw this as a challenge and was soon climbing the butte every day. It is 1 mile up and 1 mile back down. That is darn good exercise.

> **"Today and every day, I say life is good and the best is yet to be."**

It was in 2011 that I heard the shocking news: "You have stage 4 lung cancer." I was 92 years old. The diagnosis was later changed to stage 3; however, lymph nodes along my sternum were involved, and surgery was no longer an option.

My treatment consisted of seven weeks of chemotherapy and radiation. The radiation was administered five days a week; each visit, I was zapped five times from different angles.

During those seven weeks, I climbed the old butte 14 times and got to the top seven times. I made it just halfway the other seven times. The main side effect of the treatment for me was fatigue. I did my best to ignore it. Looking back, I think my positive attitude certainly helped me.

The nine years since the completion of treatment have been the best of my life. There is something about going through the diagnosis and treatment of cancer that awakens a desire to make each day the best day of your life. Today and every day, I say life is good and the best is yet to be.

In the time since treatment, I have accomplished things that I never thought of doing in the past. Four times, I have had the privilege of visiting Europe for at least a »

ART VINALL sits in a glider he helped pilot in celebration of his 101st birthday, as the flight's lead pilot, left, and friend MARIKAY DORNACH stand nearby. The lead pilot was in charge as the glider was towed to 5,000 feet, and then Vinall took the controls until the craft made its approach for landing.

IMAGES COURTESY OF ART VINALL

Born and raised on an Iowa farm, **ART VINALL** received a bachelor's degree from the University of Iowa in 1940. He spent World War 2 in North Africa and Scotland as a civilian employee of TWA airline, carrying rush cargo and personnel to the war front. He returned home to serve in a similar role in the Naval Air Transport Service before being discharged as an ensign. After that, he worked for airlines and managed travel bureaus. In retirement, Vinall lived in Florida for 14 years and has been a resident of Bend, Oregon — which he calls a perfect place to live — for 10 years.

VINALL carved two life-size carousel horses, one of which is on public display in the town where he lives.

After completing cancer treatment, VINALL painted an 8-by-7-foot mural on his dining room wall.

month. I have fulfilled my desire to know Paris better, having lived on the Left Bank for an extended period. During these visits, I spent more than five weeks in Italy.

I also found time to paint an 8-by-7-foot mural on our dining room wall.

During my long, boring sessions of chemotherapy, I wrote a book. Its title: "How I Chose to Live My Life." The story of my life turned out to be 256 pages and included more than 100 illustrations. I had a printer produce enough so that my grandchildren and great-grandchildren could each have a copy.

My lifelong hobby has been wood carving. I felt it necessary to do something fairly large, so I carved a life-size carousel horse. I later carved another that was included in "Art in Public Places" here in Bend. It hangs today at the entrance of the downtown parking structure.

Since completing treatment, I have also had a season pass for our local ski mountain, Mount Bachelor. One year I skied 44 days.

This year, I celebrated my 101st birthday by piloting a glider down from 5,000 feet. (I have a pilot's license.)

These accomplishments made me realize that, at any age, life is not over when you receive a diagnosis of serious cancer. Rather, it is time to take a new view of life and make the most of it. My life is not over.

Since age 43, VINALL has been an avid downhill skier.

SHARE YOUR STORY!

Whether you are a patient, survivor, caregiver or health care provider, we want to publish your stories about cancer and the people, places and moments of the experience. They can be funny, poignant or practical. Send stories to **editor@curetoday.com,** or share on our Facebook page at **facebook.com/curemagazine**. Submissions should be no more than 600 words and include your name, phone number and email.

We are helping to move mountains for myeloma patients

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

Since its inception in 2016, Moving Mountains for Multiple Myeloma teams have climbed Mt. Kilimanjaro, hiked the Grand Canyon, summited Mount Fuji, trekked the Inca Trail to Machu Picchu, reached Everest Base Camp and conquered Iceland's many landscapes. Our team members have raised over $2.7 million, 100% of which goes directly to the MMRF, which spearheads and funds critical myeloma research. These amazing journeys are captured via blogs, social media posts, and video.

Now in its fifth year, the program will expand to exciting new challenges in 2020. Patients, caregivers, myeloma loved ones, and others impacted directly by multiple myeloma will take on the Alaskan Kenai Peninsula, summit Mount Washington, explore the terrain of Greenland, and more! They will raise funds for multiple myeloma research and demonstrate that the advancements being made in recent years, led by the MMRF, are helping patients live longer with a higher quality of life than ever before.

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

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

LEARN MORE ABOUT OUR CLIMBS!

2020 TREK SCHEDULE

Rim to Rim Grand Canyon Hike
To be determined

Mount Washington Hike
July 10-12, 2020

Greenland Trek
July 25-August 1, 2020

Alaskan Kenai Peninsula Trek
August 10-15, 2020

Kilimanjaro Trek
September 11-22, 2020

Machu Picchu Trek
October 1-12, 2020

endurance.themmrf.org/MM4MM

MOVING MOUNTAINS for MULTIPLE MYELOMA

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Multiple myeloma MAKES US A community

BCMA MAKES US LIKE family

Not actual patients.

Just like any other family, people with multiple myeloma have something in common: B-cell maturation antigen (BCMA). It's a protein found on cancerous myeloma cells that contributes to the growth and spread of the disease.

Learn more at multiplemyelomaandyou.com

At GSK, patients are at the core of what we do, and we are committed to researching the potential of targets like BCMA in multiple myeloma.