FOR PATIENTS, SURVIVORS & THEIR CAREGIVERS

LUNG CANCER

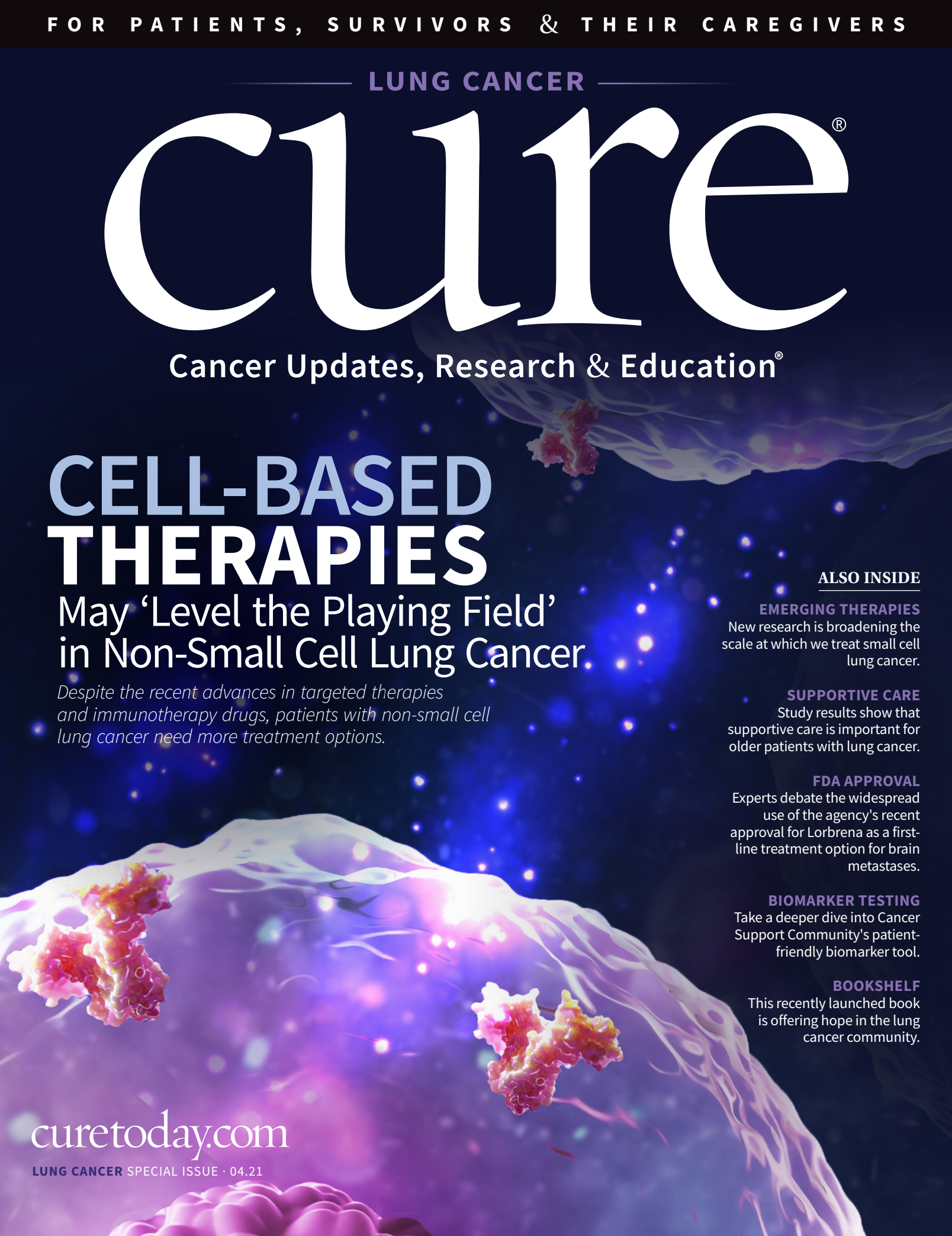
cure®

Cancer Updates, Research & Education®

CELL-BASED THERAPIES

May 'Level the Playing Field' in Non-Small Cell Lung Cancer

Despite the recent advances in targeted therapies and immunotherapy drugs, patients with non-small cell lung cancer need more treatment options.



ALSO INSIDE

curetoday.com

LUNG CANCER SPECIAL ISSUE · 04.21

KEYTRUDA IS A BREAKTHROUGH IMMUNOTHERAPY.

FOR TODAY

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

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

FOR THE FUTURE

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

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

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

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

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

IMPORTANT SAFETY INFORMATION

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

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

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

Important Safety Information is continued on the next page.

keytruda.com/lung

IMPORTANT SAFETY INFORMATION *(continued)*

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

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

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

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

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

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

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

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

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

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

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

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

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

Having trouble paying for your Merck medicine?

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

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

MERCK

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

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

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

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

Lung problems

- cough
- shortness of breath
- chest pain

Intestinal problems

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

Liver problems

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

Hormone gland problems

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

Kidney problems

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

Skin problems

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

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

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

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

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

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

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

Continued on next page.

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

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

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

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

  Females who are able to become pregnant:

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

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

How will I receive KEYTRUDA?

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

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

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

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

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

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

These are not all the possible side effects of KEYTRUDA.

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

General information about the safe and effective use of KEYTRUDA

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

Based on Medication Guide usmg-mk3475-iv-2011r036 as revised November 2020.

MERCK

CURE® CONTENTS

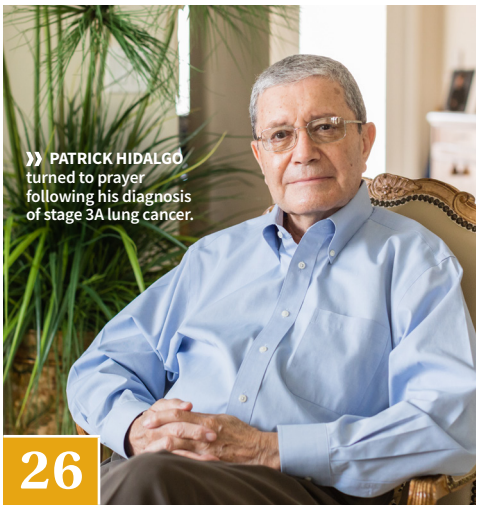
LUNG CANCER · 04.21

» DEBORAH BARKER received a dianosis of stage 4 non-small cell lung cancer in 2017.

14

« MARI CASANOVA got a second opinion to help her understand the severity of her diagnosis.

19



» PATRICK HIDALGO turned to prayer following his diagnosis of stage 3A lung cancer.

26

SCAN THE CODE

to receive our regular email newsletter with cancer updates, research and education.

cure®

SALES & MARKETING

Vice President, CURE Media Group Erik Lohrmann / elohrmann@mjhassoc.com

Vice President & Executive Producer, MJH Productions David Lepping / dlepping@mjhassoc.com

Executive Vice President, Oncology Professional Relations Donna Short, M.A.

Vice President, Strategic Alliances and Patient Engagement Strategy Sandra Shaw

Director, Patient Education Marty Murphy

Associate Director Brittany Hansen

Strategic Alliance Partnership Manager Brooke Weinstein

Senior Marketing Manager Melissa Hindle

Sales & Marketing Coordinator Samantha Gullace

OPERATIONS & FINANCE

Circulation Director Jon Severn, subscribe@curetoday.com circulation@mjhassoc.com

Vice President, Finance Leah Babitz, CPA

Controller Katherine Wyckoff

CORPORATE

Chairman & Founder Mike Hennessy Sr.

Vice Chairman Jack Lepping

President & CEO Mike Hennessy Jr.

Chief Financial Officer Neil Glasser, CPA/CFE

Chief Marketing Office Michael Baer

Executive Vice President, Global Medical Affairs & Corporate Development Joe Petroziello

Senior Vice President, Content Silas Inman

Senior Vice President Operations Michael Ball

Senior Vice President, I.T. & Enterprise Systems John Moricone

Vice President, Human Resources & Administration Shari Lundenberg

Vice President, Mergers & Acquisitions Chris Hennessy

Executive Creative Director, Creative Services Jeff Brown

EDITORIAL & PRODUCTION

Editor-in-Chief Debu Tripathy, M.D.

Editorial Director Kristie L. Kahl

Associate Editorial Director Ryan McDonald

Managing Editor Darlene Dobkowski; editor@curetoday.com

Editor Antonia DePace

Assistant Editor Colleen Moretti

Social Media Manager Jessica Skarzynski

Assistant Web Editor Jamie Cesanek

Copy Chief Jennifer Potash

Copy Supervisors Rachelle Laliberte, Paul Silverman

Medical & Scientific Quality Review Editor Stacey Abels, Ph.D.

Senior Copy Editor Kelly King

Copy Editors Cheney Baltz, Georgina Carson, Rebekah Harrison, Kirsty Mackay, Ron Panarotti

Creative Director, Publishing Melissa Feinen

Senior Art Director Gwendolyn Salas

Photo Editor & Department Coordinator Emily Hakkinen

Contributing Writers Meeri Kim, Erik Ness, Don Vaughan

Contributing Photographers Ken Carl, Arielle Gallione, Mike Kitada, Gözde Turgut, Emil White

AN MJH life sciences™ BRAND

MJH Life Sciences, LLC.
2 Clarke Drive, Suite 100
Cranbury, N.J. 08512
609-716-7777

All the stories you read in *CURE*® are reported and edited without the influence of advertisers or sponsors.

Subscriptions: *CURE*® is FREE to cancer patients, survivors or caregivers who live in the U.S. FREE bulk subscriptions are available for physicians, cancer centers and other organizations. Subscriptions may be obtained at www.curetoday.com/subscription, or by calling 800-210-2873 or requested via email to subscribe@curetoday.com.

The Different Roads of Lung Cancer

"LUNG CANCER" MAY BE only two words, but when you receive a diagnosis, they loom large. And each patient will handle their diagnosis differently.

Mari Casanova, for instance, had no experience with cancer and thought her journey would be easy. Her first doctor told her how aggressive her small cell lung cancer (SCLC) was but never mentioned the possibility of death. She didn't fully grasp the severity of her disease until she found a second oncologist who explained that she could die.

John Williams received a diagnosis of SCLC around the same time as Casanova, but he immediately grasped what this meant and had the help of a palliative care team. As we learned in one of our recent *CURE*® Educated Patient® Summits, palliative care is extremely important for any patient with cancer — and not just as a last resort. A supportive palliative care team can help patients like Williams fully understand their diagnoses and give them better quality of life during and after treatment. Unlike Casanova, Williams received his diagnosis just as emerging therapies were approved by the Food and Drug Administration — specifically, Tecentriq (atezolizumab) as a part of the first immunotherapy-plus-chemotherapy regimen for SCLC. Read more about Casanova and Williams in this special issue of *CURE*®.

> **"We all handle things differently, look at things differently and understand differently, meaning that the journey of each patient with cancer is unique."**

For another feature in these pages, we speak with an 82-year-old man who benefited from palliative care at Penn Medicine's Abramson Cancer Center during his complex treatment for non-small cell lung cancer (NSCLC). The team, who stayed at his side during more than 30 proton radiation treatments, ensured that everything went smoothly with as little impact as possible on his quality of life.

These are only three experiences out of the many cases of lung cancer, but they illustrate how each patient is different. We all handle things differently, look at things differently and understand differently, meaning that the journey of each patient with cancer is unique. But there are always similarities among the symptoms, risks and treatments.

One big risk associated with lung cancer is brain metastases, or the traveling of cancer cells from their original site to the brain. You'll read more about this as we speak with doctors regarding the most recent research and trials. Also in this issue, stay up to date on news and insights from the 2020 World Conference on Lung Cancer, including a new novel therapy for NSCLC.

MIKE HENNESSY SR.
Chairman and Founder

cure®

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

Could T-Cell Therapy Be the Next Advancement in Lung Cancer Immunotherapy?

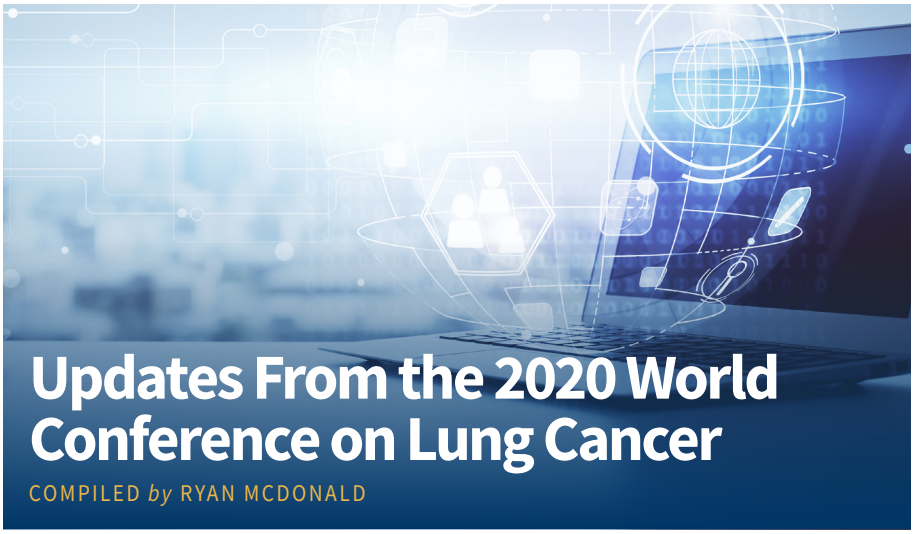
CURRENTLY, LUNG CANCER stands as the second most common cancer in both men and women. In fact, the American Cancer Society estimates that there will be about 235,760 new cases of lung cancer in the United States in 2021 — cases dropped over the past couple of decades, but it still has a high mortality rate. Over the past few years, however, lung cancer has changed significantly with improving outcomes, particularly attributable to immunotherapy, but how do we continue that trend?

Currently, cell-based therapies, including one known as chimeric antigen receptor (CAR)-T cell therapy, are in the very early stages of development for the treatment of non-small cell lung cancer (NSCLC), which makes up about 84% of diagnosed lung cancers today. The therapy, which transplants genetically engineered white cells known as CAR-T cells to specifically attack cancer cells, is leading to limitless possibilities in treating a variety of malignancies. These cells work by recognizing specific proteins expressed on cancer cells and then unleashing cytokines that kill cells on contact. Although CAR-T cells were initially developed and tested in hematological malignancies, there has been some difficulty in identifying which antigens are best for NSCLC and unique enough to cancer cells so as not to injure normal tissue. According to Dr. Adam Schoenfeld, a medical oncologist at Memorial Sloan Kettering Cancer Center in New York City, in an interview with *CURE*®: "The problem with lung cancer is that the cancer cells are constantly evolving, and they're all very different. It's very challenging to pick a specific target." Read more from Schoenfeld and others on the emergence of cell-based therapies in NSCLC in this issue's cover story.

With this in mind, researchers still prevail and are continuing to study and develop this method for a growing number of patient populations. Which brings us to the following questions: What kind of cell-based therapies are being investigated in patients with NSCLC? Why have cell-based therapies focused mainly on hematological malignancies in the past? And how do cell-based therapies — specifically, another one known as tumor-infiltrating lymphocyte (TIL) therapy — work in attacking NSCLC cells? Read more about the topic in this special issue of *CURE*®, where we identify the strengths and limits of CAR-T cell and TIL therapies, as well as other emerging treatments that could bring continued progress to the world of lung cancer.

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

MIKE KITADA



Updates From the 2020 World Conference on Lung Cancer

COMPILED *by* RYAN MCDONALD

Tagrisso Improves Survival Outcome in Patients With Non-Small Cell Lung Cancer Subset

TREATMENT WITH ADJUVANT TAGRISSO (osimertinib) was associated with an improvement in disease-free survival (the time after treatment without signs of cancer) in patients with EGFR-mutated non-small cell lung cancer (NSCLC), regardless of disease stage or prior chemotherapy treatment.

Adjuvant Tagrisso reduced the risk of death or disease recurrence by 84% in patients who had previously received adjuvant chemotherapy. The decrease was slightly lower, at 77%, in those who did not receive chemotherapy.

"The overwhelming (disease-free survival) benefit in patients in (the ADAURA trial) already supported the role of Tagrisso as a pioneering therapy in the adjuvant treatment of EGFR-mutated (NSCLC)," lead study author Dr. Yi-Long Wu, tenured professor at the Lung Cancer Institute at Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences in China, said in a news release. "The latest analysis shows the magnitude of that benefit is consistent with or without prior adjuvant chemotherapy and regardless of disease stage, reinforcing the critical role of Tagrisso in this setting."

A total of 682 patients (median age, 63 years; 70% women) with completely resected stage 1b, 2 and 3a NSCLC were enrolled onto the phase 3 trial. The main goal of the study was to assess Tagrisso's effect on disease-free survival, as well as overall survival, safety and health-related quality of life.

Preliminary results of the trial, which were presented during a medical conference earlier in 2020, demonstrated that adjuvant Tagrisso induced a significant improvement in disease-free survival in patients with stage 1b, 2 and 2a EGFR-mutated NSCLC. Median disease-free survival had not been reached with Tagrisso at that time, whereas treatment with placebo was associated with a median disease-free survival of 27.5 months.

Based on those results, the Food and Drug Administration in December approved Tagrisso for use in certain patients with EGFR-mutated NSCLC.

Updated results presented at this meeting showed that in patients who had previously received adjuvant chemotherapy, Tagrisso reduced the risk of death or disease progression by 85% in those with stage 2 disease and 87% in those with stage 3a disease. In a subgroup of patients who did not previously receive chemotherapy, Tagrisso reduced the risk of death or disease recurrence by 62% in those with stage 1b disease, 80% in those with stage 2 disease, and 90% in those with stage 3a disease.

Onivyde Produces Anti-Tumor Activity in Patients With SCLC Who Become Resistant to Chemo

DATA FROM THE PHASE 2/3 RESILIENT trial demonstrated that Onivyde (irinotecan liposome injection) shows promising anti-tumor activity in patients with small cell lung cancer who have become resistant to platinum-based chemotherapy in the first-line treatment setting.

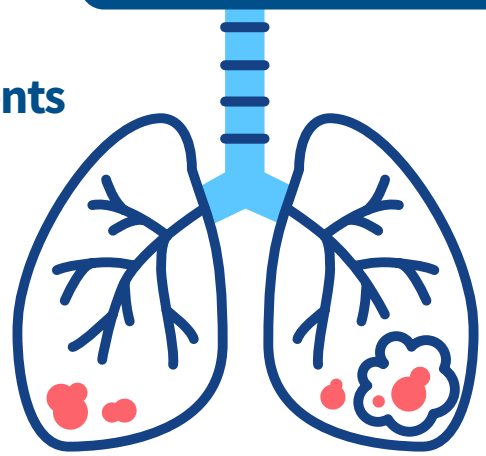
In the first part of the study, 30 patients (median age, 61.5 years; 56.7% women) received the study drug, and five of them received it at a higher dose (85 milligrams/square meter) than the rest of the patients (70 milligrams/square meter). Four of the five who received the higher dose experienced toxicities such as diarrhea and abnormal liver function and were considered to not have tolerated the dose.

Of the remaining 25 patients, one achieved a complete response, 10 achieved a partial response, seven had stable disease, five developed progressive disease and two were considered nonevaluable.

The median duration of response in the 25 patients who received the lower dose was 2.99 months, and median progression-free survival (the time from treatment to disease progression or worsening) was 3.98 months. Median overall survival reached 8.08 months in this group.

"(Onivyde) raised no new safety signals in patients with small cell lung cancer, and the anti-tumor activity observed was promising, warranting further study," study author Dr. Luis G Paz-Ares of the Hospital Universitario 12 De Octubre in Madrid said in a prerecorded presentation of the data.

Novel Therapy Shows Promise in Certain Patients With Non-Small Cell Lung Cancer



SOTORASIB (FORMERLY AMG 510), a KRAS G12C inhibitor, induced rapid responses in patients with KRAS G12C-mutated advanced non-small cell lung cancer (NSCLC).

Moreover, the data indicate that sotorasib is the first KRAS G12C inhibitor to show a progression-free survival (the time from treatment to disease progression or worsening) in a phase 2 study, according to a news release from the manufacturer of the agent, Amgen.

"These results are encouraging and clinically meaningful for patients with advanced (NSCLC) harboring the KRAS G12C mutation," lead study author Dr. Bob T. Li, a medical oncologist at Memorial Sloan Kettering Cancer Center in New York City, said in the release. "These are patients who have progressive disease after standard treatment, so they need additional treatments, and the fact that we are seeing rapid tumor shrinkages and durable responses in these patients is, for me, a step forward and a win for patients."

Previous results of a phase 1 study showed that sotorasib, among 35 previously treated patients with KRAS G12C-mutated advanced NSCLC, induced a 50% response rate.

In this phase 2 CodeBreaK 100 trial, patients received 960 milligrams of oral sotorasib once a day.

Treatment with sotorasib elicited a 6.8-month median progression-free survival in the patient population.

At a median follow-up of 12.2 months, patients who received sotorasib achieved a confirmed objective response rate (the proportion of patients who had a complete or partial response to treatment) of 37.1% and disease control rate (percentage of patients who achieved a complete or partial response and have stable disease) of 80.6%.

In terms of safety, most treatment-related side effects were mild or moderate in severity. There were no treatment-related deaths during the study. The most frequently reported all-grade treatment-related side effects included, but were not limited to, diarrhea (31%) and nausea (19%). Some patients (7.1%) discontinued therapy because of treatment-related side effects.

Patients With Lung Cancer May Need More Support, Education When Making Treatment Decisions

NEARLY HALF OF PATIENTS with and survivors of lung cancer reported that they were not knowledgeable enough about their treatment options before making a decision with their doctor, which may highlight the need for more educational materials and in-person counseling during the decision-making process.

Results from the survey also demonstrated that there may be a relationship between discussing treatment options with a doctor and a patient's involvement in the decision-making process.

Researchers assessed responses from 276 patients (mean age, 61.8 years; 67% women) with lung cancer in Cancer Support Community's Cancer Experience Registry. Patients in this study answered additional questions about their lung cancer diagnosis and treatment decision-making.

Regarding treatment decision-making, 67% of patients reported that they were quite a bit or very much involved in the process, compared with 33% who reported they were somewhat or not at all involved. In addition, 34% reported being quite a bit or very knowledgeable about their treatment options before going through the treatment decision-making process versus 66% who were somewhat or not at all knowledgeable about their options.

Findings also determined that 38% of patients would have liked more support before treatment decision-making, compared with 42% who did not feel that they needed more support. Sixty percent of patients were somewhat or not at all prepared to discuss treatment options with their doctor, compared with 40% who reported they were quite a bit or very much prepared to do so.

"Results suggest involvement alone is insufficient for an informed treatment decision-making experience and highlight a need for additional resources, such as treatment decision-making guides or in-person counseling, to enhance health care team communication surrounding treatment decision-making for individuals with lung cancer, particularly for economically disadvantaged individuals," said Kelly Clark, research manager at the Research and Training Institute at Cancer Support Community in Philadelphia, during a virtual presentation of the data. "Such efforts may provide patients better knowledge about treatment options, thus enhancing their preparation to discuss and select the appropriate treatment pathway."

LUNG ARTWORK: BACKWOODSDESIGN / STOCK.ADOBE.COM; PATIENT ARTWORK: MICROONE / STOCK.ADOBE.COM

Newly-Approved Lorbrena Shows Better Responses in Patients With Brain Metastases

The FDA recently approved an expanded indication for Lorbrena as a first-line treatment option for a subset of lung cancer that has spread to the brain. Compared to previously-approved options, experts say Lorbrena is more effective. By ANTONIA DEPACE

THE FOOD AND DRUG ADMINISTRATION (FDA) recently expanded approval of Lorbrena (lorlatinib) for use as a first-line treatment option for anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) that has also spread to the brain. That marks a step in the right direction for patients, but experts note there are still significant unmet needs.

"The difficulty we have is that the brain has a blood-brain barrier that protects itself from chemicals," Dr. Shayma Kazmi, medical director of thoracic oncology at Cancer Treatment Centers of America in Philadelphia, said in an interview with *CURE*®. "So really, systemic treatments like chemotherapy, which we used to use up until five or six years ago, would not penetrate the brain very well."

Brain metastases, or the spread of cancer cells from their original site to the brain, occurs in approximately one-third of patients with another type of cancer, according to estimates from Johns Hopkins Medicine. In general, research has shown that brain metastases are more common in certain cancers because of the biology of the disease. Lung cancer is one of the more common diseases that can spread to the brain.

Up to 40% of patients with lung cancer, according to Kazmi, develop brain metastases, and some already have it present at the time of initial diagnosis. In general, common symptoms patients should be aware of include headache, nausea, vision changes, clumsiness, forgetfulness and, under more serious circumstances, seizures.

Although it has been difficult to break the blood-brain barrier with conventional chemotherapies, there has been dramatic progress regarding treatment options for disease that has spread to the brain, Kazmi said. One is Lorbrena, which received an expanded approval on March 3. The drug had received an accelerated approval in November 2018 for the second- or third-line treatment of ALK-positive metastatic NSCLC.

The FDA based its decision to expand the indication of Lorbrena on data from the randomized, multicenter, open-label, active-controlled phase 3 CROWN trial, which was conducted in 296 patients with ALK-positive metastatic NSCLC. These patients had not previously received treatment for metastatic disease.

"The (trial) showed that Lorbrena, when compared to crizotinib (Xalkori), had better systemic responses, and almost 96% of patients didn't have brain metastases at one year, versus the 60% from crizotinib," Kazmi explained.

However, questions remain as to how to best treat metastases in metastatic NSCLCs that have no genetic mutation such as ALK or EGFR, according to Kazmi. "There's still a significant unmet need," she said.

Dr. Lecia Sequist, director of the Center for Innovation in Early Cancer Detection at Massachusetts General Hospital in Boston, questions how Lorbrena compares head-to-head with newer drugs such as Alecensa (alectinib) and Alunbrig (brigatinib), which are also showing to be effective. "These other available ALK drugs are exponentially better at getting into the brain compared with crizotinib," she said.

Sequist noted that patients should be aware of a new set of possible side effects associated with Lorbrena use since the drug was specifically designed to get into the brain. "These can cause mental and personality side effects that are a little different than we've seen with other ALK drugs, but they are usually well managed by reducing the dosage and educating people about the types of side effects," she said. Other symptoms patients should monitor are swelling of the feet and legs, weight gain and changes to the triglycerides that affect cholesterol.

When it comes to watching and treating brain metastases in general for patients with lung cancer, Sequist emphasized the importance of monitoring the brain along with the rest of the body — which can be difficult, depending on a patient's insurance. For those patients who have not received a diagnosis of brain metastases, she recommends getting an MRI at least once a year, or every six months if they are on a drug that doesn't also protect the brain, to monitor for disease spread.

cure® | LC LUNG CANCER HEROES®

Nominate your **Lung Cancer Hero** today!

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

Submit yours by June 30, 2021.

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

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

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

Founding Sponsor 2020: Takeda | ONCOLOGY

CANCER SUPPORT COMMUNITY
A Global Network of Education and Hope

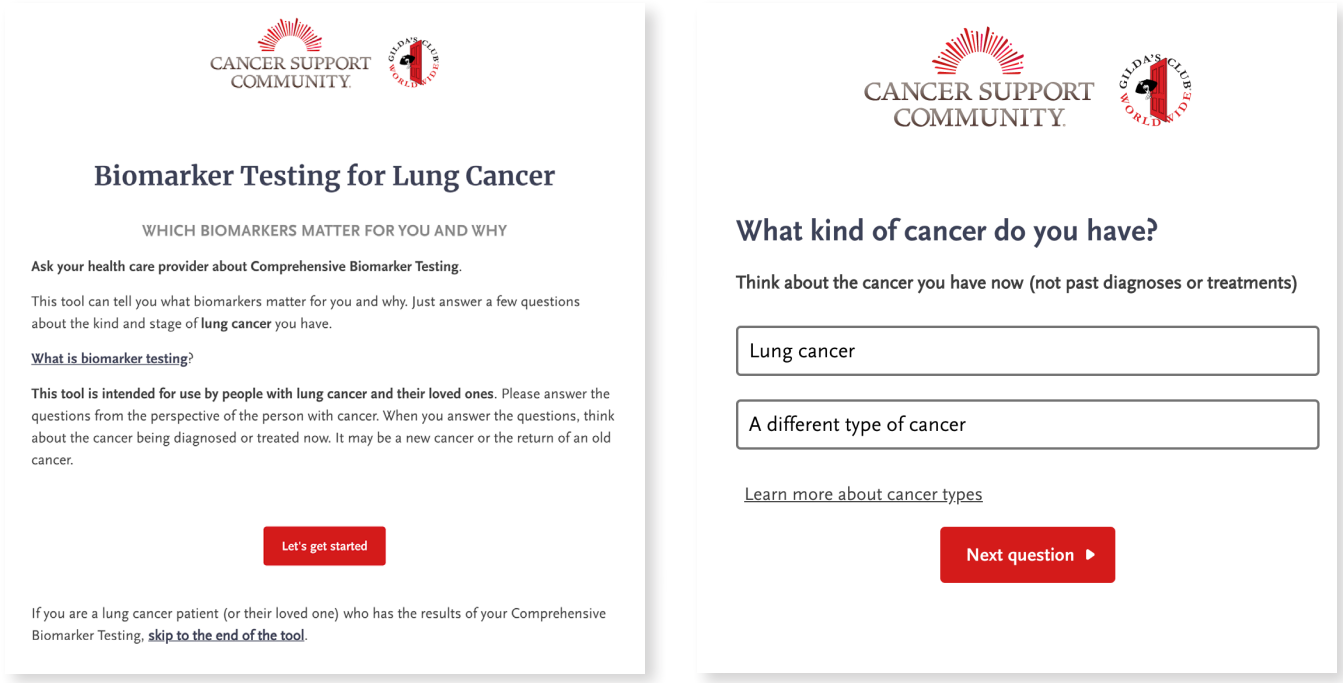
Biomarker Testing Tool Empowers Patients With Lung Cancer

By NICK POWER

TARGETED THERAPY IS CHANGING cancer treatment. Testing the tumor tissue, blood or bodily fluid of someone with cancer reveals the levels of genomic biomarkers in the person's cancer. These biomarkers — often referred to by a three- or four-letter abbreviation, such as ALK (anaplastic lymphoma kinase) or EGFR (epidermal growth factor receptor) — help identify the cancer's subtype. This process is called biomarker testing or molecular testing. Once the subtype has been found, a targeted therapy approved for that subtype can be used in treatment.

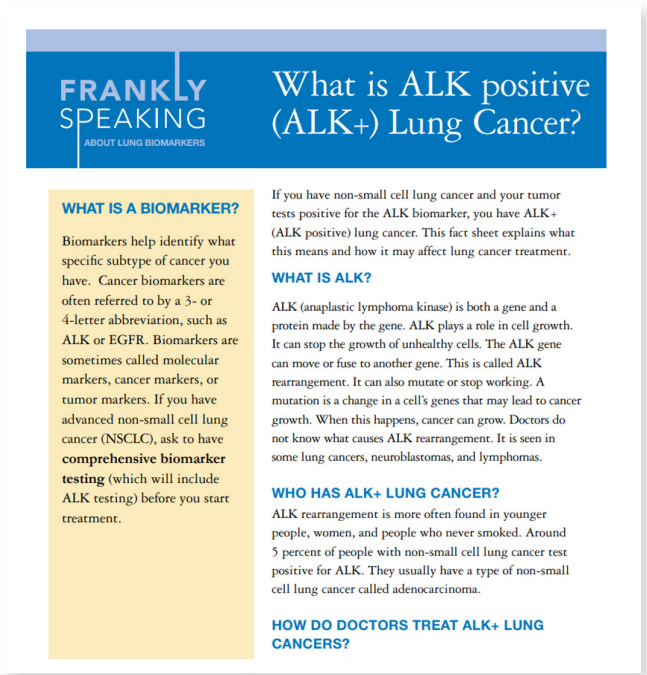
Targeted therapy drugs have been approved by the Food and Drug Administration as treatments for eight subtypes in non-small cell lung cancer alone. Like many major advances in cancer research, this has led to both improved treatment outcomes and a more complex treatment process for people with cancer. It is not always easy for people with cancer to access biomarker testing through their health care team. Even if they can, biomarker testing reports are often long and full of medical language. For these reasons, biomarker testing can be a discouraging process for people with cancer and their loved ones. This process can be made more complex by factors such as the stage of their cancer and whether it is a recurrence of cancer, which may limit or expand their targeted therapy options.

With this in mind, Cancer Support Community has developed a new tool for people with lung cancer and their loved ones. This platform asks a few brief questions and then connects users with specific information about how to receive biomarker testing, how to read results, which treatment options match their subtype, targeted therapies still in clinical trials and how to talk with their health care team about biomarker testing and targeted therapy. As targeted therapies are continually being approved for new subtypes, the tool is updated



The tool is made specifically for patients and their caregivers and asks step-by-step questions.

CANCER SUPPORT COMMUNI



After answering the questions, the tool educates users with specific biomarkers about their targeted therapy drugs.

often to make sure users have access to the most correct and complete information available.

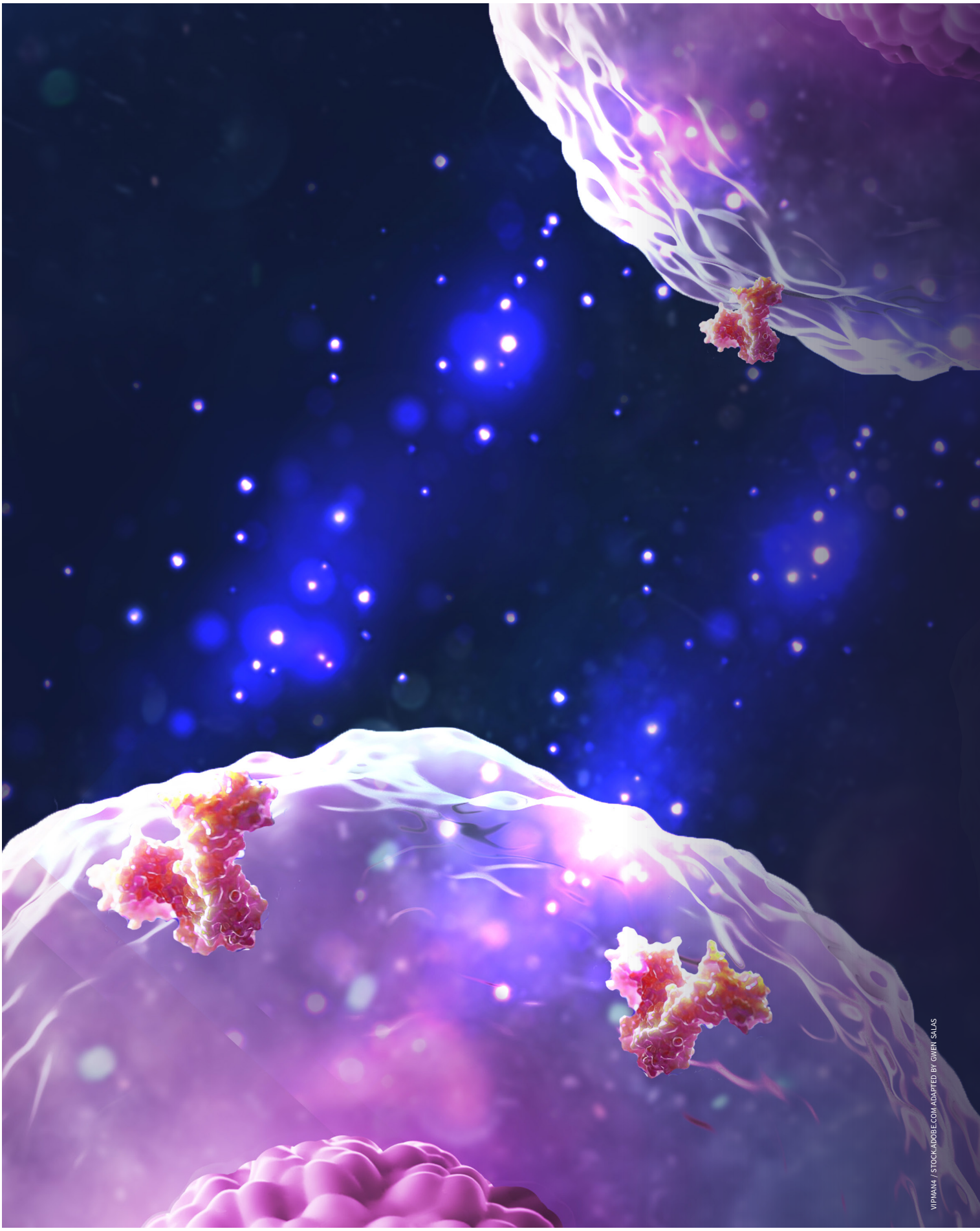
The tool also gives resources based on how much users already know about biomarker testing. Those who have not gotten biomarker testing receive information about the testing process and how to access it if it is not offered by their health care team. Those who have gotten biomarker testing and have their results receive information on how to read their results and what targeted therapy drugs may be a good fit based on their subtype.

"Oh, my God, this would have made it so much easier," says the husband of a lung cancer survivor after trying the tool, thinking about when his wife was told that targeted therapy may be an option. "I spent two months scouring the internet to educate myself. I look back and really do not know how we got through this time. If I had one website to go to, the amount of time and worry I spent searching the internet would have been much less."

The Biomarker Testing Tool can be used by any person with lung cancer no matter their cancer stage, cancer subtype or smoking history. It can also be used by caregivers and loved ones of people with lung cancer to answer the questions from the point of view of the person with cancer.

If you or a loved one is living with lung cancer,
SCAN THE QR CODE

to explore the Biomarker Testing Tool for yourself at **CancerSupportCommunity.org/BiomarkerTool**.



VIPMAN4 / STOCK.ADOBE.COM ADAPTED BY GWEN SALAS

CELL-BASED THERAPIES

May 'Level the Playing Field' in Non-Small Cell Lung Cancer

Even with all the recent advances in targeted therapies and immunotherapy drugs, patients with non-small cell lung cancer still need more treatment options. Although it's early, cell-based therapies have shown some promise, with more research underway.

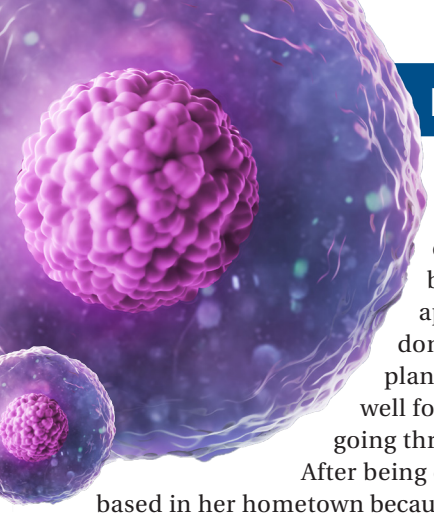
By MEERI KIM

In the fall of 2017, Deborah Barker noticed a strange pain developing on the left side of her body, around waist level. An avid scuba diver and underwater photographer, she thought it might be related to a back injury and requested an MRI from her primary care doctor.

The scan identified a lesion close to her spine, which was concerning. But she was floored after her biopsy when the pathology results came back with a diagnosis of stage 4 non-small cell lung cancer (NSCLC).

"It was really shocking. You think, 'Oh, God, this is it.' And my dad died of lung cancer in 2000," says Barker, 69, who lives in St. Petersburg, Florida. "I went through the normal, scary feelings for about a week, and then I remember being real anxious to start treatment."

Her local oncologist recommended radiation therapy right off the bat since the lesion was so close to the spine. But her tumor didn't have any of the gene mutations that would make her eligible for the newer targeted therapy drugs. Barker wasn't satisfied with receiving only the standard treatment regimen of chemotherapy and asked him about clinical trials for metastatic lung cancer. »



"I had gone through a clinical trial with my sister back in 2007. She had severe aplastic anemia and I was the donor for her stem cell transplant," she says. "That went real well for her, and it was kind of neat going through it all."

After being disqualified for a study based in her hometown because the researchers were unable to get a large enough biopsy sample, Barker headed to the much larger Moffitt Cancer Center in neighboring Tampa. There, she learned about a clinical trial for tumor-infiltrating lymphocyte (TIL) therapy, a type of cellular immunotherapy being newly tested in patients with NSCLC. It extracts immune cells present inside and presumably attacking the tumor, grows billions of them in a lab and then infuses them back into the patient.

Such approaches to immunotherapy, which involve modifying the patient's own immune cells to more successfully attack the cancer cells, were first used to treat melanoma or blood cancers such as lymphoma and leukemia. Recently, clinical trials have explored the efficacy of TIL therapy and another type called chimeric antigen receptor (CAR)-T cell therapy in other cancer types, including lung cancer. Early results appear promising and give hope to patients with metastatic disease, like Barker, who lack options.

"We have a long track record of a percentage of patients with metastatic melanoma getting durable, complete responses from TIL therapy dating back to the 1980s," says Dr. Ben Creelan, medical oncologist and principal investigator of the TIL therapy clinical trial at Moffitt. "Based on that positive experience, we wanted to take that into lung cancer and see if we could achieve similar results. Of the lung cancer patients we treated, a proportion of them have had durable responses lasting four years now, in some cases."

BREAKING DOWN CELL-BASED THERAPIES

Cell-based therapy encompasses a broad range of techniques that all include the injection or transplantation of cellular material into a patient. For example, bone marrow transplants infuse healthy, blood-forming stem cells into the body to replace damaged or diseased bone marrow. They could be cells from a donor or the patient's own cells.

Cellular immunotherapy — which includes TIL therapy, CAR-T cell therapy and others — specifically focuses on immune cells. TIL therapy extracts a patient's own TILs or immune cells that have moved from the blood into a tumor and stimulates their growth in tissue culture. CAR-T cell therapy, on the other hand, collects a type of white blood cell, called T cells, from a patient and genetically alters them to better identify cancer cells.

Both therapies then inject the modified immune cells back into the patient so they can go to work, newly empowered to attack the cancer cells. Patients usually need to receive chemotherapy before the infusion to wipe their immune system clean of other immune cells.

"The main side effects of cell-based therapies are due to this conditioning chemotherapy that can be a little bit rough," explains Dr. Erminia Massarelli, co-director of the lung cancer and thoracic oncology program and an associate clinical professor of medical oncology and therapeutics research at City of Hope in Duarte, California. "So the patient will need to be at a good stage of their well-being — we call it 'performance status' — to tolerate this type of chemotherapy. We cannot treat patients who are in a wheelchair, for example, or oxygen dependent."

Massarelli and her colleagues are currently recruiting participants for a phase 2 clinical trial investigating TIL therapy for patients with metastatic NSCLC. They are part of a recent wave of researchers hoping to transfer the success of cellular immunotherapy in hematological malignancies to lung cancer. At this point, the Food and Drug Administration has approved four types of cellular immunotherapy — all CAR-T cell therapies — for patients with different kinds of blood cancers.

These strategies have had limited efficacy in patients with solid tumors, mainly because solid tumor cells lack an easy target for immune cells to latch onto. Normally, T cells use receptors to attach to proteins called antigens on the surface of invading cells. This lock-and-key mechanism allows T cells to recognize and destroy the invading cells. CAR-T cell therapy adds a man-made receptor — the chimeric antigen receptor, or CAR — specific to a cancer-specific antigen to the patient's harvested T cells.

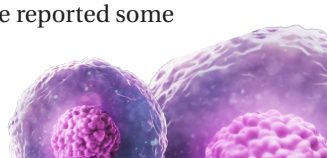
However, there isn't a widely expressed antigen in solid tumors that doesn't also appear on normal cells. So the infusion of modified cells might kill a patient's cancer cells but end up hurting healthy tissue in the process. In addition, solid tumors and their antigens mutate so frequently that using traditional CAR-T cell therapy on them becomes like shooting a moving target.

"The problem with lung cancer is that the cancer cells are constantly evolving, and they're all very different. It's very challenging to pick a specific target," says Dr. Adam Schoenfeld, a medical oncologist at Memorial Sloan Kettering Cancer Center in New York City. "Our therapies continue to evolve with new techniques, but we still face the challenge of a multitude of targets and potential resistance."

In this sense, TIL therapy has the advantage for treating lung cancer since the immune cells infiltrating a tumor are already trained against a patient's specific tumor antigens. The lymphocytes, after being extracted from the patient, go through testing in the lab to determine which ones best recognize the tumor cells. The front-runners are then chosen and allowed to multiply before going back into the patient.

ENCOURAGING EARLY RESULTS

TIL therapy remains in early stages for solid tumors other than melanoma, although recent studies have reported some



> When you're faced with stage 4 lung cancer, there's not much out there for people like me, so I didn't have one moment of hesitation about doing the clinical trial.
>
> — *DEBORAH BARKER*

« **DEBORAH BARKER** wasn't eligible for any of the newer targeted therapy drugs due to her tumor's gene mutations, so she sought out some clinical trials.

success in head and neck cancer and cervical cancer. Last year, Moffitt's phase 1 clinical trial in lung cancer demonstrated the safety and efficacy of TIL therapy for this patient population. Creelan and his colleagues recruited 20 patients with metastatic NSCLC, including Barker, and two have achieved complete responses with no evidence of disease on their scans.

"Stage 4 lung cancer traditionally has a lot of room to go when it comes to getting durable remission for patients," Creelan notes. "I would say that a good number of the patients we treated were never smokers and historically bereft of immunotherapy options, and now it seems like (TIL therapy) could level the playing field."

Overall, the clinical trial went smoothly for Barker, although things didn't happen exactly as planned. To collect the lymphocytes, a surgeon removed part of the tumor from her right upper lung with minimally invasive robotic surgery. While waiting for the immune cells to multiply in the lab, she received an immunotherapy drug called Opdivo (nivolumab) for about a month. To everyone's surprise, she fared very well on Opdivo — so much so that she didn't require TIL therapy after all.

"I was getting a good response, and then I was told, 'Well, we're not going to give you your cells,'" says Barker. "That was really interesting because I had a combination of being happy that I was responding but disappointed that I wasn't getting my cells."

Barker ended up receiving her cells almost a year later, when an imaging scan spotted a recurrence. Thankfully, Moffitt had frozen her billions of lymphocytes, and Creelan assured her they were still viable. She went through a grueling week of chemotherapy to flush her immune system clean, which left her fatigued and bedridden, and then received the infusion of cells over several hours.

Although the cell infusion itself doesn't have any notable side effects, other aspects of TIL therapy can take a toll on patients. Because of low blood cell counts, Barker needed blood transfusions after chemotherapy, and most patients in the study experienced low levels of albumin, phosphate and sodium in the blood. Other reported side effects included nausea and diarrhea. However, most of these side effects resolved after roughly 10 days. »

EMIL WHITE

In addition, all patients were put on interleukin 2, an immunotherapy drug that increases the growth and activity of T cells, for five days after infusion. Common side effects related to interleukin 2 use include fever, chills and other flu-like symptoms.

Although the initial results of this phase 1 trial seem promising, a much clearer picture should emerge within the next few years regarding the role of cell-based therapies in treating lung cancer. Investigators with phase 2 clinical trials by Massarelli, Schoenfeld and other research groups hope to publish their results by 2024 or earlier.

"I'm very curious to see the results of our current efforts with TIL-based therapies. I think the early data are encouraging, so this could be a potential option in the next few years if we have results similar to what we're seeing in melanoma translate over to lung cancer," Schoenfeld says. "One of the things we're exploring with these studies is looking at them in earlier settings and if that is potentially helpful."

WORKING IN COMBINATION

Experts believe cellular immunotherapy could be more effective if given to patients before their immune system becomes suppressed by chemotherapy and other forms of treatment. About half of the participants in Creelan's study, for instance, had not received any prior treatment.

"I wouldn't say that it's something that you would reserve for the very last line, because usually patients aren't healthy enough to go through with it if they've been through five or six different previous treatments," says Creelan. "Reserving a trial for the very end rarely works, because usually by that point, patients are too sick to be eligible for these kinds of studies."

Researchers are also exploring whether cell-based therapies could work better in combination with immunotherapy drugs like Keytruda (pembrolizumab). Early data suggest that pairing the two types of treatment may help reduce drug resistance and increase long-term response. Other studies focus on tweaking aspects of CAR-T cell therapy to make it more suitable for lung cancer, by evaluating new antigen targets that won't harm as much healthy tissue. And still others are testing less-established cellular immunotherapies for lung cancer like T-cell-receptor-engineered cells, double-negative T cells and clonal neoantigen T cells.

Regardless of the approach, one thing remains clear: Patients with NSCLC still need more treatment options, even with all the recent advances in targeted therapy and immunotherapy drugs. Not everyone responds to immune checkpoint inhibitors such as Opdivo and Keytruda or is eligible for targeted therapy drugs.

"The majority of non-small cell lung cancer patients actually don't have targetable mutations — I would say about 60% to 70% of non-small cell lung cancer patients don't have specific targets — so they are mainly treated with chemotherapy and immunotherapy," Massarelli says. "So cell-based therapies are very good options for these kinds of patients."

DEBORAH BARKER received TIL therapy through a clinical trial at Moffitt Cancer Center.

EMIL WHITE

After receiving TIL therapy through the clinical trial at Moffitt, Barker has been in remission since June and celebrated her three-year survival in October. She looks forward to getting back into the water with her scuba gear as soon as the weather warms up.

Although she normally travels to exotic destinations like the Galapagos Islands, the Philippines and Indonesia for her dives, the COVID-19 pandemic has thrown a wrench into Barker's international travel plans. But there are plenty of local options in her home state of Florida, and she feels an overwhelming sense of gratitude to have her life and health back.

"My quality of life has been great, and I feel completely blessed," Barker notes. "When you're faced with stage 4 lung cancer, there's not much out there for people like me, so I didn't have one moment of hesitation about doing the clinical trial."

Now Enrolling:

Lung Cancer Study

ONE-TIME THERAPY

Non-randomized, open-label (no placebo) trial

Tumor Infiltrating Lymphocytes (TIL) therapy: derived from your own immune cells.

Investigational TIL cell therapy clinical trial for participants with non-small cell lung cancer.

You or someone you know may qualify for the trial if certain criteria are met:

- Diagnosis of metastatic Non-Small Cell Lung Cancer (NSCLC)
- Progression on or following a single line of systemic therapy with an immune check point inhibitor + chemotherapy
- Fully active or able to carry out light work or activity
- At least one tumor that can be safely removed by surgery for TIL generation

If these key eligibility criteria are met, you may be eligible to participate in our clinical study program. There are additional eligibility criteria that must be met and can only be assessed by a study physician.

To learn more about the trial, call 1–866–565–4410

(Press option 3)

Email clinical.inquiries@iovance.com or,
Visit iovance.com/clinical/our-clinical-program/

Full eligibility details at clinicaltrials.gov
(Search: NCT04614103)

TIL Therapy is an investigational therapy and has not been approved for any indication by the Food and Drug Administration (FDA) or any other regulatory agency. The safety and effectiveness of this study has not been determined.

TRIAL SPONSOR

IOVANCE BIOTHERAPEUTICS

ADVANCING IMMUNO-ONCOLOGY

NO *SMALL* CHALLENGE

In recent years, research in treating small cell lung cancer has broadened, bringing emerging therapies like immunotherapy to the forefront.

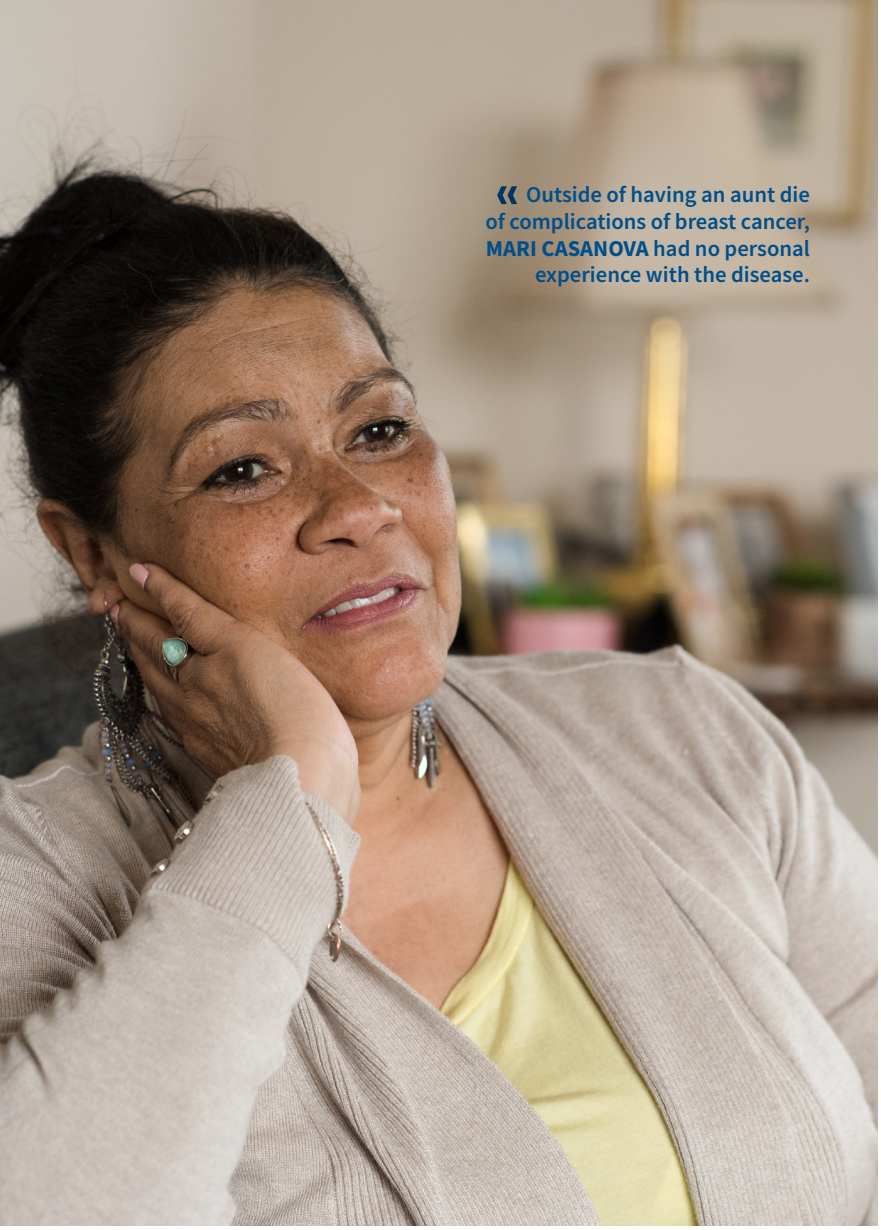
By ERIK NESS

For Mari Casanova, it started with a weird, dry cough. Her doctor wasn't alarmed and suggested cough medicine. But a few weeks later, the morning after a Pilates class in November, Casanova felt an unusual lump in her armpit. At first she wondered if she had pulled a muscle. Then she realized it was the size of small lemon, so she cleared her schedule and headed to her neighborhood hospital in Chicago.

> "'In three months, I'm going to be fine. I'm going to beat this.' I had no fear because I didn't understand that I could die."
>
> — MARI CASANOVA

A needle biopsy indicated cancer, but for nearly two months, her doctors couldn't pin down the origin. Finally, they located a spot, about the size of the back of an earring, in her right lung. She received a diagnosis of small cell lung cancer (SCLC). Her doctors said the lump in her arm was already spreading, and she was scheduled to begin three months of chemo 10 days later. A second opinion didn't happen. "I didn't have time to get the right doctor," she says. »

AVECTOR / STOCK.ADOBE.COM



« Outside of having an aunt die of complications of breast cancer, **MARI CASANOVA** had no personal experience with the disease.

On the treatment side, SCLC has been described as "a graveyard for drug development" in several studies, including one published in *Frontiers in Oncology* in 2020, where chemo alone was the standard for more than 40 years. And on the patient communication side, it was even more retro: Casanova's doctor never told her she was facing one of the most aggressively dangerous cancers known. "Yeah, he forgot the part about death," she says.

An aunt had died from breast cancer years ago, but otherwise, Casanova had no close personal experience with cancer. "I said, 'This is going to be easy for me' because I had no clue what chemo was," she says. "'In three months, I'm going to be fine. I'm going to beat this.' I had no fear because I didn't understand that I could die."

She tolerated the chemo well. Meanwhile, her sister Martha had questions and had been doing some research. She came along for what was supposed to be the last appointment. And when Martha started to ask hard questions, the doctor shooed her away with a gesture and left the room. Casanova collected her records and found another oncologist.

"And the first thing he did was explain to me that I could die." She pauses a bit at the memory. "Yeah, in a very sweet kind of way." He laid out a treatment plan: one more round of chemo and some radiation for the spot on her lung and to prevent brain metastases.

Casanova was fortunate in that patients with SCLC are often very overwhelmed by their symptoms. "They usually come in in pretty significant distress," explains Dr. Stephen Liu, director of thoracic oncology at Georgetown Lombardi Comprehensive Cancer Center in Washington, D.C. "This is not a subtle finding."

"My approach is to be very upfront, very open, very honest," Liu says. "Small cell lung cancer is an exceptionally lethal subtype of lung cancer. And I try to prepare patients for the journey that we're going on." Because it moves so fast, SCLC is almost always picked up at an advanced stage, and there's almost no role for surgery. Median survival for people receiving treatment like Casanova was only 10 months.

"It's a heartbreaking, terrible disease," adds Trudy Oliver, a lung cancer researcher at Huntsman Cancer Institute and an associate professor of oncological sciences at the University of Utah in Salt Lake City. "It's why we're in the lab trying to find things that will make a difference so that it doesn't have to feel like such a such an overwhelming death sentence."

UNDERSTANDING SCLC

According to the Centers for Disease Control and Prevention, lung cancer is the third most common cancer in the United States after skin and breast/prostate cancers, but most of that is non-small cell lung cancer (NSCLC). Its treatment has improved dramatically over the past two decades, marking one of the great success stories of modern oncology. SCLC makes up approximately 15% of lung cancers overall, or nearly 30,000 cases annually. Most SCLC can be linked to cigarette smoking. Its poor prognosis leaves few survivors, and the added burden of tobacco's social stigma means that SCLC hasn't benefited much from patient advocacy. But for more than a decade now, a dedicated cadre of researchers has been trying to crack one of the most challenging types of tumors in oncology.

"There was a period of time when small cell was largely ignored," says Dr. Charles Rudin, medical oncologist and chief of thoracic oncology at Memorial Sloan Kettering Cancer Center in New York City. "People really felt like this disease was too hard and nothing worked." That sort of negative reinforcement led to less research focus. Rudin's lab undertook one of the first major projects to turn this around: sequencing the small cell cancer genome. That knowledge base led to trying to define new targets for SCLC and accelerated the critical process of defining subsets of disease. "There's an opportunity to tease apart the biology of this disease and start to develop better and

KEN CARL

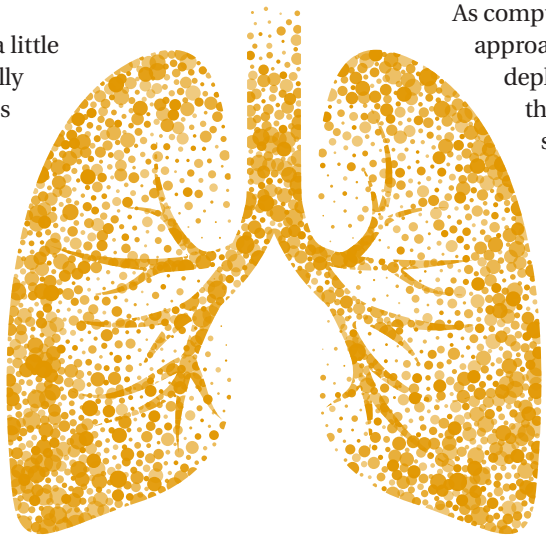
more focused therapeutic approaches," Rudin says. "It's not an uncommon disease at 15% of lung cancer. And there are few therapies that work, so patients are super eager to try something that's going to change their fate. I think it really was just waiting for people to come to the table and start to work on it."

Oliver took up this challenge after learning that existing mouse models of SCLC were slow, with tumors developing in the second year. The wait slowed research and limited its value in such short-lived organisms. Engineering a mouse to study a particular cancer is complex science. But after years of work, her lab succeeded: Its mice would get sick in just a few months. In the process, the researchers unlocked some small cell secrets.

"The tumors looked and behaved a little differently," Oliver says. "That was really our first clue that not all SCLC behaves the same way." Working with a group in Germany, she discovered her model was very sensitive to a particular class of drugs. SCLC could no longer be viewed as one disease, and that makes a difference in the clinic.

Dr. Lauren Averett Byers, an associate professor in the Department of Thoracic/Head and Neck Medical Oncology at The University of Texas MD Anderson Cancer Center in Houston, also jumped into the SCLC challenge. Her group is also focused on defining — and attacking — the molecular subtypes of SCLC.

Among the first things Byers worked on was defining SCLC's differences at an elemental level. SCLC is considered a neuroendocrine tumor, which is a cancer that begins in neuroendocrine cells with similar traits to hormone-producing cells and nerve cells. Its fundamental biology is rooted in how the cells of the nervous and hormonal systems work. NSCLC features a number of highly accessible biologic targets that have allowed major therapeutic advances. SCLC is more cryptic, Byers says. "It wasn't going to be as straightforward."



As computational biology advanced, one approach was to let the data talk. Her team deployed a battery of algorithms to analyze the growing library of SCLC tissue samples. "How many types of small cell lung cancer are there?" she asks. "Let's not be biased by what we think we know. Let the data tell us."

IMPACT OF IMMUNOTHERAPY

A year after Casanova began her SCLC treatment, John Williams was running a snowblower on his block. He was a few miles away, also in Chicago, and a heavy snow had been falling that January night. »

JOHN WILLIAMS started chemotherapy with Tecentriq a day after receiving his diagnosis; the FDA had just approved the drug as a part of the first immunotherapy-plus-chemotherapy regimen for SCLC.

ARIELLE GALLIONE

JOHN WILLIAMS was given two to four months, possibly a year, to live after receiving his diagnosis.

ARIELLE GALLIONE

Now 77, Williams is fit and retired, and he takes pleasure in helping out his neighbors. He had already cleared the sidewalks and was finishing a neighbor's driveway when it suddenly became difficult for him to breathe. He struggled to make it back to his house and collapsed into a chair. A few days later, he was still having breathing issues and was admitted to the hospital. They drained two liters of fluid from his lungs and ran a battery of tests: a PET scan, CT scan, an MRI, blood tests and a needle biopsy.

A few days later, Williams met with an oncologist, who told him he had SCLC and started talking about palliative care. She forecasted he had two to four months, maybe a year. "This can't be me," he thought, his mind shifting into overdrive. "I'm the active, 'go get 'em' kind of guy."

But it was him, and the very next day, he was getting chemo. And not just chemo. In March 2019, the Food and Drug Administration (FDA) approved Tecentriq (atezolizumab) as part of the first immuno-therapy-plus-chemotherapy regimen for SCLC. But the data that would lead to this approval had been released in September 2018, and Williams' doctors were already putting it to use. Williams laughed when his infusion nurses couldn't pronounce the drug name and suggested they call it "Bob."

"This is what I call a really major stroke of luck," he says, and he spent a lot of time thinking about his circum-stances. "I've got absolutely no control over the doctors, the medication, the progres-sion of the disease. I can do nothing. The only thing I can control, really, is my attitude. I can be negative or I can be positive," he says. "So I focused on the positive from that point forward. And that's an extremely difficult road because there's so much negativity around." He can't prove it, but he thinks the combination worked. "I'm thinking that the Tecentriq and attitude had a major, major effect on my physiology."

Williams was playing golf by the time the season opened a few months later. He lost his hair and discovered — to the detriment of his golf game — that eyebrows actually serve a purpose: They help keep the wind out of your eyes.

In fact, once the fluid was gone from his lungs, he felt no symptoms of his cancer. One of the major challenges comes with the tumor location; SCLC can quickly encroach on major airways and blood vessels. This challenge is mitigated by the disease being responsive to so many types of chemotherapy. "You can see double-digit response rates to over a dozen different chemotherapy drugs or two- or three-drug combinations," Liu says. "You can actually get

response rates that are quite high." Although patients might feel like things have gone back to normal, maintaining that response and preventing relapse is the real challenge. "We can't rest on the laurels of that initial response," Liu says. "We have to prepare for what will be in many cases an inevitable relapse."

Tecentriq improved those odds for the first time in more than 30 years. It didn't move the bar much, adding just a couple of months, but Liu still considers it a breakthrough. "I appreciate that it's not necessarily the breakthrough that everyone wanted, that the survival gains aren't of the magnitude that people are waiting for, that patients deserve," he says. "I'd consider it the first step; hopefully, the first step of many. When we add immunotherapy to chemotherapy, we improve survival. There's no doubt about it."

In 2020, a second immunotherapy agent, Imfinzi (durvalumab), was granted FDA approval in combination with chemo. It is not the same as Tecentriq, but both are anti-PD-L1 agents with very similar survival results. In Liu's mind, they are equivalent.

Rudin also acknowledges that although Tecentriq and Imfinzi don't extend survival tremendously, they represent a significant advance. "A subset of patients between 10% and 15%, maybe 20%, do derive significant benefit from immunotherapy. That can be transformative for those patients," he says, providing hope even for patients with advanced stage disease. "That gives us an important proof of principle that this is a disease that can be amenable to appropriate therapy."

A quick look at the numbers makes it easy to tell when a subset of patients in a clinical trial is doing significantly better, raising expectations like an A student breaking the curve. The real challenge comes in finding out why. Often the idea behind a drug points the way, and simply testing biomarkers for the drug pathway yields the answer.

SCLC hasn't been so transparent, which is part of what drove Byers' computational group. As expected, their analysis confirmed three of the major variations the field has been defining. But the project also unmasked a fourth group, which they described as inflamed SCLC. It hadn't been on anybody's radar. "It was incredibly exciting because we've really struggled in SCLC to understand who gets the most benefit from immunotherapy," she says. Although obvious biomarkers haven't worked out, this new, computationally defined group appears to survive almost twice as long as the other groups treated with chemo plus immunotherapy.

Inflamed SCLC had higher markers of immune infiltration and of important immune checkpoints. Immunotherapy works by manipulating the body's immune system, and now researchers have a footprint to work with. "There are obviously many questions and things left to test," Byers says.

LOOKING TO THE FUTURE

Tecentriq worked for Williams for an estimated 10 months (from February to December 2019), then he was put on Abraxane (paclitaxel). In the autumn of 2020, his cancer returned and is now trying to take hold in his liver. Relapse is a scary time for all patients with cancer, but particularly for patients with SCLC. "Our first shot is always our best shot, and part of that is because when small cell lung cancer does relapse, it does so unforgivably," Liu says. Many patients never get more than first-line treatment.

> **"The only thing I can control, really, is my attitude. I can be negative or I can be positive."**
> *—JOHN WILLIAMS*

But once again, Williams is just in time for another new treatment. Zepzelca (lurbinectedin) received FDA accelerated approval in June 2020, the first approved use of the new agent. It is exciting for patients with SCLC because the only other approved chemo drug at this stage is topotecan, known for its extensive list of uncomfortable and brutal side effects. Zepzelca presents its own difficulties but is generally easier to handle and can be effective against cells that have developed early resistance to platinum-based chemo.

Zepzelca is a welcome addition to a limited armamentarium, though its future was clouded when its phase 3 trial came up short of expectations in December 2020. "We see a lot of patients with recurrent disease," Rudin adds. "We're exploring many of the new therapeutic targets in patients with recurrent disease."

Oliver describes the unique challenge of SCLC using M&M's. Imagine your newly treated cancer is a bag of blue M&M's, and you're fortunate to have a cancer drug that wipes out blue M&M's. "If my bag of M&M's was all blue, I could wipe out that bag pretty quickly," she says. But if your bag contains five colors of M&M's, the blue drug is going to be limited. With SCLC, what actually happens is that some blue M&M's die, but others change color. "That ability to evolve and change rapidly and easily? That's a massive challenge," Oliver says.

"That's how they escape or adapt," Byers adds. Researchers need to figure out how they're switching colors and how to block that. They can also refine the classic cancer strategy of combining drugs that hit more than one color. "I think that's doable," she says. As hard as drug development has been for SCLC, she says it may be one of the most amenable tumors for developing a so-called liquid biopsy: using genetic information available in blood to target the disease.

"My hope is that within the next five years, we will start having biomarker testing to guide treatment," Byers says. C

EARLY Introduction to Supportive Care Greatly Benefits Older Patients With Lung Cancer

Because of their age, disease state and comorbid conditions, older patients need supportive care.

By DON VAUGHAN

When Frank Giunta, 82, of Collegeville, Pennsylvania, was diagnosed with non-small cell lung cancer (NSCLC) in August 2020, he was assured by his caregivers at Penn Medicine's Abramson Cancer Center in Philadelphia that he would not be alone during his treatment journey. Accompanying him would be a multidisciplinary supportive care team dedicated to ensuring that everything went smoothly, with as little impact as possible on his quality of life.

Giunta's treatment was complex. He received more than 30 proton radiation treatments and multiple sessions of chemotherapy. A feeding tube was inserted when esophagitis from the radiation treatments made swallowing painful. He spent 17 days in the hospital, and three days after he returned home, his wife died from complications of lung and breast cancer. »

MONGKOLCHON / STOCK.ADOBE.COM

"It was a difficult journey made more comfortable by supportive care," Giunta says. A nurse visited twice a week and taught his two daughters how to care for him. A physical therapist assisted with balance issues, and a speech therapist helped him overcome swallowing difficulties related to the esophagitis.

"I wouldn't have known what to do without supportive care," Giunta says. "They made my life and recovery much easier."

Giunta's experience is typical among patients with lung cancer, who tend to skew older. According to the American Society of Clinical Oncology, the average age at the time of diagnosis for advanced lung cancer is 70. This age group also tends to have more comorbidities that can affect treatment type, outcomes and quality of life.

The good news: A growing body of research suggests that the early introduction of supportive care greatly benefits older patients with lung cancer physically, emotionally and psychologically.

"Supportive care is essentially the many different measures we put in place to take care of the whole person," says Dr. Christine Ciunci, an assistant professor of clinical medicine and section chief of hematology oncology at Penn Medicine. "We provide treatments, either curative or palliative, to help patients live the best life that they can and feel their best for the longest amount of time possible. It's a multidisciplinary approach that includes cancer treatments as well as the prevention and treatment of side effects, social work, nutrition, physical therapy, speech therapy, home care, palliative care and management of comorbidities such as COPD, heart disease and diabetes. Supportive care encompasses all of these things and is what I spend a lot of focus on as an thoracic medical oncologist."

> "It was a difficult journey made more comfortable by supportive care."
> — FRANK GIUNTA

Supportive care for older patients with lung cancer has evolved in recent years as researchers explore its need, scope and efficacy. Key aspects are a greater appreciation of the complexity of cancer care and the increased role of supportive care throughout the process, says Dr. Arif Kamal, an associate professor of medicine at Duke University School of Medicine and a member of the Duke Cancer Institute in Durham, North Carolina. "Referral to a specialist, such as an endocrinologist for diabetes, makes sense because it's good care to provide that extra layer of support to the patient," he explains. "Cancer care delivery in 2021 is a team sport, and as a team sport, we can't be shy about asking for help when we need it."

Equally important is acknowledgement that supportive care is most effective when started early in the treatment process. Helping to drive this concept are the findings of a seminal 2010 study published in the *New England Journal of Medicine,* which found that among patients with metastatic NSCLC, early palliative care led to big improvements in quality of life and mood. In addition, compared with patients receiving standard care, patients receiving early palliative care had less aggressive care at the end of life but longer survival.

"Over the years, palliative care has evolved and become a standard of care for these patients," Ciunci says "We have more options to help patients and more supportive measures in place than we did even just a few years ago. It has been very beneficial for our patients."

Supportive care goes by a number of different names, Kamal notes. The majority of programs call themselves palliative care, some call themselves supportive and palliative care, and others call themselves supportive care only. Among them, the services are essentially the same. "We advocate for multidisciplinary care that involves physicians, nurses, chaplains and social workers, at a minimum, but also care navigators, physical therapists and others," Kamal says. "We find large variability across the country."

Patients with lung cancer commonly require more supportive care than patients with other types of cancer due to their age, the stage of their disease and the presence of comorbid conditions, sometimes including intrinsic lung disease. "Patients with lung cancer can have significant symptom burden at the time of diagnosis, especially those with metastatic disease," notes Dr. Robert Daly, a thoracic medical oncologist at Memorial Sloan Kettering Cancer Center (MSK) in New York City. "They can have underlying pain from their metastases, as well as fatigue, loss of appetite, shortness of breath and cough, so there is a clear need within this patient population."

Patients with lung cancer may also experience psychological and emotional issues related to existential distress. Former smokers, for example, may feel depressed because they blame their lifestyle for their cancer. Others may experience conflict with their spirituality, questioning why they developed cancer despite living a healthy life, or believing that their cancer is some sort of punishment. Kamal recalls a patient who had received an abortion in her teens and refused pain management for her cancer because she felt she had to atone for her perceived sin.

"I don't have the skills to deal with that, but I do have people on my team, such as chaplains, who do," Kamal says. "It affects everything."

Not all patients experience a crisis of faith, however. Patrick Hidalgo, 79, of Boynton Beach, Florida, turned to prayer to help him deal with post-operative pain and other issues following a diagnosis of stage 3A lung cancer

PATRICK HIDALGO received post-surgical wound care through a visiting nurse and was placed on an exercise regimen by a physical therapist to help him regain strength.

in May 2020. "I don't like taking drugs, and prayer was very effective for me," Hidalgo says.

A patient's need for supportive care is commonly determined through a close assessment of their disease, symptoms, physical condition, home support, transportation options and much more. Through candid conversation, the supportive care team can help the patient determine their specific goals, whether curative or palliative, and create a plan to achieve those goals.

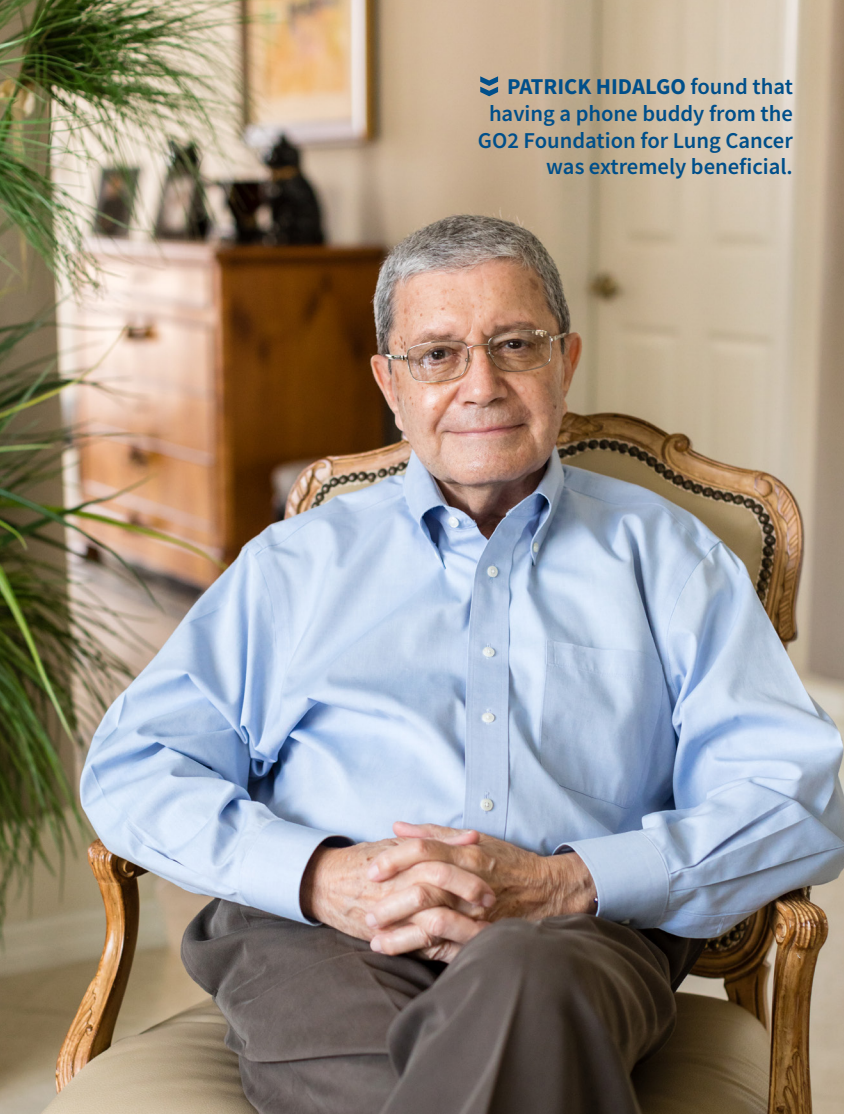
"The medical oncologist works closely with the patient to manage their symptoms, from the disease and from any toxicities resulting from treatment," Daly explains. "But involvement of a supportive care specialist also helps benefit the patient by integrating their expertise with that of the medical oncologist."

Supportive care is typically tailored to the patient, though certain aspects are common to all, Ciunci says. These include addressing the side effects of treatment and ensuring access to a social worker. "This is important to ensure the patient has all the resources they need at home," Ciunci explains. "Home care is highly valued for these patients."

Hidalgo received post-surgical wound care through a visiting nurse, who also taught Hidalgo's wife, Josie, how to help him as needed. In addition, a physical therapist placed him on an exercise regimen to keep his body strong while he healed. The process was an eye-opener. "I was in great shape," Hidalgo says. "I was riding a bike 10 miles a day. Then I got sick and everything changed."

The early introduction of supportive care can have a positive effect on treatment outcomes and quality of life. "There are good studies that show that timing does matter," says Kamal. "When we think about best-practice palliative and supportive care, we are talking within 12 weeks of diagnosis. The reason for that is, an ounce of prevention is worth a pound of cure when we talk about distress. If we start supportive care at the same time we start treatment, we can prevent complications from happening, anticipate them and have a plan in place to manage them. This keeps »

GÖZDE TURGUT



PATRICK HIDALGO found that having a phone buddy from the GO2 Foundation for Lung Cancer was extremely beneficial.

the patient from having to go to the emergency room at 2 a.m. when the pain worsens."

Older patients with lung cancer sometimes encounter barriers to receiving supportive care. A lack of transportation is one of the most common, especially for those who may depend on family, friends or public transportation to get around. Many cancer centers have turned to telehealth to make visits with doctors and other care providers easier but, as Ciunci notes, a large percentage of older people do not have smartphones or laptops. "It can sometimes be difficult to connect patients to these valuable resources due to a lack of comfort with certain technologies," she observes.

Financial difficulties also can be an obstacle to supportive care, Ciunci says. A patient who is seen by the oncology team once a week, for example, may be overburdened if required to return for a palliative care visit or physical therapy session on a separate day. Financial issues may include the expense of child care, lost work time, and even the cost of gas and parking. Additionally, many patients cannot afford certain basics integral to their care, such as nutritional supplements and home health equipment.

"We may be able to provide access to samples, coupons and programs, but it doesn't take care of everything," Ciunci says. "Some patients may be reluctant to come in for visits because they simply can't afford the copay. Luckily, at Penn Medicine, we are able to offer financial assistance and specialized resources, but not every program can."

Over the past year, patients with lung cancer faced another unexpected obstacle: the COVID-19 pandemic. When it came time for him to begin chemotherapy, Hidalgo decided to have it done at MSK, where COVID-19 cases were dropping, rather than in Florida, where cases were spiking. The supportive care he received from his oncology team at MSK was primarily process oriented, he says, as they guided him through the realities of treatment, side effects and more.

Supportive care is an essential key to the effective treatment of lung cancer, and older patients are encouraged to become their own advocates. "My advice is for patients to ask their oncology team early and often about supportive and palliative care resources, to add all the extra layers of support they can to their team, so that several minds are thinking about their distress from all angles," Kamal says. "I would ask (as a patient), 'What supportive or palliative care resources do you think could help me?' and predicate the question on a clear and mutual understanding of what quality-of-life issues the patient and their family are facing. If everyone isn't on the same page, there is a real risk of the oncologist underappreciating the unmet needs that can be addressed through additional services."

Find a team that you work well with, Ciunci adds. "Your oncologist should be asking, 'What are your goals for your cancer treatment, and what do you want for the future?' I think that's extremely important so that your team can tailor your treatment approach based on your objectives," she notes. "And of course, if you haven't been given access to a social worker, nutritionist, physical therapist or palliative care provider, you should ask. These are things that should be readily available to you during treatment."

From a patient perspective, Hidalgo encourages others to reach out to support organizations such as the GO2 Foundation for Lung Cancer. Hidalgo benefited greatly from a phone buddy there and now works in a similar capacity helping others. "My interaction with the GO2 Foundation was the most impactful component of my recovery," he says. "Now I help out by reaching out to others in the lung cancer community."

GÖZDE TURGUT

CANCER

Did you know you can sell your life insurance for immediate cash?

- *No Fees*
- *No Obligation*
- *Most Settlements are Tax Free*
- *No Doctor Visits Necessary*
- *Private and Confidential*
- *Immediate Cash*

For peace of mind, confidentiality, and expert advice, trust in the strength and stability of an industry leader.

Call Greg or Lisa today.

- *Group Life*
- *Term Life*
- *FEGLI*
- *Whole Life*
- *Universal Life*

Available in most states.

Working with cancer patients and their families for over 23 years.

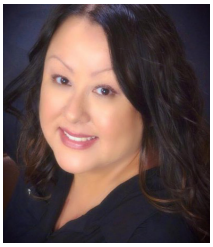
LIBI
LIFE INSURANCE BUYERS, INC.
Since 1995

1-800-936-5508

www.lifeinsurancebuyers.com

Quelling COVID-19 and Cancer Fears

As part of its "Speaking Out" video series, CURE® spoke with Katie Brown from LUNGevity about challenges that have arisen from the COVID-19 pandemic — including delays in screening — and resources to help patients through these trying times. By KRISTIE L. KAHL



KATIE BROWN

A YEAR AFTER PEOPLE were told to stay home for two weeks to "flatten the curve," the COVID-19 pandemic still affects many, especially those with cancer.

Amid reports that many people have delayed important screenings and/or treatment during the pandemic, and with many feeling the psychosocial impact of social isolation, organizations such as LUNGevity are offering a variety of resources to help patients with lung cancer.

As part of its "Speaking Out" video series, *CURE®* spoke with Katie Brown, vice president of support and survivorship programs at the LUNGevity Foundation, about the challenges patients have experienced throughout the pandemic and ways the organization can help those in need.

Q: *CURE®*: To start, should there be a concern regarding delayed treatments and disease progression or mortality related to the COVID-19 pandemic?

A: **Katie Brown:** I feel like individuals who are at high risk of developing lung cancer are not showing up for their lung cancer screenings. And this will definitely increase the number of patients who will be diagnosed with advanced stage lung cancer. Also, I think what concerns us and health care professionals are patients who are canceling or postponing not only their scans and their follow-up scans but also their wellness visits due to COVID-19 fears.

Q: How can we try to address these fears and combat the potential challenges?

A: I think that information is key. It's important to convey to patients that hospital systems are taking great care to protect against COVID-19 spread within the hospital. I know that in some hospitals, COVID-19 patients and critically ill persons enter through different parts of the hospital than (patients coming in for) scans and office visits. Hospital staffs are also screening everyone who enters for COVID-19 symptoms and limiting who can go into the hospital. And because we know that early detection saves lives, patients should not skip their treatments or appointments or even their yearly wellness exams.

Q: You mentioned that one challenge is patients skipping their appointments. What are some of the additional hurdles we've seen in lung cancer during the pandemic?

A: You know, all of us are experiencing challenges right now during the pandemic. What I'm seeing universally across all of our communities is the feeling of social and emotional isolation.

Q: What can we do to address that kind of challenge and help others feel less socially isolated?

A: A huge benefit is the technology that we have today at LUNGevity. We have many online communities for patients to utilize. Last year, when the pandemic began, we pivoted our in-person events to a virtual platform, and we partnered with other organizations to engage within our lung cancer community. We also have a virtual patient and caregiver meetup via Zoom four times a week, and we're considering doing it daily to meet all the challenges that our patients face.

Q: Are there other resources available that patients can turn to during these trying times?

A: Yes, absolutely. Patients can use our lung cancer help line for professional psychosocial support, financial support and access to resources. We also have a lung cancer mentor program called LifeLine that patients can sign up for, and that's where they can request a support mentor. We also have many vibrant online communities and message boards.

Q: To bring it all together, what is your biggest piece of advice for an individual who has lung cancer and is trying to make their way through this pandemic?

A: My biggest piece of advice would be to let them know that they are not alone. Although we can't physically be together, there are ways that a patient can plug into our community for social interaction, peer support and advice.

LUNG FORCE™

American Lung Association.

Lung Cancer Patient Virtual Meetup

Save the Date

May 11 | **12:00 – 5:00 PM ET** Exhibit Hall will open at 11:30 AM

The Lung Cancer Patient Virtual Meetup program is designed for lung cancer patients and caregivers to learn more about the latest trends, resources and research surrounding lung cancer. With our new meeting platform, you will feel like you're attending an in-person conference but from the comfort of your own home. Join us for this dynamic event where we will provide you with the latest need-to-know information about your specific lung cancer.

Registration is Free

Learn more at Lung.org/Patient-Meetup.

Sotorasib Shows Promise in Non-Small Cell Lung Cancer Subset

Treatment with sotorasib induced a 6.8-month median progression-free survival in patients with KRAS G12C–mutated advanced non-small cell lung cancer. *by* RYAN McDONALD

DATA FROM THE PHASE 2 CodeBreaK 100 trial demonstrated that treatment with sotorasib, a KRAS G12C inhibitor, induced rapid responses and encouraging progression-free survival outcomes in previously treated patients with KRAS G12C–mutated advanced non–small cell lung cancer (NSCLC).

"Because of the way that mutant RAS protein interacts with some of the proteins in the cell, it is a really hard target for drug development," study author Dr. Vamsidhar Velcheti, director of thoracic medical oncology at NYU Langone's Perlmutter Cancer Center, said in an interview with *CURE*®. "Because of that, a lot of efforts by several cancer researchers over several decades have failed because we could not develop good drugs against this RAS gene."

As Velcheti noted, recent advances led to novel therapies that target the RAS mutation. But, he said, the story has been different for patients with the KRAS G12C mutation, which occurs in approximately 10% to 15% of all lung cancers.

"Previously, we've not had any targeted therapy treatment options for these patients," he said. "And the CodeBreaK 100 trial demonstrates that this drug, sotorasib, can shrink cancers and is extremely well tolerated compared to traditional chemotherapy."

Data from a prior phase 1 trial of the investigational therapy showed similar results in 35 previously treated patients with KRAS G12C–mutated advanced NSCLC. At the time, the study results demonstrated that sotorasib induced a 50% response rate in these patients.

In the phase 2 CodeBreaK 100 trial, 126 patients were given 960 mg of oral sotorasib once daily.

Eighty-one percent of patients had previously progressed after receiving platinum-based chemotherapy and PD-1/PD-L1 inhibitors; the remainder had progressed after receiving one of these therapies. The data cutoff date was Dec. 1, 2020.

The results of the phase 2 trial showed that sotorasib induced a 6.8-month median progression-free survival (the time from treatment to disease progression or worsening) in patients with KRAS

CONTINUED ON PAGE **36**

Real-World Patients May Have More Side Effects From Immunotherapy for Lung Cancer

Results of a study focused on patient-reported experiences found that aching joints, sore muscles and fatigue were more common than initially found in clinical trials.

by DARLENE DOBKOWSKI, M.A.

STUDY FINDINGS BASED ON patient-reported outcomes demonstrated that the rate of side effects from immune checkpoint inhibitors to treat lung cancer were higher than previously shown in clinical trials.

The study, which was published in *Cancers*, was one of the first studies to use patient-reported outcomes to assess this area compared with clinical trials, which often enroll healthier patients than those in the real-world setting.

"What's really exciting about this study is that it focused on patients in the real world — primarily those not treated on a clinical trial — who had received immune checkpoint inhibitor therapy for lung cancer," said Dr. Heather S.L. Jim, senior member of the Department of Health Outcomes and Behavior and co-leader of the health outcomes and behavior research program at Moffitt Cancer Center in Tampa, Florida, in an interview with *CURE*®. "Patients who participate in clinical trials tend to be younger, healthier and less racially and ethnically diverse than patients who are treated with these agents as part of standard of care."

Dr. Adam P. Dicker, senior vice president, professor and chair of the Department of Radiation Oncology, and director of the Center for Digital Health & Data Science at the Sidney Kimmel Cancer Center at Thomas Jefferson University in Philadelphia, told *CURE*® about some of the distinct differences between patients in a clinical trial and those in the real world. "In general, clinical trials … will have patients who are more fit, whose performance status is better or feeling better, etc., and people are certainly motivated to go on clinical trials," Dicker said. "In the real world, the patient may not be as healthy, and they have other comorbidities or other medical conditions that may not have allowed them necessarily to go on the clinical trial but certainly allows them to use medication that is appropriate to treat their cancer."

In this study, researchers analyzed outcomes reported by 226 patients (mean age, 61 years; 75% women) who participated in the GO2 Foundation's Lung Cancer Registry. In particular, this registry included patients with lung cancer who were

BEARSKY23 / STOCK.ADOBE.COM

treated with immune checkpoint inhibitors such as Imfinzi (durvalumab), Tecentriq (atezolizumab), Keytruda (pembrolizumab) and Opdivo (nivolumab).

"When all of these checkpoint inhibitors came on the scene, it really was a paradigm shift because there are patients who previously were noncurable, and the disease this study focused on is lung cancer," Dicker said. "There's no question it's a game changer. What's been appreciated is that when you release the brakes on the immune system, there's a variety of side effects that occur, and that hasn't been as well studied as the clinical aspects in terms of whether patients respond or not, what the cure rate is, etc."

All patients completed a survey focused on quality of life, which allowed researchers to evaluate the rates of common side effects with these immune checkpoint inhibitors.

Patient responses from these surveys showed that quality of life was worse compared with that of the U.S. population and patients from previous clinical trials. During treatment with immune checkpoint inhibitors, the most common side effects considered moderate to severe included aching muscles (20%), aching joints (27%) and fatigue (41%).

"One of the most striking findings in this particular study was the fact that fatigue and aching joints and muscles were among the most common side effects that patients reported," Jim said. "That's useful information because there are empirically supported treatments for fatigue, for aching joints and aching muscles, in people with cancer, and so we can begin to address some of these issues with better supportive care for these patients."

In addition, 11% of patients reported a visit to the emergency room, 25% reported a delay in treatment, and 9% reported being hospitalized, all of which were associated with toxicity.

> **"It's really important that we hear from a wide diversity of patients because it helps us to better understand the patient experience more broadly."**
>
> *—DR. HEATHER S.L. JIM*

"It's kind of eye-opening that 1 out of 10 patients — or at least in the patients we looked at with lung cancer — are going to visit an emergency room and about the same percentage were hospitalized," said Dicker.

Both Jim and Dicker mentioned that could be improved through remote monitoring, using technology to track a patient's activity and side effects. This is an active area of interest at the Jefferson Center for Digital Health & Data Science and part of the Sidney Kimmel Medical College curriculum for medical students.

"We're entering an exciting time in behavioral science," Jim said. "With the rise of smartphones and smartwatches, people can become citizen scientists. If you view them as experts in their own experience, and they are able to share that experience with researchers, it really helps us understand larger patterns in cancer survivorship." This is an active area of research for the doctors at their respective institutions.

Jim added that collecting data in this manner requires little effort from the patient. "This can be a form of passive monitoring in the sense that as long as the patient gives us permission to access this data, there's really very little burden to them," she said. "They're just going about their daily routine. It's really a treasure trove of data for behavioral scientists. The data are collected in a way that protects the privacy of patients."

Dicker said studies focusing on patients reporting their experience can potentially empower them to participate in more registries and studies. "By being at the table, by contributing and making sure that these types of studies get more popular and that they give back to the patient, I think you'll get greater involvement," he said. "Then, ultimately, you want patients who are part of the design process of the registry process. People talk about patient advocates. It's more than just advocating; they're playing an active role in the design of that study. I think that really then comes full circle. This is a step in that direction."

Not only do patients have the opportunity to report on their own experiences, but these surveys also allow researchers to access more information on a broader patient population.

"It's really important that we hear from a wide diversity of different patients because it helps us to better understand the patient experience more broadly," said Jim. "Then we can use that information to provide better data to the patients themselves."

In the meantime, Jim also emphasized the importance of patients talking with their doctor about any side effects experienced throughout treatment. "If patients have questions about some of the side effects they're experiencing, (they should) talk to their doctor as a reliable source of information," she said. "Anecdotal stories from other patients may not be generalizable to their own experience. Seeking out good, reliable sources of information about their side effects is really critical."

CONTINUED FROM PAGE 34

G12C–mutated advanced NSCLC.

Moreover, results from the phase 2 cohort demonstrated that 80% of patients achieved disease control after treatment with sotorasib. After a median follow-up of 12.2 months, patients who received the study drug achieved a 37.1% confirmed objective response rate (the proportion of patients who had a complete or partial response to treatment) and a disease control rate of 80.6% in this patient population. The median duration of response was 10 months.

The median best tumor shrinkage among all responders (46 patients) was 60%, with a median time to objective response of 1.4 months.

Aside from its efficacy, the study drug also was associated with a favorable benefit-risk profile. Most treatment-related side effects were of grade one or two, and no treatment-related deaths occurred. Grade three and four (considered more serious or severe) treatment-related side effects occurred in 25 (19.8%) patients and one patient (0.8%), respectively.

The most common treatment-related side effects patients reported experiencing included, but were not limited to, diarrhea (31%) and nausea (19%). Some patients (7.1%) discontinued treatment because of the side effects.

These data, Velcheti said, represent a new approach for this population of patients with NSCLC.

"For patients who have already progressed on chemotherapy and immunotherapy, if they have a KRAS G12C mutation, right now the standard treatment option is docetaxel or gemcitabine, a salvage chemotherapy option," he said. "Unfortunately, the response rate and the side effect profiles for these drugs are not that great. So patients essentially have a lot of side effects, and the response from these drugs is very modest. This treatment (sotorasib) is definitely a big advance for those patients who have that KRAS G12C mutation because the response rates are much higher, and patients respond better."

Sotorasib was recently granted breakthrough therapy designation by the Food and Drug Administration (FDA) for use in patients with KRAS G12C–mutated locally advanced or metastatic NSCLC, as determined via an FDA-approved test, following at least one prior systemic treatment.

At-Home Prehab May Improve Outcomes Following Lung Cancer Surgery

Recent study results demonstrated that an at-home prehabilitation program may improve surgical outcomes in patients with lung cancer. *by* BRIELLE BENYON

PATIENTS MAY EXPERIENCE improved outcomes following lung cancer surgery by participating in a virtual prehabilitation program before the procedure, according to study results.

"Prehabilitation is the practice of enhancing a patient's functional capacity before surgery with the aim of improving postoperative outcomes," co-study author Stephanie Wynne, physiotherapist and prehabilitiation at Guy's Cancer Centre, Guy's and St. Thomas' NHS Foundation Trust, London, explained while presenting at a recent medical conference. "In lung cancer surgery, (prehabilitation) is associated with improved functional capacity and quality of life and reduced hospital length of stay, postoperative complications and readmission."

Additionally, a prehabilitation program may boost a patient's eligibility for lung cancer surgery: Wynne explained that lung resection is the most common radical treatment for lung cancer, yet only 10% to 30% of patients referred are candidates. Others are deemed not eligible for surgery because of their disease stage, surgical risk factors, advanced age, performance status, comorbidities or reduced cardiopulmonary reserve.

Although prehabilitation traditionally takes place face-to-face, a virtual option that occurs via telephone or videoconferencing is particularly attractive amid the COVID-19 pandemic, when patients and providers alike are trying to limit unnecessary clinic visits.

The study included 20 patients who were undergoing lung surgery at a National Health Service trust in London. They were all given a personalized home-based exercise program and a diary to monitor adherence. Patients also were given written advice and counseling for symptom management and had virtual follow-ups weekly or every other week.

Participants were assessed before and after the interventions on the following outcomes:

- Medical Research Council dyspnea scale.
- Physical activity levels, measured by the Godin Leisure-Time Exercise Questionnaire (GLTEQ).
- Dietary needs.
- Mood, measured by the Hospital Anxiety and Depression Scale.
- Fatigue, measured by Functional Assessment of Chronic Illness Therapy-Fatigue.
- Exercise capacity, measured by the 1-minute sit-to-stand test.

There was a 45.9-point improvement in the average of GLTEQ scores, meaning that patients' self-sufficiency improved. With the intervention, all the study participants met recommended levels of daily physical activity, and there was an average improvement of 5.1 points in the sit-to-stand score.

"Our findings demonstrate that remote, home-based prehab is feasible, and it may improve a patients' presurgical physical activity and exercise level," Wynne said. "This is pertinent given the ongoing uncertainty surrounding COVID-19 and its impact on face-to-face health care delivery."

This study showed that at-home prehabilitation is safe and feasible but should be investigated further, especially for elderly or vulnerable patients who may have limited access to technology.

"We're now designing a triage tool to best support patients based on their therapeutic needs and access to technology," Wynne said.

Offering Hope in the Lung Cancer Community

In partnership with CURE®, Bonnie J. Addario and the GO2 Foundation for Lung Cancer will release "The Living Room: A Lung Cancer Community of Courage," a collection of stories from patients, caregivers and survivors taking a personal approach to cancer care. By KRISTIE L. KAHL

"HOPE IS DEFINED AS an optimistic state of mind, with the expectation of positive outcomes in respect to circumstances or an event in one's life."

"Hope." That word is stenciled boldly across a wall at the GO2 Foundation, which hosts a monthly education/support group for patients and caregivers called the Living Room. And now, hope can be found in a collection of stories in the soon-to-be-released book published in partnership with *CURE*® and titled "The Living Room: A Lung Cancer Community of Courage."

To launch the book, a collection of stories from patients, caregivers and survivors taking a personal approach to cancer care, Bonnie J. Addario — now a 17-year survivor and co-founder and chair of the GO2 Foundation — recounted the first Living Room event.

"The majority of those coming through the door are lung cancer survivors. Many are accompanied by family members or caregivers, while others are alone," Addario wrote. "They've all come for support, but this is no ordinary support group. Our plan, starting with this first night, is to bring in the foremost opinion leaders to speak about every facet of lung cancer, from diagnosis, screening, profiling and treatment options to ongoing research and clinical trials. And our goal is to empower patients to become advocates themselves as a direct result of what they learn in the Living Room."

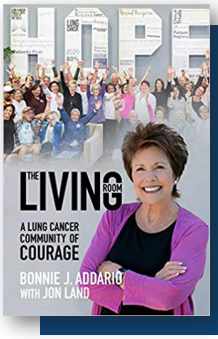
The organization did just that. Since 2008, the series and other programs have reached close to 1 million people in 144 countries. With the publication of "The Living Room," the stories of 22 powerful and inspiring profiles of men and women affected by lung cancer can reach even more.

Stories of hope within the pages of the book will include the experiences of:

- **Lucy and her husband, Dr. Paul Kalanithi**, a neurosurgical resident entering his final year of training. The couple brought their baby girl, Cady, into the world just eight months before his death. Kalanithi wrote the epilogue and published her husband's bestseller, "When Breath Becomes Air."
- **Hank "The Big Hug" Baskett**, a U.S. Air Force chief master sergeant (retired), whose deployments took him all over the world. Baskett received a diagnosis of lung cancer, but the physician treating him hadn't done the proper biomarker testing and did not realize he was eligible for a targeted therapy.
- **Gina Hollenbeck**, a not yet 40-year-old and the nonsmoking, healthy mother of two boys. Hollenbeck looked the picture of health when she walked into the emergency room holding her X-rays under her arm and had to convince the doctors that something was seriously wrong with her.
- **Matt Hiznay**, a lifelong nonsmoker who was just 24 when he learned he had lung cancer. Early treatment saved his life.
- **Juanita Segura**, a 51-year-old healthy eater and CrossFit enthusiast. The first doctor told her she had asthma and prescribed an inhaler. Then the wheezing turned into a horrible cough. The next doctor had to deliver the news that she had lung cancer. "Dude," she said to him, "I don't even smoke."

"They are my new heroes, the very definition of what it means to be brave," Addario wrote in the book. "They don't give in and they don't give up, men and women who come to the Living Room hopeless and leave hopeful. So come right in. Join us and make yourself comfortable. Our session is about to begin."

All proceeds from the book will go directly to research and patient services.



"The Living Room: A Lung Cancer Community of Courage" will be released May 4.

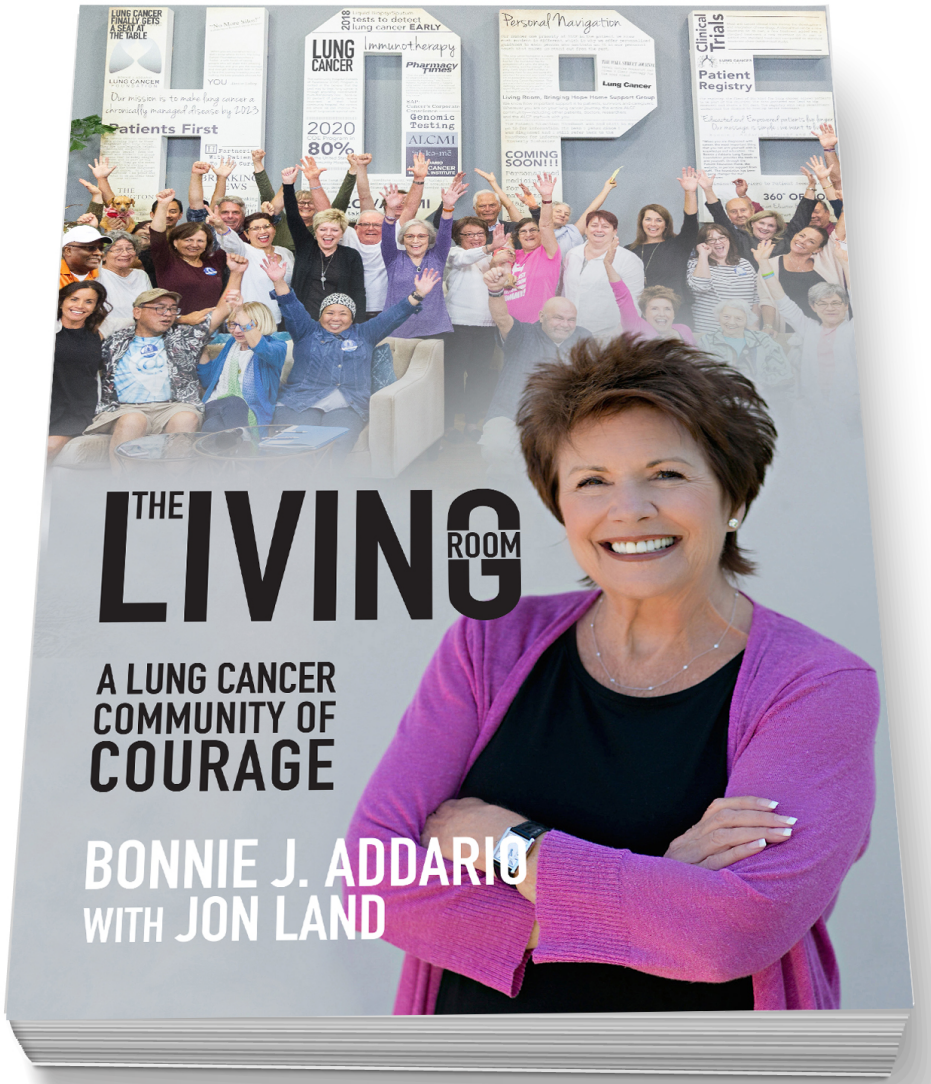
To purchase a copy, SCAN THE QR CODE.

BETTER TOGETHER

The people you will meet will make you believe that miracles happen, every day. One just might happen to the next lung cancer patient who picks up this book.

" ... a book with clear echoes of Mitch Albom's* Tuesdays with Morrie *... Addario writes from the inside out as an empathetic friend and guide ...* THE LIVING ROOM *speaks to the heart as well as the head, a seminal treatise on the human condition with overriding themes that extend far beyond even a disease as pernicious as lung cancer."

— Readers Digest



Bonnie J. Addario – 2020 recipient of CURE Media's Lifetime Achievement Award

★★★★★

Available at amazon

"The Living Room," draws its name from a virtual support and education group live-streamed internationally once a month.
www.go2foundation.org

GO2 FOUNDATION FOR LUNG CANCER

Post Hill Press

Distributed by Simon & Schuster (bestsellers include *HOPE, GRACE & FAITH*, *THE FIVE SECOND RULE*, *THE PATH*, and *HELLO DARKNESS, MY OLD FRIEND*)