NON-SMALL-CELL LUNG CANCER

FOCUS ONN



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GENE ANALYSIS DRUG DISCOVERY

When non-small-cell lung cancer spreads beyond the lungs, immunotherapy medications are an option. But, doctors can't predict who will benefit from which drugs. A new study may help. Researchers analyzed genes in the tumors of 1,003 people who received one of two immunotherapy drugs. For both drugs, the researchers discovered gene mutations in the tumors that helped predict whether the drugs would work. Two specific mutations predict poor response to both drugs. Another gene mutation was a sign that one of the drugs might work well. Doctors could one day use this gene analysis to help recommend the best treatment for patients.

SOURCE: International Association for the Study of Lung Cancer



Percentage of lung cancer cases that are non-small-cell.

SOURCE: American Society of Clinical Oncology

228,820

Estimated number of lung cancer diagnoses expected this year.

SOURCE: American Society of Clinical Oncology

TERMINATE TUMORS

Non-small-cell lung cancer commonly spreads to tissue, called pleura, that lines the lungs. The fluid that accumulates in this tissue seems to create a safe environment where tumors can grow and thrive. New research gives insight into why this may be and how to fight it. In a genetic analysis of pleural fluid in people who have non-small-cell lung cancer, researchers identified specific substances that can weaken the immune system and promote tumor growth. The finding could lead to development of drugs that might block those substances and prevent the spread of tumors. SOURCE: Oncotarget



ARTIFICIAL INTELLIGENCE ASSISTANCE

Several weeks into treatment for non-small-cell lung cancer, doctors order a CT scan of the lungs to see how well the treatment is working. Radiologists analyze the image and offer their take as to whether the cancer is retreating. But, sometimes it's not so easy to tell. Artificial intelligence may provide the perfect second opinion. When researchers trained computers to analyze lung scans for signs of tumor shrinkage or growth, the machines evaluated the images accurately up to 82% of the time.

SOURCE: Clinical Cancer Research

5 QUESTIONS

WHAT DOCTORS WANT YOU TO KNOW ABOUT NON-SMALL-CELL LUNG CANCER

By Barbara Brody Reviewed by Brunilda Nazario, MD, WebMD Senior Medical Editor

Non-small-cell lung cancer is more treatable today than ever before. David Carbone, MD, director of the Thoracic Oncology Center at The Ohio State University Comprehensive Cancer Center, and Jorge Gomez, MD, clinical director of thoracic oncology at Mount Sinai Hospital in New York City, provide information to help you better deal with the disease.

Q. WHEN CAN I START TREATMENT?

Don't be surprised if you have to wait a few weeks or even months. Nowadays, the best treatment is personalized, and step one entails having your tumor undergo molecular analysis to determine if it will respond to a targeted therapy that homes in on a specific mutation. The goal is to find the best match for *your* cancer, Carbone says. The testing process can take a while, but it's usually worth the wait because targeted treatments are very effective.

Q. SHOULD I BRACE MYSELF FOR BAD SIDE EFFECTS?

Not necessarily. "All the time I have patients who expect to become horribly sick and debilitated, but many of the treatments we use today don't cause any noticeable side effects or only very mild ones," Carbone says. He adds, "Side effects rarely occur with the newer targeted therapies and immunotherapies (which harness the power of your own immune system). Meanwhile, radiation and even surgery have become less invasive. Chemotherapy side effects may still include nausea and fatigue, but your doctor can prescribe medication to help."

Q. WHAT IS A REALISTIC PROGNOSIS FOR ME?

Someone diagnosed with stage I non-small-cell lung cancer has an 80% to 90% chance of survival. If you have stage IV (metastatic cancer), however, it's important to know that there is no cure. "This is a difficult conversation, but it's useful to understand that [patients with stage IV] will most likely die from this disease," Gomez says. "You should have a serious conversation with your doctor about your goals and expectations. Do you want to spend the next year and a half focused only on treatment, or are you going to try to enjoy your time with family and friends?" He also advises setting up a health care proxy so that someone else will be able to make medical decisions for you if you

reach a point when you are no longer able to do so.

Q. HOW IMPORTANT ARE DIET AND EXERCISE?

They are important, but not complicated, Gomez says. Just walk as much as you can and eat a healthy, well-balanced diet. Limit refined sugar and eat plenty of fruits and vegetables. That's really the same plan that everyone (including those without cancer) ought to be following. If you have advanced lung cancer, make not losing weight a priority, Carbone adds. "When cancer is out of control it makes people lose their appetite," and weight loss makes you more frail, he explains.

Q. IS IT SAFE TO TRY ALTERNATIVE THERAPIES?

Maybe, but your oncologist needs to know about them. "The majority don't have any scientific evidence behind them," but they may be safe to try along with whatever proven treatment your oncologist recommends, Gomez says. "But some may be harmful, and some have interactions with chemotherapy or other cancer treatments you may be getting."



GETTY IMAGES



KNOW YOUR Options

FIND OUT WHAT MIGHT WORK BEST FOR YOU

By Barbara Brody **Reviewed by** Brunilda Nazario, MD, WebMD Senior Medical Editor The silver lining to being diagnosed with non-small-cell lung cancer? People are living longer with it than ever before. "The median survival rate has increased significantly since about 2016," says Jorge Gomez, MD, clinical director of thoracic oncology at Mount Sinai Hospital in New York City.

That increase comes largely thanks to major advances in treatment. The best treatment(s) for you will depend on the stage of your cancer as well as the size and location of tumors, Gomez says. Here are some options your oncologist might recommend.

SURGERY

Many people who are diagnosed with non-small-cell lung cancer will have surgery to remove cancerous tissue as well as nearby lymph nodes to see if the cancer has spread. Some people with small, early stage tumors might only need surgery; those with more advanced cancer and/ or larger tumors might need chemotherapy and/or radiation as well, Gomez says. Surgery can range from minimally invasive procedures that are aided by video or robotic technology to the removal of an entire lung.

RADIOFREQUENCY ABLATION

Some people with very small tumors near the edge of the lungs may be eligible for radiofrequency ablation, a minimally invasive technique that involves heating and destroying the cancer with high-energy radio waves.

RADIATION

Many patients with stage II and stage III lung cancer will need radiation, Gomez says. Some will have radiation before or after surgery; others will only get radiation (often along with chemotherapy) because the cancer is too difficult to remove surgically.

CHEMOTHERAPY

As with radiation, many patients with stage II and stage III lung cancer will need chemotherapy, Gomez says. Generally speaking, people with stage II will have surgery first followed by chemotherapy. Those with stage III might have chemotherapy first (perhaps along with radiation) in an effort to shrink the tumor before surgery.

TARGETED THERAPY

Targeted therapies—drugs that home in on specific genetic mutations—are one of the biggest advances in recent years. Gomez estimates that about 20% of lung cancer patients have a tumor with a mutation that makes them good candidates for this option.

Some mutations include those in the EGFR (epidermal growth factor receptor), ALK (anaplastic lymphoma kinase), ROS1 (c-ros oncogene 1), and PD-L1 (programmed death-ligand 1) genes. Some targeted therapies are on the market, but others are still experimental.

IMMUNOTHERAPY

Immunotherapy works by activating your body's immune system so it can better fight the cancer. Gomez says, "Until recently, immunotherapy was only for patients with stage IV lung cancer, but we're now trying it in patients with earlier stage cancers." He adds that results from clinical trials have been highly successful. Many of these trials entail giving patients a few immunotherapy treatments before surgery.

"Many have had tumors disappear, meaning that when a surgeon goes to take it out, they find dead tumor or 90% dead tumor," he says. "It's a very promising area." For certain adults with newly diagnosed metastatic non-small cell lung cancer (NSCLC) that tests positive for PD-L1



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Results may vary. OPDIVO® + YERVOY® is not approved for patients younger than 18 years of age.

Indication & Important Safety Information for OPDIVO (nivolumab) + YERVOY (ipilimumab)

Only your healthcare professional knows the specifics of your condition and how OPDIVO in combination with YERVOY may fit into your overall therapy. The information below does not take the place of talking with your healthcare professional, so talk to them if you have any questions.

What are OPDIVO and YERVOY?

OPDIVO and YERVOY are prescription medicines used to treat people with a type of advanced stage lung cancer called non-small cell lung cancer (NSCLC). OPDIVO may be used in combination with YERVOY as your first treatment for NSCLC when your lung cancer has spread to other parts of your body (metastatic), **and** your tumors are positive for PD-L1, but do not have an abnormal EGFR or ALK gene.

It is not known if OPDIVO and YERVOY are safe and effective when used in children younger than 18 years of age.

What is the most important information I should know about OPDIVO and YERVOY?

OPDIVO and YERVOY are medicines that may treat certain cancers by working with your immune system. OPDIVO and YERVOY 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 serious or life-threatening and can lead to death and may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when OPDIVO is used in combination with YERVOY.

YERVOY can cause serious side effects in many parts of your body which can lead to death. These problems may happen anytime during treatment with YERVOY or after you have completed treatment.

Call or see your healthcare provider right away if you develop any symptoms of the following problems or these symptoms get worse. Do not try to treat symptoms yourself.

• Lung problems (pneumonitis). Symptoms of pneumonitis may include: new or worsening cough; chest pain; shortness of breath

- Intestinal problems (colitis) that can lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea (loose stools) or more bowel movements than usual; mucus or blood in your stools or dark, tarry, sticky stools; stomach-area (abdomen) pain or tenderness; you may or may not have fever
- Liver problems (hepatitis) that can lead to liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes; nausea or vomiting; pain on the right side of your stomach area (abdomen); drowsiness; dark urine (tea colored); bleeding or bruising more easily than normal; feeling less hungry than usual; decreased energy
- Hormone gland problems (especially the thyroid, pituitary, and adrenal glands; and pancreas). Signs and symptoms that your hormone glands are not working properly may include: headaches that will not go away or unusual headaches; extreme tiredness or unusual sluggishness; weight gain or weight loss; dizziness or fainting; changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness; hair loss; feeling cold; constipation; voice gets deeper; excessive thirst or lots of urine
- Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include: decrease in the amount of urine; blood in your urine; swelling in your ankles; loss of appetite
- Skin problems. Signs of these problems may include: skin rash with or without itching; itching; skin blistering or peeling; sores or ulcers in mouth or other mucous membranes
- Inflammation of the brain (encephalitis). Signs and symptoms of encephalitis may include: headache; fever; tiredness or weakness; confusion; memory problems; sleepiness; seeing or hearing things that are not really there (hallucinations); seizures; stiff neck
- Problems in other organs. Signs of these problems may include: changes in eyesight; severe or persistent muscle or joint pains; severe muscle weakness; chest pain

Additional serious side effects observed during a separate study of YERVOY alone include:

 Nerve problems that can lead to paralysis. Symptoms of nerve problems may include: unusual weakness of legs, arms, or face; numbness or tingling in hands or feet



www.OPDIVOYERVOY.com 1-855-OPDIVOYERVOY

• Eye problems. Symptoms may include: blurry vision, double vision, or other vision problems; eye pain or redness

Get medical help immediately if you develop any of these symptoms or they get worse. It may keep these problems from becoming more serious. Your healthcare team will check you for side effects during treatment and may treat you with corticosteroid or hormone replacement medicines. If you have a serious side effect, your healthcare team may also need to delay or completely stop your treatment with OPDIVO and YERVOY.

What should I tell my healthcare provider before receiving OPDIVO and YERVOY? Before you receive OPDIVO and YERVOY, tell your healthcare provider if you: have immune system problems

(autoimmune disease) such as Crohn's disease, ulcerative colitis, lupus, or sarcoidosis; have had an organ transplant; have lung or breathing problems; have liver problems; have any other medical conditions; are pregnant or plan to become pregnant. OPDIVO and YERVOY can harm your unborn baby. **Females who are able to become pregnant:** Your healthcare provider should do a pregnancy test before you start receiving OPDIVO and YERVOY.

- You should use an effective method of birth control during and for at least 5 months after the last dose. Talk to your healthcare provider about birth control methods that you can use during this time.
- Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment. You or your healthcare provider should contact Bristol Myers Squibb at 1-800-721-5072 as soon as you become aware of the pregnancy.
- Pregnancy Safety Surveillance Study: Females who become pregnant during treatment with YERVOY are encouraged to enroll in a Pregnancy Safety Surveillance Study. The purpose of this study is to collect information about the health of you and your baby. You or your healthcare provider can enroll in the Pregnancy Safety Surveillance Study by calling 1-844-593-7869.

If you are breastfeeding or plan to breastfeed: It is not known if OPDIVO or YERVOY passes into your breast milk. **Do not** breastfeed during treatment and for 5 months after the last dose.

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

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

What are the possible side effects of OPDIVO and YERVOY?

OPDIVO and YERVOY can cause serious side effects, including:

- See "What is the most important information I should know about OPDIVO and YERVOY?"
- Severe infusion reactions. Tell your doctor or nurse right away if you get these symptoms during an infusion of OPDIVO or YERVOY: chills or shaking; itching or rash; flushing; difficulty breathing; dizziness; fever; feeling like passing out

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

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

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

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

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

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MYLIFE WITH NON-SMALL-CELL LUNG CANCER

LEARNING TO MANAGE AND TAKE CONTROL

By Frank Sierawski

Reviewed by Brunilda Nazario, MD, WebMD Senior Medical Editor

I had a cough that started in late fall, and it gradually got worse. It became so disruptive that I wasn't sleeping well. I had a chest X-ray and the doctor diagnosed me with pneumonia, and gave me an inhaler and antibiotic, but the cough didn't get better.

GETTY IMAGES; INSET IMAGE BY MICHELE ZEPHIER PHOTOGRAPHY

Eventually, I saw a pulmonologist who ordered a CT scan and then did a bronchoscopy. During this procedure I was sedated, and he used a thin tube with a camera at one end to look at my airway and lungs. That's when he spotted a tumor in my left lung. I learned that I had lung cancer a few days before my 35th birthday.

It was a surprise to me because I'd never smoked. It

was a scary time, especially for my wife, Katijo. She's a registered nurse and she caught on to the seriousness of this before I did. Our sons were just 7, 5, and 3 then, and there were a lot of what-ifs.

A physician friend recommended that I get a second opinion at the Mayo Clinic where she works, so Katijo and I drove five hours to see doctors there. They did two more bronchoscopies, one to biopsy the tumor, and a second to remove it. That opened my airway and helped the coughing.

The biopsy showed that I had a non-small-cell adenocarcinoma that had spread to a rib, a vertebra, and some lymph nodes. I

chose to undergo biomarker testing to determine if this cancer had targetable mutations that would respond to treatment. My medical team found that my cancer was ALK-positive, an abnormal receptor on some types of cancer cells. When it is turned on, it causes changes within the cell that make cancer cells grow quickly. I took two pills a day. I didn't need infusions or lose my hair. When I went back for scans a month later, the lung tumor was melting away, and the bone metastases were gone.

About 10 months later, my medical team suggested that I would be a good candidate for surgery to remove the bad part of my left lung, given that I had responded so well to the drug and I was young and heathy. I decided to undergo the lobectomy. I have half a left lung now and a pretty awesome scar, and the surgery was a success.

I visit the medical center every three months for checkups, which include scans and bloodwork. I'm so comfortable with the team up there, and I like to drive, so the five-hour trip for appointments is the least of my concerns.

I'm feeling pretty great. I work full time, and I can play



FRANK'S TIPS

for Managing Non-Small-Cell Lung Cancer

Meet others. My wife and I got

Keep your diet healthy, but reasonable. My wife's very

outside with my sons, who are now 12, 9, and 7, and into soccer, baseball, and basketball. Six years after my diagnosis, days will go by without cancer crossing my mind.

NON-SMALL-CELL LUNG CANCER

FACTS AND STATS

By Sonya Collins Reviewed by Brunilda Nazario, MD, WebMD Senior Medical Editor



SOURCES: American Society of Clinical Oncology, American Lung Association, American Cancer Society, Medscape, Translational Lung Cancer Research



BUILD YOUR COMMUNITY

TAP INTO ONLINE AND IN-PERSON RESOURCES TO EASE THE JOURNEY THROUGH TREATMENT AND BEYOND

By Barbara Brody **Reviewed by** Brunilda Nazario, MD, WebMD Senior Medical Editor

Although your physical health is top priority when you're dealing with cancer, your emotional health ought to be a close second. "A diagnosis like lung cancer can be difficult to navigate on your own and may leave you feeling isolated and confused," says Gina Hollenbeck, RN, who has stage IV lung cancer. She says that joining ALK Positive, an online support group, "saved my life," because connecting with other patients was so informative and empowering.

Here are a variety of resources designed to help you get connected.

LOCAL RESOURCES

Most major cancer centers and even some smaller community hospitals host cancer support groups. Ask your oncologist to refer you to one, or search the American Cancer Association's database at cancer.org/treatment/ support-programs-and-services.html. (Click on "Search For Programs In Your Area" in the blue box. Then, enter your zip code and choose a program. Select "Support - Lung" from the drop-down menu under Program Type and then click on "Find Resources" in the blue box.)

LUNGEVITY

lungevity.org

Online messages boards, a phone helpline, and a one-on-one matching program connects people who have lung cancer. The organization also maintains an online Survivor Resource Center that features survivor stories, links to emotional support resources, and tips for navigating payment/ insurance issues.

INSPIRE LUNG CANCER SURVIVORS COMMUNITY

inspire.com/groups/american-lungassociation-lung-cancer-survivors More than 90,000 lung cancer patients and caregivers come together through this online group that's run in partnership with the American Lung Association. Log on to read stories from other survivors, get tips about nutrition, learn about complementary therapies, and much more.

GO2 FOUNDATION FOR LUNG CANCER

go2foundation.org

This organization is the result of a 2019 merger between the Bonnie J. Addario Lung Cancer Foundation and the Lung Cancer Alliance. The combined group offers an array of resources for patients and caregivers, including access to mental health professionals, a database of support groups that take place throughout the country, and a peer-to-peer Phone Buddy Program. The foundation also hosts a monthly online "Lung Cancer Living Room" with oncologists and scientists who help educate patients and their families.

MUTATION-SPECIFIC SUPPORT GROUPS

Many lung cancers are caused by mutations to specific genes. When a patient has a biopsy, tissue from their tumor is tested to see if it contains a mutation to a gene such as ALK (anaplastic lymphoma kinase), EGFR (epidermal growth factor receptor), or ROS1 (c-ros oncogene 1), among many others.

Patients with ALK-positive lung cancer, including Gina Hollenbeck, connect through the ALK Positive (alkpositive.org) support group. "ALK-positive only accounts for about 4% of non-small-cell lung cancer patients; therefore few oncologists have taken care of an ALK-positive patient," she explains. "Connecting through Facebook allows ALK-positive patients from all over to come together."

Lung cancer patients who instead test positive for EGFR can join EGFR Registers (*egfrcancer.org*). Those who are ROS1 positive can explore The ROS1ders (*ros1cancer.com*).

FACT OR FICTION?

CAN YOU DETECT THE MYTHS ABOUT NON-SMALL CELL LUNG CANCER (NSCLC)? TAKE THIS QUIZ TO FIND OUT.

By Erin O'Donnell

Reviewed by Brunilda Nazario, MD, WebMD Senior Medical Editor

1. Non-small-cell lung cancer is a rare type of lung cancer.

○ True ○ False

- 2. Most people with NSCLC have a history of smoking.
 - O True O False
- 3. Chemotherapy is the only treatment available for NSCLC.
- 4. The right lung has three lobes, while the left lung has two.
 - True False
- 5. NSCLC is usually diagnosed in its early stages.
 - O True O False



ANSWERS:

1. **False.** Roughly 80% to 85% of all cases of lung cancer are NSCLC. These cancers include adenocarcinoma, squamous cell carcinoma, and large-cell carcinoma.

2. **True.** Smoking is the top risk factor for NSCLC. If you smoke and are diagnosed with NSCLC, it is important to do what you can to quit; this makes your treatment more effective and increases your chance of a good outcome. But one type of NSCLC is the most common form of lung cancer among people who have never smoked: adenocarcinoma.

3. **False.** Chemotherapy is just one tool used to treat NSCLC. The tools used by your medical team depend on the stage of

your cancer, and can include a combination of surgery, radiation, chemotherapy, targeted therapy, immunotherapy, and laser therapy.

4. **True**. Each lung contains sections known as lobes, which are filled with spongy tissue. The right lung contains three lobes, and the left lung contains just two to make space for the heart.

5. **False.** NSCLC is rarely spotted early. It does not often cause symptoms until the cancer has advanced and moved to other organs. Symptoms of NSCLC may include a cough that gets worse and does not go away, coughing up rust-colored phlegm, and shortness of breath.

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