LUNG CANCER TREATMENTS


What you need to know about...

reading a biomarker test report






LUNGEVITY

Thank you to the lung cancer survivors who have given their permission to be featured on the cover of this booklet.

foreword

About LUNGevity

LUNGevity is the nation's leading lung cancer advocacy organization, focused on improving clinical outcomes for people with lung cancer through research, policy initiatives, education, support, and engagement for patients, survivors, and caregivers. LUNGevity seeks to make an immediate impact on the quality of life and survivorship for everyone touched by the disease—while promoting health equity by addressing disparities throughout the care continuum. LUNGevity works tirelessly to advance research into early detection and more effective treatments, provide information and educational tools to empower patients and their caregivers, promote impactful public policy initiatives, and amplify the patient voice through research and engagement. The organization provides an active community for patients and survivors—and those who help them live longer and better lives.

LUNGevity's support services help people live better with lung cancer and create a support network for all impacted by the disease. Comprehensive resources include our medically vetted and patient-centric website, peer-to-peer support through the LifeLine program, the toll-free HELPline answered by oncology social workers, and survivorship conferences like HOPE Summit and the International Lung Cancer Survivorship Conference. Online communities, hosted in private Facebook groups, weekly virtual meetups, or the Lung Cancer Support Community message board, offer connections with fellow survivors and caregivers. LUNGevity Foundation is proud to be a four-star Charity Navigator organization.

About the LUNGevity PATIENT EDUCATION SERIES

LUNGevity has developed a comprehensive series of materials for patients with lung cancer and their caregivers, focused on understanding how lung cancer develops, how it can be diagnosed, and how it is treated. Whether you or someone you care about has been diagnosed with lung cancer, and is concerned about lung cancer risk, we have resources to help you.

The medical experts and lung cancer survivors who provided their valuable expertise and experience in developing these materials all share the belief that well-informed patients make their own best advocates.

In addition to this and other booklets in the LUNGevity patient education series, information and resources can be found on the LUNGevity website at www.LUNGevity.org.

LUNGevity would like to thank the Association of Community Cancer Centers (ACCC), the Association for Molecular Pathology (AMP), the Advanced Practitioner Society for Hematology and Oncology (APSHO) and the International Association for the Study of Lung Cancer (IASLC) and their practicing clinical experts for their participation providing invaluable feedback on this patient education booklet:

ACCC
Association of Community Cancer Centers

AMP Association for Molecular Pathology

APSHO
Advanced Practitioner Society for Hematology and Oncology

IASLC
International Association for the Study of Lung Cancer

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introduction

Biomarker testing is used among diagnosed patients with non-small cell lung cancer (NSCLC) to determine the presence of specific mutations or proteins associated with cancer. It ensures that patients get matched to the right treatment at the right time, based on their biomarker test results. The results can also provide a complete overview of the therapies and clinical trials available to them specific to their biomarker(s).

It should be noted that biomarker test reports are not the same across all labs that run them. This booklet, therefore, will cover the general information that most biomarker test reports contain. It explains the different biomarkers that cancers are tested for, what the results mean, how available therapy options are reported, and how to evaluate the clinical trial options in partnership with your healthcare provider.

This booklet will help you:

- Understand the results of a biomarker test report
- Recognize how identifying key biomarkers can affect treatment decisions
- Identify potential therapy options based on test results
- Define a basic strategy for selecting a clinical trial
- Develop a list of key questions to ask your healthcare provider

The field advances quickly and new biomarkers and treatments are constantly being developed; therefore, it is important to discuss specific findings with your healthcare provider.

YOU'LL FIND A GLOSSARY TOWARD THE END OF THIS BOOKLET. Words included in the glossary appear **blue** the first time that they are used in the text.

01 biomarker testing overview

What is a biomarker?

A **biomarker** is any molecule that can be measured in blood, other bodily fluids, or tissues. Presence of a biomarker may be a sign of an abnormal bodily process or condition or disease.

Biomarkers can be used to:

- Determine whether a disease or condition is present
- Describe the prognosis (likely outcome) of the disease
- Predict how well the body will respond to a specific treatment

What is biomarker testing? Why is it important to patients with lung cancer?

Lung cancer treatment options for patients with NSCLC include a number of **targeted therapies** and **immunotherapies**. Biomarker testing is necessary in order for the healthcare team to prescribe any of these treatments.

In biomarker testing for patients with lung cancer, the two types of biomarkers currently tested for are:

- **Driver mutations** within the cancer's **DNA**
- **Programmed death-ligand 1 (PD-L1)** protein level

The results of these tests help determine whether any of the U.S. Food and Drug Administration (FDA)-approved lung cancer targeted therapies or a particular immunotherapy drug may be appropriate as part of the patient's treatment plan.

When is biomarker testing used?

Biomarker testing is done in patients with lung cancer to understand the specific type of cancer the patient has, in order to guide treatment options. It can also be done if a patient's cancer comes back after treatment, or if a certain treatment stops working.

Cancer therapies often work well for some time but then may stop working. This is known as **acquired resistance**. When this occurs, a new biopsy and biomarker testing may be needed to better understand the causes of this resistance. These tests may show a change in the cancer or a new cancer.

A healthcare provider will order the testing to be done in a lab. All biomarker lab results are recorded in a biomarker test report. For this booklet, we will focus on some of the common sections that are covered in most reports. We will start with the results summary section.

Note: For more information on biomarker testing, please refer to the "What you need to know about biomarker testing" booklet, available on the LUNGevity website.

02 understanding the test results

The biomarker test report generally starts at the top with patient information—name, date of birth, sex, medical records number—and the ordering healthcare provider's information. Within this background information section, additional details may include specifics on the specimen collected that was used for the biomarker test, such as "lung tissue" or "adenocarcinoma." The report will usually list when the specimen was collected by your healthcare provider and when it was received by the lab. It may also describe the pathology (cause of disease) of the specimen and define the amount of tumor cells found in the specimen that was collected.

EXAMPLE INFORMATION SECTION

LUNG TUMOR PROFILER | FINAL REPORT

PATIENT	SPECIMEN	PHYSICIAN
Patient 0000 **Sample Patient** **Patient Name:** Sample, Patient **Patient DOB/Sex:** 01/01/1999/X Address City, State 00000 **Phone:** (000) 000-0000 **Email:** sample.patient@example.com	**Specimen Type:** Lung Tissue **Specimen ID:** X99-99 **Accession/CaseNo:** 9999999/XXX99-9999999 **Collection Date:** 01/01/2021 **Received Date:** 01/02/2021 02:14:00 PM EDT **Report Date:** 01/17/2021 03:04:00 PM EDT **MRN:** 9999999	**Ordering Physician(s):** Sample Doctor, MD

Please note that this is one illustrative example of an Information section. Individual reports may vary.

Following this information, the report typically goes straight into the test results summary section.

Overview of the test results summary

The results summary is the section of the biomarker test report that lists the biomarker(s) that the cancer tested positive for. As mentioned earlier, FDA-approved therapies are linked to two general biomarkers: the presence of genetic driver mutations and the levels of PD-L1. The cancer may also have been tested for biomarkers that do not currently have targeted therapy drugs available; sometimes the report will also list these biomarkers along with their respective clinical trials (more on that in “Understanding the clinical trial options” section).

The results summary varies based on the lab running the biomarker tests—there may be differences with respect to the level of detail included or even the format of the results summary. However, in general, results summaries first list information on treatable driver mutations that currently have available therapies.

What is included in the test results summary?

The results summary provides a range of information, which may include the following:

- Biomarker(s) tested for
- Type of diagnostic test/methodology used to check for the biomarker
- **Analyte**, or the biological substance being measured in that specific test
- Result of that specific test

EXAMPLE RESULTS SUMMARY TABLE

BIOMARKER	METHOD	ANALYTE	RESULT
ALK	NGS	RNA-Tumor	Fusion Detected
	IHC	Protein	Positive | 3+, 100%
	NGS	DNA-Tumor	Pathogenic Variant Exon 25 | p.G1269A
PD-L1	IHC	Protein	Positive, High Expression, TPS: 50%
BRAF	NGS	DNA-Tumor	Mutation Not Detected
EGFR	NGS	DNA-Tumor	Mutation Not Detected
ROS1	NGS	RNA-Tumor	Fusion Not Detected

Please note that this is one illustrative example of a Results Summary table. Individual reports may vary.

Now let's walk through the details found in the Results Summary table.

Tested biomarkers

Testing for biomarkers provides information vital to choosing the best treatment option. Biomarker driver mutations tested in patients with NSCLC include but are not limited to: ALK **gene fusions**, *BRAF V600E, EGFR, KRAS, MET* ***exon*** *14 skipping, NTRK* fusions, *RET* fusions, and *ROS1* fusions. Additionally, biomarker testing will also evaluate levels of PD-L1 proteins.

- **Testing positive for a driver mutation:** Biomarker test results will provide information about biomarkers that are treatable, such as driver mutations. Driver mutations are able to be treated by available drug therapies specifically designed to target them. If a cancer tests positive for a biomarker with an available therapy, the therapy may be listed on the report, or the healthcare provider will discuss treatment options during a follow-up appointment. Note that the specific genetic mutation details matter. For example, there are many different types of *KRAS* mutations, and not all of them are linked to an effective therapy.
- **Testing positive for PD-L1:** Biomarker test results will also show the levels of PD-L1 on cancer cells. Patients with tumors that have high levels of PD-L1 and no actionable driver mutations may be more likely to respond to immunotherapy treatments (more on this in the "Understanding the available therapies" section). However, even those with tumors that do not express PD-L1 may be able to respond to these treatments. Your healthcare provider will be able to answer any questions and provide more guidance on the options.
- **Testing positive for multiple biomarkers:** If more than one biomarker is detected, one may be more important than the other(s). Your healthcare provider will need to discuss the recommended treatment course when this occurs.

Types of diagnostic tests and their methodologies

Depending on which lab runs the biomarker test, it may run multiple diagnostic tests to identify biomarkers. The following describes some of the most common diagnostic tests used, including details about how the test is run and what a positive (or negative) result from each respective test looks like.

For more of the latest information on types of diagnostic tests, the Association for Molecular Pathology (AMP) is a valuable resource: https://outreach.amp.org/resources/cancer/

NGS (Next-Generation Sequencing)

- **Method:** Looks for mutations by examining DNA and/or **RNA** from a tissue or liquid biopsy sample. All the driver mutations can be detected through next-generation sequencing. Note that the report may only reflect results from a type of testing called polymerase chain reaction (PCR)-based sequencing. Similar to NGS, PCR-based testing also looks for gene mutations in DNA but is not as comprehensive in what it can identify.
- **Result:** For DNA sequencing results, the report may list the specific type of mutation, or **variant**, detected (more on that in the "Identifying biomarker variants" section). For RNA sequencing results, the term "Fusion Detected" may be used. This means that the RNA sequencing test has found a gene fusion, which is a type of mutation that results from a change in the structure of DNA.

IHC (Immunohistochemistry)

- **Method:** Uses antibodies, which are proteins that bind specifically to target proteins, to detect levels of the target proteins from a tissue sample. Typically used to detect levels of PD-L1, but also can be used to detect *ALK* and *ROS1* expression, which is indicative of a fusion.

- **Result:** The report may show IHC as a percentage (**TPS**, or **tumor proportion score**)—this refers to the percentage of tumor cells that express the protein of interest. IHC results may also be shown as a number ranging from 0–3+. This is a numerical scoring system used when testing for the ALK and ROS1 biomarkers in IHC. The scoring system varies with each antibody used for the IHC test, but the result will list whether the biomarker tested for is "positive," "negative," or "uncertain," depending on the score.

FISH (Fluorescence In Situ Hybridization)

- **Method:** Uses fluorescent dyes and fluorescent microscopes to detect cancer-promoting abnormalities in specific parts of the DNA from a tissue sample. FISH can be used to detect *ALK*, *ROS1*, and *RET* fusions, among other biomarkers.
- **Result:** FISH test results are reported as either "positive" or "negative" based on the percentage of cells with the fusion detected.

Identifying biomarker variants

Biomarker summary reports may just list the biomarker(s) that tested positive, but some may also list the variant, which is the specific type of mutation of a given biomarker. This highly clinical information may be listed right next to the biomarker, in a separate table, or even in the text section of the report. Reports may present this information as "variant interpretation"—this is the result of the specific test, showing whether a mutation was detected and if the mutation is pathogenic (disease-causing). Sometimes reports may even describe these biomarker variants in more detail, listing the exact change to the DNA sequence (**DNA alteration**) or protein code (**protein alteration**), and the percentage of cancer cells that express the mutation (**variant frequency**). There may be many variants for a given biomarker; e.g., the KRAS G12C mutation is a variant—a single type of KRAS mutation.

Knowing the exact variant of the biomarker will provide key information regarding drug **sensitivity** and response, providing the necessary information to choose the proper treatment plan.

EXAMPLE BIOMARKER VARIANTS TABLE

GENE	METHOD	ANALYTE	VARIANT INTERPRETATION	PROTEIN ALTERATION	EXON	DNA ALTERATION	VARIANT FREQUENCY %
ALK	NGS	RNA-Tumor	Fusion Detected	EML4-ALK	-	-	-
	NGS	DNA-Tumor	Pathogenic Variant	p.G1269A	25	c.3806G>C	9
CDKN2A	NGS	DNA-Tumor	Variant of Uncertain Significance	p.E119K	2	c.355G>A	29
	NGS	DNA-Tumor	Likely Pathogenic Variant	p.R87L	2	c.260G>T	26
KIT	NGS	DNA-Tumor	Variant of Uncertain Signifiance	p.V852I	18	c.2554G>A	50

Please note that this is one illustrative example of a Biomarker Variants table. Individual reports may vary.

Concerns with navigating biomarkers

If a cancer has multiple biomarkers...

A cancer may test positive for a driver mutation as well as PD-L1 because driver mutations occur in DNA, while PD-L1 is a protein found on the surface of cancer cells. If there are multiple positive biomarkers, your healthcare provider can help determine which treatment option is best. In some cases the order of treatment is very important, so this must be discussed in detail with your healthcare provider.

If a cancer has no biomarkers...

A cancer may not have any actionable biomarkers that can be identified for treatment with targeted therapies. In this situation, it is especially important to evaluate PD-L1 levels to identify proper immunotherapy strategies. However, be sure to discuss the test with your healthcare provider to ensure testing results are reliable.

In some cases, the biopsy specimen that was tested could have been too damaged prior to testing to have confidence in a negative result. For example, in a bone biopsy, some of the agents used in the processing of the bone damage the DNA and RNA, making it harder to find mutations. In addition, the various steps during specimen handling can sometimes result in degradation of DNA/RNA and protein, resulting in inaccurate test results. Similarly, liquid biopsy or blood-based biomarker testing may miss some biomarkers, especially if the amount of cancer in the circulating blood is low. Therefore, if no biomarkers are found, ask your provider if additional testing is needed.

QUESTIONS TO ASK YOUR HEALTHCARE PROVIDER ABOUT THE TEST RESULTS SUMMARY:

- Did my cancer undergo complete biomarker testing for all of the biomarkers listed in evidence-based clinical practice guidelines (e.g., National Comprehensive Cancer Guidelines, CAP/IASLC/AMP Molecular Testing Guideline)?
- Was my test accurate? Will I need additional testing to help determine my best course of treatment?
- Will I ever need to repeat my testing?
- If the cancer has a driver mutation and high PD-L1 levels, do you recommend targeted therapy or immunotherapy?

03 understanding the available therapies

What are the different types of therapies?

The biomarker test report may list the therapies that are available for the detected biomarker(s). Some reports list the therapies in tandem with the biomarker(s) found in the results summary, while other reports list therapies in their own stand-alone section. If there are no therapy drugs listed in the biomarker test report, consult with your healthcare provider regarding options for treatment.

Targeted therapy drugs and immunotherapy are the two general types of FDA-approved therapies for biomarkers. If the cancer tests positive for a driver mutation, it may respond to targeted therapy drugs designed for that specific biomarker. Assessing PD-L1 levels may help in deciding if immunotherapy is the right treatment. It is helpful to remember that therapies are always evolving and improving, so the following is the latest information on the current targeted therapy and immunotherapy drugs used to treat NSCLC.

Targeted therapy drugs

As of August 2022, the targeted therapy drugs for driver mutations currently approved by the FDA are (drugs listed alphabetically):

Driver mutation	FDA-approved targeted therapy drug(s)	Role
ALK	**Alectinib (Alecensa®), Brigatinib (Alunbrig®), Ceritinib (Zykadia®), Crizotinib (Xalkori®), Lorlatinib (Lorbrena®):** ALK inhibitors	ALK inhibitors target the abnormal ALK protein that causes cancer cells to multiply.
BRAF V600E	**Dabrafenib (Tafinlar®):** BRAF inhibitor **given in combination with Trametinib (Mekinist®):** MEK inhibitor	BRAF inhibitors target the altered BRAF protein that causes cancer cells to grow. MEK inhibitors target the altered MEK protein that causes cancer cells to grow.
EGFR	**Afatinib (Gilotrif®), Dacomitinib (Vizimpro®), Erlotinib (Tarceva®), Gefitinib (Iressa®), Osimertinib (Tagrisso®):** EGFR inhibitors used for exon 19 deletion or exon 21 L858R substitution mutation **Osimertinib (Tagrisso®):** EGFR inhibitor used for T790M mutation **Amivantamab (Rybrevant®), Mobocertinib (Exkivity®):** EGFR inhibitors used for exon 20 insertion mutation	EGFR inhibitors block the signal from the EGFR protein that tells cancer cells to grow.
KRAS G12C	**Sotorasib (Lumakras™):** KRAS inhibitor	KRAS inhibitors attach to the abnormal KRAS protein on cancer cells to keep the cells from growing. This is effective only for KRAS G12C and not for other KRAS mutations.
MET exon 14 skipping	**Capmatinib (Tabrecta®), Tepotinib (Tepmetko®):** Treat tumors with MET exon 14 skipping mutations	MET inhibitors attack the abnormal MET protein in cancer cells that makes them grow.
NTRK	**Entrectinib (Rozlytrek®), Larotrectinib (Vitrakvi®):** Target proteins made by NTRK genes	NTRK inhibitors target and disable the abnormal NTRK protein in cancer cells that makes them grow.
RET	**Pralsetinib (Gavreto®), Selpercatinib (Retevmo®):** RET inhibitors	RET inhibitors attack the abnormal RET protein in cancer cells that makes them grow.
ROS1	**Crizotinib (Xalkori®), Entrectinib (Rozlytrek®):** Target cells with ROS1 gene changes	ROS1 inhibitors target the abnormal ROS1 protein that causes cancer cells to multiply.

For the latest list of FDA-approved targeted therapy drugs for driver mutations, please refer to the LUNGevity website: https://www.lungevity.org/for-patients-caregivers/navigating-your-diagnosis/treatment-options/targeted-therapy

Immunotherapy drugs

As of August 2022, the immunotherapy drugs currently approved by the FDA are (drugs listed alphabetically):

Targeted biomarker	FDA-approved targeted therapy drug(s)	Role
PD-L1	**Atezolizumab (Tecentriq®), Durvalumab (Imfinzi®):** PD-L1 inhibitors	PD-L1 inhibitors target PD-L1 to prevent its interaction with PD-1 on immune cells. Blocking PD-L1 keeps the cancer cells vulnerable to being killed by the immune system.
	Cemiplimab (Libtayo®), Nivolumab (Opdivo®), Pembrolizumab (Keytruda®): PD-1 inhibitors	PD-1 inhibitors target PD-1 to prevent its interaction with PD-L1 on cancer cells. Blocking PD-1 allows the immune system to better attack cancer cells, delaying tumor growth.
	Ipilimumab (Yervoy®): CTLA-4 inhibitor	Ipilimumab (Yervoy®) is used with Nivolumab (Opdivo®) to treat advanced NSCLC. CTLA-4 inhibitors block CTLA-4 on immune cells to better allow them to attack cancer cells.

For the latest list of FDA-approved immunotherapy drugs, please refer to the LUNGevity website: https://www.lungevity.org/for-patients-caregivers/navigating-your-diagnosis/treatment-options/immunotherapy

What is included in the therapy association section?

If the report includes a therapy association section, it may include information about the association of a specific therapy to a biomarker. A specific therapy may be described as “associated” or “relevant,” or “beneficial,” but they all mean the same thing.

EXAMPLE ASSOCIATED THERAPIES TABLE

THERAPY ASSOCIATION	BIOMARKER LEVEL
Brigatinib	Level 1
Ceritinib	Level 1
Alectinib, Crizotinib	Level 1
	Level 3A
Pembrolizumab	Level 1
Atezolizumab	Level 2
Durvalumab, Nivolumab	Level 3A
Dabrafenib and Trametinib Combination Therapy	Level 1
Vemurafenib	Level 2
Erlotinib, Gefitinib	Level 1

Please note that this is one illustrative example of an Associated Therapies table. Individual reports may vary.

What does “level of evidence” mean?

If a report lists the therapies associated with a specific biomarker, it will usually include the “level of evidence” for the association of each drug and the target biomarker. The level of evidence uses evidence from research, past clinical trials, and survival/quality of life to essentially “rank” the efficacy of a specific drug to the paired specific biomarker. Each report may describe the level of evidence in a slightly different way, including “biomarker level” or “tier.” Though most healthcare providers will opt to make treatment recommendations using a Level 1 recommendation when possible, the following is a general example of how ranking of the different levels of evidence may be described:

EXAMPLE OF BIOMARKER LEVELS FOR AN FDA-APPROVED BIOMARKER TEST

Biomarker Level	Description
Level 1	Signifies the highest level of clinical evidence and/or biomarker association included in the drug label
Level 2	Signifies strong evidence of clinical significance and is endorsed by standard clinical guidelines
Level 3A	Signifies potential clinical significance; evidence exists **in tumor type**
Level 3B	Signifies potential clinical significance; evidence exists **in other tumor type(s)** (no evidence in NSCLC)

QUESTIONS TO ASK YOUR HEALTHCARE PROVIDER ABOUT AVAILABLE THERAPIES:

- What do you recommend if the report does not list any therapies? What are my next steps?
- What if there are multiple therapies recommended for one biomarker? Which one do you recommend?
- If the cancer has multiple biomarkers, do you recommend therapies to treat them all?
- Which of these therapies is the most effective? Which is best tolerated?
- Does using one therapy prevent me from receiving other therapies in the future?
- Is there a specific sequence of treatment that is best?
- Are there clinical trials we should explore?
- Will I know if any recommended therapies could lead to acquired resistance, when a cancer therapy works well for some time but then may stop working?

04 understanding the clinical trial options

When to join a clinical trial

Clinical trials are research studies that test whether a new drug is a safe and effective treatment. If there is no FDA-approved targeted therapy currently available for the identified biomarkers, participating in a clinical trial may be an option to pursue. Even if the biomarker has an FDA-approved targeted therapy, joining a clinical trial may provide access to treatments that are not yet available everywhere and may be more effective.

Biomarker test reports may include information on clinical trials that are testing treatments for the cancer's biomarker(s); including the **phase** of the trial, the location of the trial, and the up-to-date progress of the trial. Biomarker test reports may also provide links on where to sign up for clinical trials. Information on clinical trials might be included in the same table where the biomarkers and therapies are listed, but is usually found in its own stand-alone section of the report, after the results summary and therapies. Biomarker test reports may also list information on **investigational agents**, or the drugs being tested in the clinical trials, with the corresponding biomarker that the drug is meant to target.

EXAMPLE OF CLINICAL TRIAL INFORMATION IN A BIOMARKER TEST REPORT

Clinical Trials Finder

For a comprehensive list of clinical trials currently open for enrollment, visit Clinical Trials Finder, a web-based service that offers personalized, clinical trial information with advanced searching capabilities including, but not limited to:

- **Location:** Filter by geographic area
- **Biomarker(s):** Identify biomarkers associated with open clinical trials
- **Drug(s):** Look for specific therapies
- **Trial Sponsor:** Find trials based on the organization supporting the trial(s)

Visit our website to view all trials that you have been matched with. Therapeutic agents listed below may or may not be FDA-approved for the tumor type tested as of now.

TARGETED THERAPY CLINICAL TRIALS (199)

DRUG CLASS	BIOMARKER	METHOD	ANALYTE	INVESTIGATIONAL AGENT(S)
Immunomodulatory agents (185)	PD-L1	IHC	Protein	MEDI4736, MK-3475, MPDL3280A, MSB0010718C, atezolizumab, avelumab, durvalumab, nivolumab, pembrolizumab
Multikinase inhibitors (14)	ALK	IHC	Protein	AP26113, PF-06463922, RXDX-101, X-396, brigatinib, ceritinib (LDK378)
	ALK	NGS	DNA-Tumor	
	ALK	RNA-Seq	RNA-Tumor	

(#) = Total number of clinical trials identified for the specified drug class or table.

Please note that this is one illustrative example of the clinical trial information. Individual reports may vary.

How to enroll and find updated information on clinical trials

If the biomarker test report does not list any information on where to find clinical trials, your healthcare provider can share whether clinical trials are an option. The following websites may also be helpful for up-to-date information on clinical trials in all types of cancer around the world:

- **American Society of Clinical Oncology (ASCO):** https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/about-clinical-trials
- **LUNGevity:** https://www.lungevity.org/for-patients-caregivers/navigating-your-diagnosis/find-clinical-trial
- **National Institutes of Health (NIH):** https://clinicaltrials.gov/ct2/search
- **National Institutes of Health (NIH) - National Cancer Institute:** https://www.cancer.gov/about-cancer/treatment/clinical-trials/search

QUESTIONS TO ASK YOUR HEALTHCARE PROVIDER ABOUT CLINICAL TRIALS:

- Am I eligible to join a clinical trial?
- Is additional biomarker testing needed for me to enroll in a clinical trial?
- Can I do a clinical trial and standard treatment simultaneously?
- What is the goal of each phase of a clinical trial? How do I know which phase to join the clinical trial in?
- Will I know if I am in the standard treatment control group?
- What is the out-of-pocket cost versus what is covered by insurance when joining a clinical trial?
- Where will I go for treatment throughout the entirety of the clinical trial?
- What are the advantages and disadvantages of joining a clinical trial versus taking standard treatment or chemotherapy?
- If I begin to have side effects from a clinical trial treatment, can I stop it and go on a different treatment?
- Who will take care of me if I have side effects caused by participating in the clinical trial?

05 glossary

For a comprehensive glossary of terms related to lung cancer, please refer to the LUNGevity website: https://www.lungevity.org/for-patients-caregivers/helpful-resources/glossary

Acquired resistance—Describes the clinical scenario in which a cancer initially responded to the treatment but after a period of time, it relapsed and progressed

Analyte—The biological substance being measured in a biomarker test

Biomarker—Any molecule that can be measured in blood, other bodily fluids, or tissues. Presence of a biomarker may be a sign of an abnormal bodily process or condition or a disease

Control group—The group of people in the clinical trial who receive the "standard of care" (what we know works) and a placebo, an inactive substance that is meant to look like the therapy drug being tested. The control group will not be exposed to the trial treatment, so that researchers can compare the "standard of care" results against the results of the group introduced to the studied treatment

DNA—Hereditary material inside cells that carries the organism's genetic information

DNA alteration—The specific mutation in the DNA that makes up the gene

Driver mutation—A mutation that causes cancer

Exon—The segment of the gene that codes for a protein

Gene fusion—A type of mutation that results from a change in the structure of chromosomes, where two independent genes join together to form a hybrid gene

Immunotherapy—A type of cancer therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. Some types of immunotherapy only target certain cells of the immune system. Others affect the immune system in a general way

In tumor type/In other tumor type—Sometimes an available therapy may have clinical evidence in treating the same biomarker in a different tumor type (for example, a therapy for the same biomarker that has worked in breast cancer). In this case, the report may list the therapy and specify this information, either through the "biomarker level" or "tier" information, or by directly stating that the therapy has been shown to work in another tumor type

Investigational agent—A substance that has been approved by the FDA to be tested in people in clinical trials

Phase—The steps a clinical trial must go through. There are 3 main phases – Phases I to III. Patients may enter a clinical trial at any phase if they qualify, and also may leave at any phase for any reason

Phase I—The general goal of this phase is to learn if the drug is safe for people and what the preferred dose/dosing schedule of the drug(s) should be. This is usually the first time the drug will be given to people, so healthcare providers will assess dosage and side effects

Phase II—The general goal of this phase is to assess how the drug works for a specific type of cancer

Phase III—The general goal of this phase is to compare the efficacy and safety (side effects) of the drug against the standard treatment

Programmed death-ligand 1 (PD-L1)—A protein that helps keep immune cells from killing tumor cells in the body

Protein alteration—The specific mutation in the protein that is made by the biomarker gene that results in altered protein expression or function

RNA—Hereditary material inside cells that contains instructions from DNA for making proteins

Sensitivity—Describes a drug that is effective against the selected biomarker

Targeted therapy—A treatment that uses drugs to attack specific types of cancer cells with less harm to normal cells. Some targeted therapies block the action of certain enzymes, proteins, or other molecules involved in the development, progression, and/or spread of the cancer

Tumor proportion score (TPS)—The percentage of tumor cells with a particular protein of interest

Variant—Refers to the specific type of mutation of a biomarker. Can also be described as DNA or protein alteration

Variant frequency—The percentage of the DNA from your sample that contained a given variant; variant frequency is used to estimate the proportion of cancer cells containing that variant

06 notes

LUNGEVITY

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