A glass vase containing a bouquet of small white and yellow flowers is the central focus. In the background, a string of warm-toned bokeh lights is visible against a blurred green backdrop. A dark, cylindrical object hangs from the top left.

TARGETED THERAPY

FOR LUNG CANCER

Patient and
Caregiver Guide

GO₂
FOUNDATION
FOR LUNG
CANCER



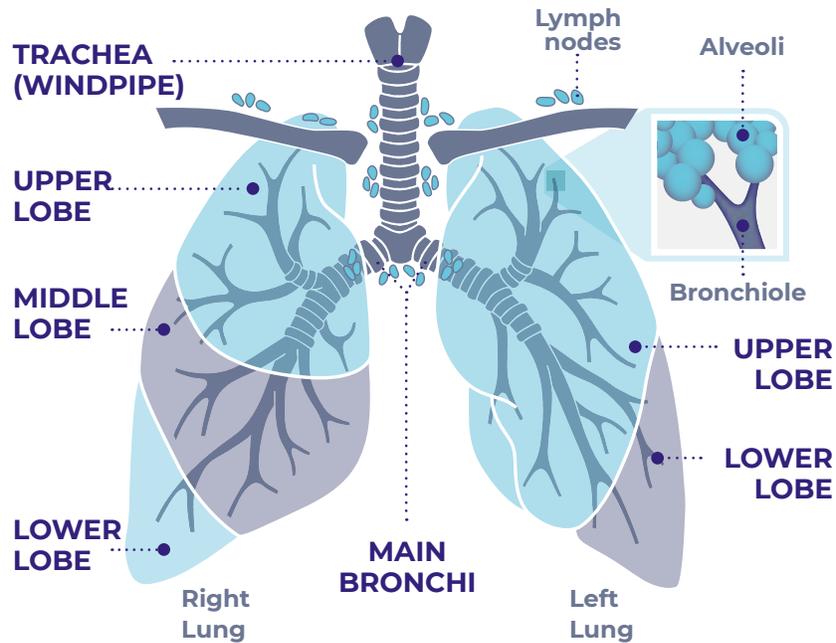
TARGETED THERAPY

FOR LUNG CANCER

Patient and Caregiver Guide

TABLE OF CONTENTS

Why Targeted Therapy?.....	2
Lung Cancer Basics.....	2
Changes in Lung Cancer.....	3
Biomarker Testing.....	5
Targeted Therapies.....	7
Drugs That Target EGFR.....	8
Drugs That Target ALK.....	8
Drugs That Target ROS1.....	8
Drugs That Target BRAF.....	9
Drugs That Target RET.....	9
Drugs That Target MET.....	9
Drugs That Target NTRK.....	9
Drugs That Target KRAS.....	9
Other Targeted Therapies.....	9
Things to Know.....	11
Clinical Trials.....	12
About GO2 Foundation for Lung Cancer.....	13



WHY TARGETED THERAPY?

Until the mid-2000s, treatment choices were mostly limited to surgery, chemotherapy and radiation. Now, people living with lung cancer often have newer, more personalized treatment options.

The goal of targeted therapy is to directly target your unique tumor. This allows treatments to work better and with fewer side effects. This brochure will help you understand targeted therapies and what they mean for you.

Knowing the type and subtype of your lung cancer is important. That information guides treatment choices.

LUNG CANCER

Cancer that starts in the lungs – lung cancer – is one of the most common cancers in the United States. But lung cancer is not one disease; there are many types of lung cancer.

THE BASICS

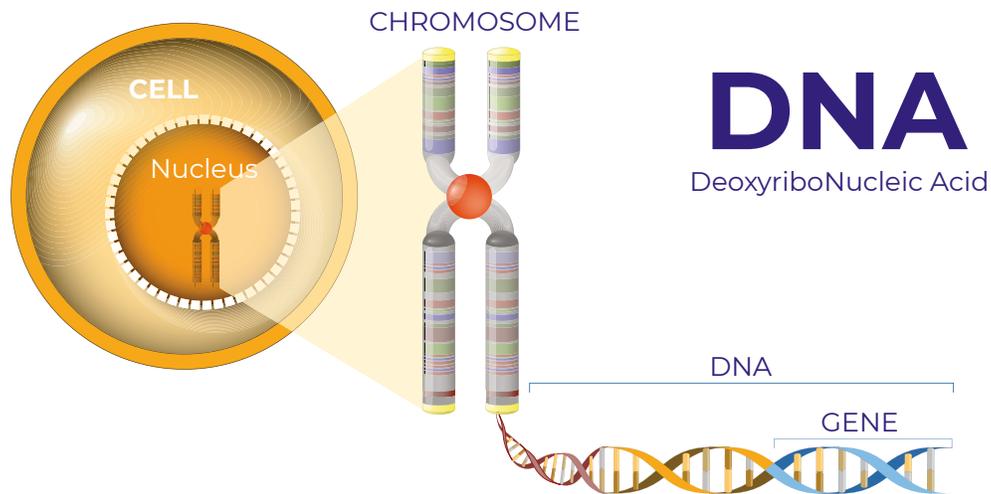
There are two main types of lung cancer based on how the cancer looks under a microscope:

NON-SMALL CELL LUNG CANCER (NSCLC), the most common type. Two subtypes of NSCLC found most often are:

- Adenocarcinoma
- Squamous Cell Carcinoma

SMALL CELL LUNG CANCER (SCLC), less commonly diagnosed and made up of cells that are smaller in size than most other cancer cells.

If you would like more information about the different types of lung cancer, check out our *Understanding Non Small Cell Lung Cancer*: <https://go2foundation.org/understanding-nsclc/> and *Understanding Small Cell Lung Cancer* booklets: <https://go2foundation.org/sclc/>



CHANGES LEADING TO LUNG CANCER

Research has found drugs called “targeted therapies” that attack cancer cells in new ways. Before we discuss targeted therapies, we will look at how cells work and how they can change into cancer.

Changes in genes can cause too much or uncontrolled growth of cells that can lead to cancer

Cells are the basic unit in our body. They make up all our organs and structures. Cells have many jobs that are carried out by parts inside the cell. The cell nucleus holds genes that control how the cell works. The genes are carried on chromosomes, 23 from each parent. They are made up of DNA

(deoxyribonucleic acid). The genes control what proteins the cell will make. Proteins perform the work of a cell.

There are many ways that normal cells in the lungs change into cancer. You will read and hear terms like *mutations, overexpression, fusions, alterations, translocations, deletions* and *rearrangements* and others. These are all types of changes that happen inside cells.

Over time, genes and the proteins they make can change. The changes may happen over generations or over a lifetime due to things to which we are exposed or what we eat and drink. These changes may also happen by random chance. Some changes are helpful. Some do not make a difference one way or the other. But other changes can lead to diseases. Changes causing too much or uncontrolled growth of the cells can lead to cancer.

COMMON GENE AND PROTEIN CHANGES IN LUNG CANCER

Genes are often called by their gene symbol (letters which stand for a longer name). It is helpful to know the name of the changes in your lung cancer. Some changes can be treated with a targeted therapy.

SYMBOL	NAME
PD-L1	Programmed death-ligand 1 (also known as cluster of differentiation 274)
CTLA-4	Cytotoxic T-Lymphocyte Associated protein 4
TMB	Tumor Mutational Burden
EGFR	epidermal growth factor receptor
ALK	anaplastic lymphoma receptor tyrosine kinase
ROS1	ROS proto-oncogene 1, receptor tyrosine kinase
BRAF	B-Raf proto-oncogene, serine/threonine kinase
RET	ret proto-oncogene
MET	MET proto-oncogene, receptor tyrosine kinase
NTRK1,2,3	neurotrophic receptor tyrosine kinase 1, 2, and 3
VEGFR	vascular endothelial growth factor receptor
KRAS	Kirsten rat sarcoma viral oncogene homolog
ERBB2/ HER2	erb-b2 receptor tyrosine kinase 2 (also known as human epidermal growth factor receptor 2)
PARP	Poly ADP-ribose polymerase
STK11	Serine/threonine kinase 11
NRG1	Neuregulin 1
FGFR1	fibroblast growth factor receptor 1
PIK3CA	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha
DLL3	delta like ligand 3



BIOMARKER TESTING

WHAT'S THE DIFFERENCE?

To know what kinds of gene and protein changes happened in the cancer, it must be tested. This testing has many names. This brochure uses the terms *biomarker testing* or *molecular testing*. These terms cover testing for all the types of changes that can be found in the cancer.

There are changes that are common in each type of lung cancer. If one of these changes is found in the cancer, it is said to have tested “positive.”

Many of the gene changes found in lung cancer only happen in small numbers of people. Right now we do not have therapies to treat all of the gene changes we know about. A lot of research is being done to find treatments to target all of the known changes.

Genetic Testing

Molecular Testing Mutation Testing

Biomarker Testing

Tumor Testing Molecular Profiling

Know your options

New ways to understand and treat lung cancer are being tested and approved more quickly than ever before. Knowing your treatment options makes you an active and empowered member of your team.

If you have not had biomarker testing, we can help you get it. Call our treatment specialists at 1-800-298-2436 or visit www.lungmatch.org.

LungMATCH

TESTING DURING DIAGNOSIS AND MONITORING

A tissue biopsy takes tissue from the cancer for testing. Doctors will look at a piece of the biopsy under the microscope. From that, they will know if you have lung cancer and what type. Most biomarker testing is also done with tissue biopsy samples. See our brochure *Understanding Lung Cancer Biopsies* to learn more.

Talk to your doctor about getting biomarker testing done at diagnosis.

We encourage patients with non-small cell lung cancer (NSCLC) to get their cancer tested at diagnosis, regardless of whether they have a smoking history or not. This will make sure you know all the possible treatment choices. If possible, you should have a “panel” test. A panel test checks for many biomarker changes at one time rather than just one or two changes. This will use less biopsy tissue than having many single gene tests.

As lung cancer spreads, it can keep changing. Knowing how the cancer changes over time can suggest new treatment choices. So if your cancer comes back, it should be tested again with a new biopsy.

Liquid biopsy is a newer way to do biomarker testing. Small amounts of the cancer DNA can be found in your blood or other fluids. Liquid biopsy is when this DNA can be tested instead of DNA from the cancer tissue. Liquid biopsy can be used for biomarker testing, but cannot be used for diagnosing cancer or to know what type.

Liquid biopsy works best when the cancer has spread outside of the lung. It may be a good choice if there is not enough tumor tissue to do biomarker testing from the original biopsy. It may also be a good choice if the cancer needs to be tested again, but a tissue biopsy is not possible. Liquid biopsy is also easier and less risky for the patient.

If you are not sure if your cancer has been tested, ask your health care team. If you have not had testing, ask why not. If you have been tested, talk with your team to make sure you understand the results of your tests.

Testing your cancer helps you know your treatment choices.

If you have received biomarker testing and are unsure what the results mean, we can help you understand them. Contact our LungMATCH specialists by phone at 1-800-298-2436 or by email at support@go2foundation.org

LungMATCH



TARGETED THERAPIES

Targeted therapies are aimed at a certain “target” in cancer cells. Their goal is stopping the change that is making the cancer grow.

Targeting the change in the cancer can spare the rest of the body from side effects. Chemotherapy kills cells that grow fast. These include cancer cells, but may also include normal cells that grow fast. This is what often causes side effects. Targeted therapies instead attack the differences between normal and cancer cells. They target the changes that are in your cancer. As a result, targeted therapy may have fewer side effects.

The Food and Drug Administration (FDA) approves drugs for use. The FDA has approved targeted therapies for some NSCLC gene changes. These include changes in the genes EGFR, ALK, ROS, BRAF, RET, MET and NTRK. This booklet describes the FDA approved drugs for changes in each of these genes.

Other types of cancer may have drugs approved to treat other gene changes. Your cancer might have a gene change more common in another cancer type.

If so, the doctor may suggest a therapy normally used for that other cancer type. Combinations of targeted therapies are starting to be used in clinical trials. Your doctor may suggest off label or compassionate use of either more than one targeted therapy at a time, targeted therapies in combination with chemotherapy, or targeted therapies in combination with immunotherapy.

HOW DO I TAKE A TARGETED THERAPY?

There are two methods to deliver targeted therapies. Some are pills taken by mouth. Others are man-made proteins. These are called *monoclonal antibodies*. They are given through a vein over several hours in a clinic.

All drugs have two names, a generic name and a brand name. You can tell if a therapy is oral or by vein by looking at the generic drug names.

GENERIC DRUG NAMES

Oral Targeted Drugs

Ends in -ib
Example: Xalkori's generic name is crizotinib

Monoclonal Antibodies

Ends in -mab
Example: Avastin's generic name is bevacizumab

DRUGS THAT TARGET

EGFR

GILOTRIF (afatinib)
IRESSA (gefitinib)
TAGRISSEO (osimertinib)
TARCEVA (erlotinib)
**TARCEVA (erlotinib) WITH
CYRAMZA (ramucirumab)**
VIZIMPRO (dacomitinib)

Some of the most common changes in NSCLC are changes in the EGFR gene. Gilotrif, Iressa, Tagrisso, Tarceva and Vizimpro are oral drugs that can all be prescribed as first treatment. They are used to target many different types of EGFR changes.

You should talk with your treatment team about which one of these drugs is best for you. All of them target the most common EGFR changes, but some of the drugs can also target less common changes in the EGFR gene. For example, Gilotrif is approved for the EGFR S768I, L861Q and G719X changes and Tagrisso can target EGFR with the T790M change. Gilotrif is also approved for use in patients with squamous cell non-small cell lung cancer. If you have received chemotherapy and have squamous cell non-small cell lung cancer, ask your doctor if Gilotrif is an option for you.

EXKIVITY (mobocertinib)
**RYBREVANT
(amivantamab-vmjw)**

Exkivity and Rybrevant have been approved for NSCLC with the exon 20 insertion mutation in EGFR.

GILOTRIF (afatinib)
PORTRAZZA (necitumumab)

Portrazza targets EGFR and is given by vein. Both Gilotrif and Portrazza have been approved for a type of NSCLC called squamous cell. Portrazza is given with chemotherapy.

ALK

ALECENSA (alectinib)
ALUNBRIG (brigatinib)
LORBRENA (lorlatinib)
XALKORI (crizotinib)
ZYKADIA (ceritinib)

Changes involving the gene ALK can also be found in NSCLC. These oral drugs are approved to treat such "ALK positive" lung cancer when it has spread. Alecensa, Alunbrig, Xalkori and Zykadia are all approved as first treatments, but can also be given as later treatments.

Lorbrena is approved for use after the cancer has stopped responding to at least one prior ALK treatment.

Importantly, some of these drugs work to treat cancer in the brain and spinal cord better. Some are better if your cancer has certain changes in ALK. Some may also have fewer side effects. It is important to talk with your healthcare team about which therapy is best for you.

ROS1

ROZLYTREK (entrectinib)
XALKORI (crizotinib)

Changes in the ROS1 gene also occur in NSCLC. Xalkori and Rozlytrek also target changes in this gene and are approved for treatment only when the cancer has spread.

Talk to your health care team about biomarker testing and if targeted therapy is right for you. For more information, call our treatment specialists at 1-800-298-2436 or visit www.lungmatch.org.

DRUGS THAT TARGET

BRAF	MEKINIST (trametinib) WITH TAFLINAR (dabrafenib)	BRAF is another gene that can change in NSCLC. These two oral drugs are approved for NSCLC with a change in BRAF called V600E. The drugs are approved only for cancer that has spread.
RET	GAVRETO (pralsetinib) RETEVMO (selpercatinib)	Changes in the RET gene can be found in 1-2% of all NSCLCs. Gavreto and Retevmo target changes in this gene and has been approved for cancers that have spread with changes in RET.
MET	TABRECTA (capmatinib) TEPMETKO (tepotinib)	Changes in the MET gene can be found in 1-3% of all NSCLCs. These drugs target a specific change in this gene known exon 14 skipping. In addition to Tabrecta and Tepmetko, there are several drugs currently in clinical trials for cancers with different changes in MET.
NTRK	ROZLYTREK (entrectinib) VITRAKVI (larotrectinib)	<p>Changes involving the NTRK genes, known as NTRK gene fusions, can be found in less than 1% of all NSCLCs.</p> <p>NTRK gene fusions can produce abnormal TRK proteins which can cause cancer to develop and grow in sites throughout the body. There can be gene fusions of NTRK1, NTRK2, or NTRK3.</p> <p>Vitakvi and Rozlytrek are oral 'TRK inhibitors' that work by blocking signals that the abnormal TRK proteins send to cells to grow and divide uncontrollably. By blocking this signal, Vitakvi stops the growth and spread of the cancer cells.</p>
KRAS	LUMAKRAS (sotorasib)	The most common genetic change in NSCLC is a change in the KRAS gene occurring in 20-40% of patients. So far, only patients whose cancer has the specific KRAS G12C mutation have an approved treatment, but other variants of the KRAS mutation are under investigation in clinical and pre-clinical trials.
Other Targeted Therapies	AVASTIN (bevacizumab) CYRAMZA (ramucirumab) MVASI (bevacizumab-awwb)	<p>Some targeted therapies work in a different way. These drugs target proteins that cause blood vessel growth. The goal is to "starve" the cancer by cutting off the blood supply that feeds it. Unlike other targeted therapies, these therapies do not need biomarker testing.</p> <p>The VEGF protein family causes blood vessel growth around cancers. Avastin targets VEGF-A. It can be taken in combination with chemotherapy and as a first treatment. It is given by vein. Mvasi is nearly the same therapy as Avastin. It is called a biosimilar.</p> <p>Cyramza targets VEGFR2. It can be used after the cancer has grown during prior treatment. It is given together with chemotherapy or Tarceva (for patients with changes in the EGFR gene). It is given by vein.</p>

DRUG RESISTANCE

Often targeted therapies work well for some time, but then stop working. This is known as “resistance” to the therapy.

Resistance happens in different ways. There may be new changes in the cancer. When cancer begins to grow again, you may need a new biopsy and biomarker testing. This testing looks for causes of resistance. For some types of resistance, there are drugs already approved.

For example, if your cancer is positive for ALK, you may take Alecensa. It may work well for months or years. Then the drug stops working and the cancer starts to grow again. If you develop resistance due to other changes in the ALK gene, you may be eligible for other ALK targeted drugs like Lorbrena. If you develop resistance due to changes in a different gene, there may be different options that are available.



THINGS TO KNOW

Targeted therapies may have fewer side effects than chemotherapy, but they can sometimes be severe. The most common side effects are rash and diarrhea. Talk with your treatment team about how you might manage them. Other less common side effects may include:

- Vision problems
- Liver problems
- Tiredness
- Nausea
- Heart problems
- Lung problems

For additional information on coping with side effects, visit our website at www.go2foundation.org.

We are still learning how to best use targeted therapies. Studies are underway to use them with other treatments. These other treatments include chemotherapies or immunotherapies. Please see our *Understanding Immunotherapies* brochure for more information on these new treatments. Treatments that include several different types of drugs may become more common in the future.

Targeted drugs can be costly. Drug companies often have programs that may help. We can direct you to the right program. Call our HelpLine at 1-800-298-2436.



CLINICAL TRIALS

Research is moving quickly. There are many clinical trials for different gene changes. When you have your cancer tested, the results may suggest a clinical trial for your gene changes.

A clinical trial is a research study to determine whether a new drug, combination of drugs, procedure or medical device is safe and effective.

There are also new types of clinical trials which test many gene changes at once. They then put you in a part of the trial for your gene changes. Examples are LUNG-MAP and NCI-MATCH. Talk to your treatment team about whether a clinical trial is right for you.

To learn more and find clinical trials near you, call our clinical trial specialists at 1-800-298-2436 or visit www.lungmatch.org.

ABOUT GO2 FOUNDATION

Founded by patients and survivors, GO2 Foundation for Lung Cancer transforms survivorship as the world's leading organization dedicated to saving, extending, and improving the lives of those vulnerable, at risk, and diagnosed with lung cancer.

GO2 Foundation works to change the reality of living with lung cancer by ending stigma, increasing public and private research funding, and ensuring access to care.

For more information about lung cancer and current treatments, to discuss support options or for referral to other resources, please contact us:

HELPLINE | 1-800-298-2436 or support@go2foundation.org

**BIOMARKER TESTING &
CLINICAL TRIAL MATCHING** | lungmatch.org

WEBSITE | go2foundation.org



Empower Everyone. Ignore No One.



GO₂ FOUNDATION FOR LUNG CANCER

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