YOUR PATIENTS ARE CONFUSED!

CLEARING THE MUDDY WATERS OF TESTING IN OVARIAN CANCER

Patients need confidence to know that they are receiving a treatment that gives them the best chance of survival. Communication from health care providers (HCPs) about their treatment plans can help provide this confidence. Molecular testing is necessary in order to plan treatment for patients with ovarian cancer. The National Comprehensive Cancer Network (NCCN) recommends that all patients with ovarian cancer receive germline testing for BRCA1/2. Tumor testing is necessary when the patient is negative for BRCA1/2 mutations.

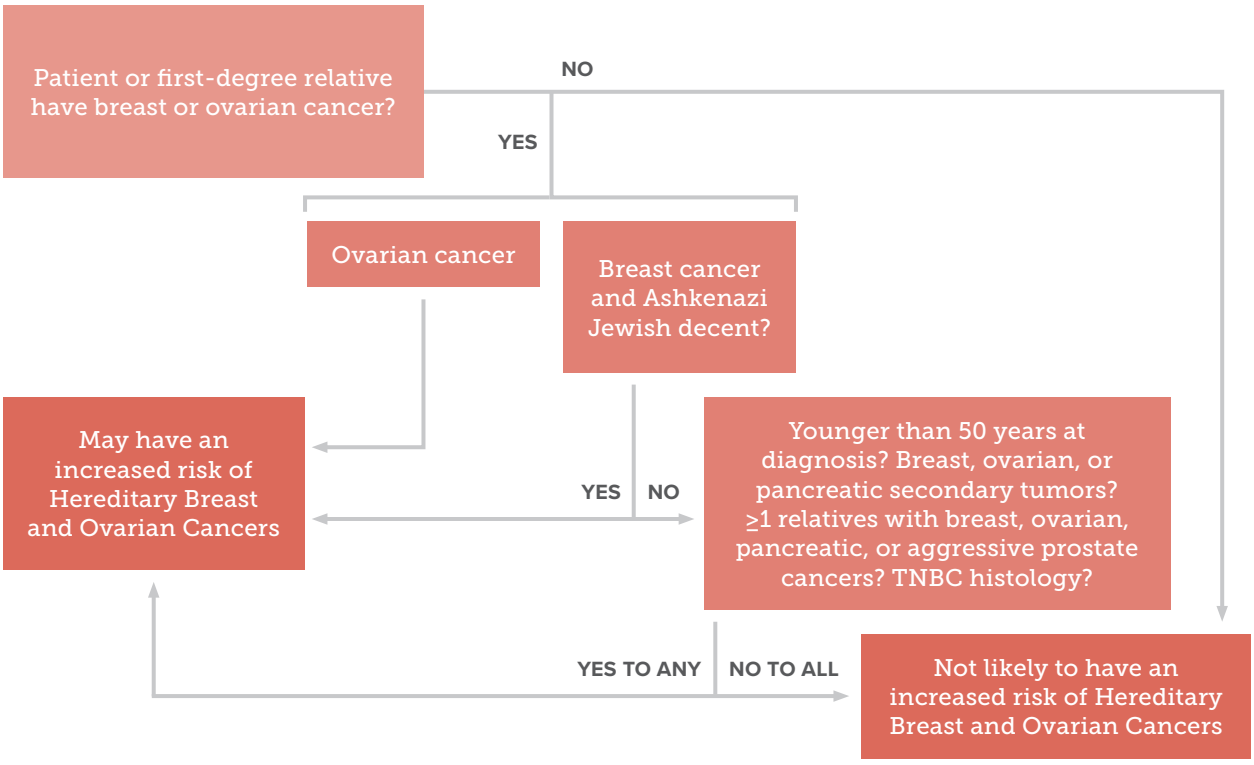
However, the terminology related to genetic testing and relevant to treatment options in patients with ovarian cancer can be confusing to patients. It is easy for HCPs, who use these terms on a daily basis, to forget that patients have varying levels of health literacy. This toolkit gives HCPs a list of commonly used terms, that patients may encounter, defined in easy-to-understand language. This HCP toolkit also includes some key points that an HCP may use to help a patient understand more about how testing results inform ovarian treatment plans.

Mutation and Biomarker Testing for Ovarian Cancer Treatment

WHY IS TESTING IMPORTANT?

When diagnosed with ovarian cancer, ALL patients are recommended to undergo genetic and tumor testing. Genetic and tumor testing allows treatment plans to incorporate medications that have demonstrated the ability to improve outcomes in patients whose genetics or tumors exhibit specific biomarkers or mutations. It is recommended that all women with a diagnosis of ovarian cancer receive genetic and biomarker testing. Similar to how we test bacteria to determine which antibiotic will work best when we have an infection, we can also look at mutations and markers in our genes and in the tumor itself to predict whether some treatments will work. Currently, a few specific mutations and biomarkers are used to direct therapy in ovarian cancer. These can be germline (inherited) and somatic (in the tumor). Many clinical trials have helped shape guidelines to best utilize the information that is discovered from testing. Additionally, receiving testing that looks for a broad range of mutations and biomarkers is preferred because there are clinical trials that you may be eligible to participate in based, in part, on your results. Clinical trial participation is highly recommended. At a minimum, clinical trials provide treatments that are considered standard of care and additionally they offer the possibility of receiving new medications or medications earlier in the course of treatment than guidelines currently recommend.

Risk of Hereditary Breast and Ovarian Cancers*



*It is recommended to consider having patient consult with genetic counseling services

Biomarker testing is a way to look for genes, proteins, and other substances (called biomarkers or tumor markers) that can provide information about cancer. Each person's cancer has a unique pattern of biomarkers. Some biomarkers affect how certain cancer treatments work. Biomarker testing may help you and your doctor choose a cancer treatment for you.

There are also other kinds of biomarkers that can help doctors diagnose and monitor cancer during and after treatment. To learn more, visit the **NCI Tumor Markers** fact sheet.

Biomarker testing for cancer treatment may also be called:

- tumor testing
- tumor genetic testing
- genomic testing or genomic profiling
- molecular testing or molecular profiling
- somatic testing
- tumor subtyping

Biomarker testing is different from genetic testing that is used to find out if someone has inherited mutations that make them more likely to get cancer. Inherited mutations are those you are born with. They are passed on to you by your parents. Tumor biomarker testing identifies mutations that contribute to tumor growth or are associated with tumors preferentially compared to normal (non-cancerous) tissue.

HOW ARE BIOMARKER TESTS USED TO SELECT TREATMENTS FOR OVARIAN CANCER?

Biomarker tests can help you and your oncologist or oncology team select a cancer treatment that is tailored for you. Some cancer treatments, including targeted therapies and immunotherapies, may be more effective for people whose cancers have certain biomarkers.

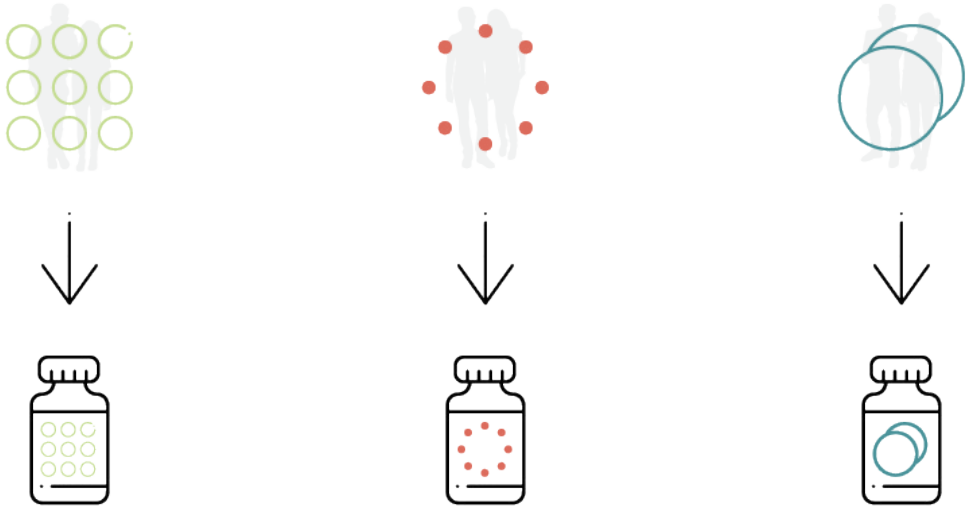
For example, people with ovarian cancer with certain genetic changes that cause defects in DNA repair pathways may benefit from agents called PARP inhibitors, that work with this defect to target the cancer. When MSI-H or dMMR biomarkers are found, treatment with PD-1 inhibitors are considered. When tumors are found to have other biomarkers, such as *NTRK* gene fusion or *BRAF* V600E mutations, other targeted agents may be helpful. In each of these cases, the treatments may not be considered unless there are mutational biomarkers that indicate that the treatment may work better than without the treatment.

Biomarker testing could also help you find a clinical trial that you may be able to join. Clinical trials are opportunities to access emerging therapies before they gain approval for widespread use.

For example, studies like **NCI-MATCH**, **NCI-COG Pediatric MATCH**, and **NCI-ComboMATCH** are using biomarker tests to match people to treatments based on the genetic changes in their cancers. To find out if there are open trials for which you may be eligible, use the search tool at **Find Clinical Trial**. Or, contact the **Cancer Information Service** for help.

Precision Medicine: The Right Drug to the Right Patient

Patients with tumors that share the same genetic change receive a drug that takes advantage of that genetic change.



ARE THERE DIFFERENT TYPES OF BIOMARKER TESTS?

Yes, there are many types of biomarker tests that can help select cancer treatment. Most biomarker tests used to select cancer treatment look for genetic markers. But some look for proteins or other kinds of markers.

Some tests check for a single biomarker. Others check for many biomarkers at the same time and may be called multigene tests or panel tests. Some tests are for people with a certain type of cancer, like melanoma. Other tests look for biomarkers that are found in many cancer types, and such tests can be used by people with different kinds of cancer. Your doctor will choose a test that informs treatment of ovarian cancer.

Some tests, called whole-exome sequencing, look at all the genes that direct the production of proteins in your cancer. Others, called whole-genome sequencing, look at all the DNA (both genes and the genetic material in between genes) in your cancer.

Still other biomarker tests look at the number of genetic changes in your cancer (what's known as "tumor mutational burden"). This information can help figure out if a type of immunotherapy known as immune checkpoint inhibitors may work for you.

WHAT DO THE RESULTS OF A BIOMARKER TEST MEAN?

The results of a biomarker test could show that your cancer has a certain biomarker that is targeted by a known therapy. That means that the therapy may work to treat your cancer. The matching therapy may be available as an FDA-approved treatment, an off-label treatment, or through participation in a clinical trial.

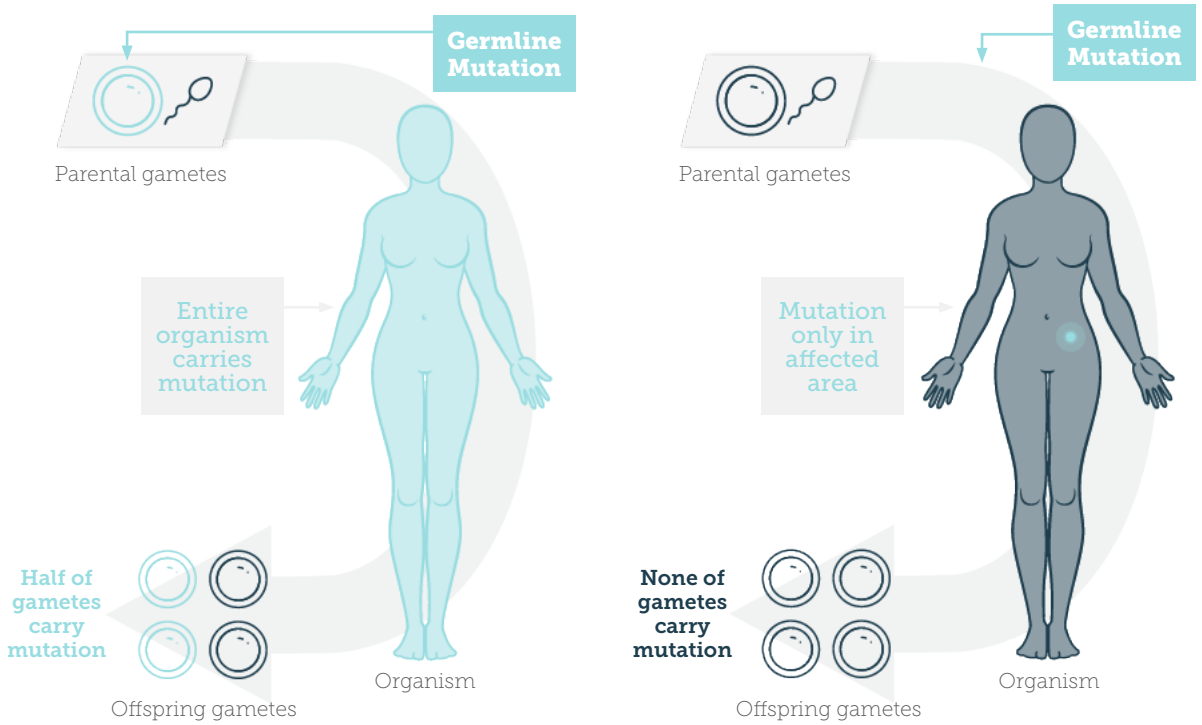
The results could also show that your cancer has a biomarker that may prevent a certain therapy from working. This information could spare you from getting a treatment that won't help you.

In many cases, biomarker testing may find changes in your cancer that won't help your doctor make treatment decisions. For example, genetic changes that are thought to be harmless (benign), whose effects are not known ("variant of unknown significance"), or against which there are not any available drugs and are not used to make treatment decisions.

Based on your test results, your health care provider may recommend a treatment that is not FDA approved for your cancer type but is approved for the treatment of a different type of cancer that has the same biomarker as your cancer. This means the treatment would be used off-label, but it may work for you because your cancer has the biomarker that the treatment targets.

Some biomarker tests can find genetic changes that you may have been born with (inherited) that increase your risk of cancer or other diseases. These genetic changes are also called germline mutations. If such a change is found, you may need to get another genetic test to confirm whether you truly have an inherited mutation that increases cancer risk. For instance, mutations in the *BRCA*1 and *BRCA*2 genes are associated with an increased risk of breast and ovarian cancers. However, tumors can acquire mutations in these genes, without the mutations being germline. If your doctor suspects that you may have a germline mutation that increases the risk that cancer may affect you and your family, they may recommend that you speak with a genetic health care provider (such as a genetic counselor, clinical geneticist, or a certified genetic nurse) to help you understand what the test results mean for you and your family.

Germline vs Somatic Mutations



Germline mutations are inherited and found in all cells.
Somatic mutations are not inherited and are found within the tumor.

IN SUMMARY

Treatment options for patients with ovarian cancer now include a number of targeted therapies aimed at particular mutations and several immunotherapies aimed at a patient's own immune system. Each of these treatments can provide substantial benefits—but not to all patients. Comprehensive biomarker testing is used among patients with ovarian cancer to determine the presence of particular mutations or of a particular protein. It is the first step in ensuring that a patient is matched to the right treatment at the right time, based on the unique features in each patient's cancer.

To get more information about biomarker testing, please visit the **National Cancer Institute**.

LANGUAGE RELATED TO TESTING:

Biomarker

Biological component, such as a protein or genetic mutation, that can be quantified to determine cancer growth or remission, as well as suggest a prognosis or predictive treatment.

Clinical Treatment Guidelines

A set of instructions for best practices in the treatment of specific disorders or conditions, written by leading experts in the field, using the most current understanding of the disease.

Clinical Utility

Something, such as a drug or information derived from a diagnostic test, that is useful in the treatment or prevention of disease.

DNA (Deoxyribonucleic Acid)

Organic chemical structure within the nucleus that serves as hereditary material for encoding almost all of an organisms' proteins.

Gene

DNA that can be transcribed into RNA then usually translated into protein. A gene is the original copy of genetic material, stored as DNA.

Gene Sequencing

A method for examining the order of DNA base pairs with genes.

Genetic Counseling

Informing and advising by a geneticists or other health care professional about genetic test results regarding a patient's health and their family health.

Genetic Counselor/Geneticist

A health care provider team member with a skillset in diagnosis and genetic testing. Specifically, a geneticist would advise the patient about the impact of germline mutations that may be passed from parent to offspring.

Genetic Mutation

An alteration in DNA that leads to a change in the DNA sequence. These changes can be good, bad, or inconsequential to a cell.

Genetic Testing

An assessment of patient genomic code in search of specific mutations leading to cancer or other diseases.

Germline Mutation

A congenital and hereditary mutation in patient's DNA.

mRNA (ribonucleic acid)

A genetic replica of hereditary material encoded within DNA, which is often used to direct the synthesis of proteins. Whereas DNA is the original copy of information, mRNA is the "working copy."

MSI Screening

Measuring specific DNA microsatellite length in tumors to help determine if tumor cells have fully functional DNA repair mechanisms and to choose a possible treatment.

Mutation

An alteration in DNA that leads to a change in the DNA sequence. These changes can be good, bad, or inconsequential to a cell.

Next Generation Sequencing (NGS)

Method consisting of sequencing millions of DNA segments at one time from a single tissue sample.

Panel Test

A measurement of multiple analytes within a single diagnostic test, such as tumor profiling. The CBC (complete blood count) or blood chemistry tests that most people receive at their annual physical exam are panel tests.

Predictive Biomarker

A biomarker used to identify individuals who are more likely than similar individuals without the biomarker to experience a favorable or unfavorable effect from exposure to a medical product or an environmental agent.

Prognostic Biomarker

A biomarker used to identify likelihood of a clinical event, disease recurrence, or progression in patients who have the disease or medical condition of interest.

Prognostic Test

A diagnostic test used to examine clinical health outcomes. These tests help doctors determine the expected outcomes of a given treatment or disease course. Doctors may use phrases like good or bad prognosis indicating whether the disease course or the treatment options are expected to result in favorable or unfavorable outcomes.

Single Analyte Test

A diagnostic test that measures and analyzes the chemical makeup of a single substance.

Somatic mutation

A spontaneous genetic mutation within tissue or cancer cells that is not heritable.

BIOMARKERS THAT HELP DETERMINE IF CANCER IS PRESENT:

CA-125

Mucin glycoprotein family member that can be detect via liquid biopsies (blood tests) and serve as biomarker for ovarian cancer.

Carcinoembryonic Antigen (CEA)

Mucin glycoprotein family member that can be detect via liquid biopsies (blood tests) and serve as biomarker for ovarian cancer.

Circulating Tumor DNA (ctDNA)

DNA segments found in blood that are identifiable by the genetic mutations associated with cancer.

MUTATIONAL BIOMARKERS THAT HELP GUIDE TREATMENT:

***BRCA*1**

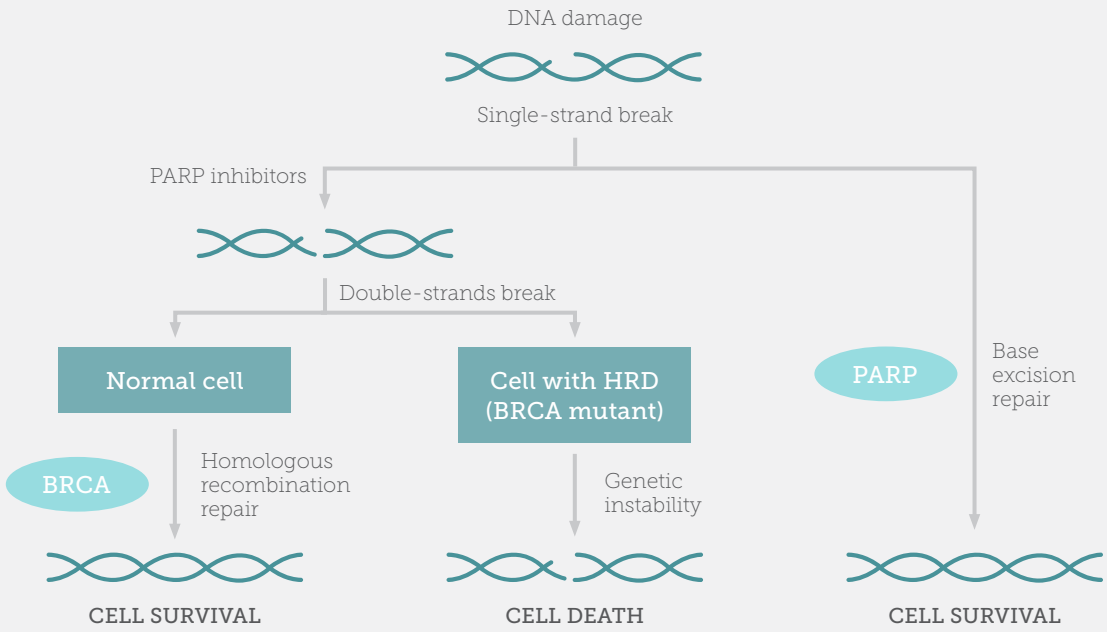
A human gene involved in DNA repair and transcription. Germline mutations of these genes can lead to hereditary cancers, including ovarian cancer.

***BRCA*2**

A human gene involved in DNA repair and transcription. Germline mutations of these genes can lead to hereditary cancers, including ovarian cancer.

***BRCA*1/2**

Both BReast CAncer gene 1 and 2 can synthesize proteins responsible for DNA repair. Two copies are passed down from each parent. They suppress tumor development by reducing the occurrence of gene mutations, which may lead to cancer development.



Homologous Recombination Deficiency (HRD)

An inability to perform DNA double stranded break repair. A deficiency in HR indicates that tumor cells will struggle to repair themselves. Tumors that are "HRD+" are those that have deficiencies in DNA repair. "HR proficient" cells have normal DNA repair function.

Loss of Heterozygosity (LOH)

The loss of one of the two copies of a gene that is normally carried in all cells. In losing one copy, the cell becomes homozygous.

Microsatellite Instability (MSI)

Short tandem DNA repeats that accumulate when DNA mismatch repair is malfunctional.

Mismatch Repair (MMR)

A DNA repair mechanism that functions to detect and correct small mistakes in DNA, such as deletions or insertions of base pairs into DNA to conserve genomic stability

Tumor Mutational Burden (TMB)

Quantity of mutations within tumor cell DNA, which can serve as a biomarker and inform treatment options. High TMB is associated with deficiencies in DNA repair pathways.

LANGUAGE RELATED TO MEDICATIONS:

Immune Checkpoint Inhibitors (ICIs)

Type of immunotherapy used to "rev up" the immune system. Tumor cells produce proteins that disable a patient's immune system from eradicating the cancer. By inhibiting this

interaction—that is, “immune checkpoint”—these drugs restore the ability of immune cells to recognize cancer cells as dangerous.

Immunotherapy

A treatment option that employs the immune system to defend against cancer via targeting immune or cancer cell proteins.

PARP inhibitors

All normal cells contain multiple DNA repair mechanisms. Often, cancer cells have defects in one DNA repair pathway (for example, BRCA1/2). These inhibitors introduce block the remaining DNA repair mechanism leading to selective cancer cell death.

Precision Medicine

A personalized treatment or preventative care approach based on a patient’s own genetic profile.

Systemic therapy

A therapy, like chemo-, hormone, or targeted therapy, that can treat cancer cells that reside anywhere within the body.

Targeted (cancer) therapy

Therapy option that targets a particular molecule or pathway associated with a tumor cell or cellular pathway that occurs with greater frequency in cancer cells.

LANGUAGE THAT YOUR ONCOLOGY TEAM MAY USE WHEN TALKING ABOUT THE BENEFITS OF TREATMENTS:

Overall Survival

Time length from diagnosis or treatment of disease that a patient remains alive

Progression Free Survival

Period of time a treated patient is alive without symptoms of disease progressing.

REFERENCES

1. https://www.fightcancer.org/sites/default/files/Improving%20Access%20to%20Biomarker%20Testing.pdf
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer, Version 5.2022. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed October 3, 2022.
3. National Cancer Institute https://www.cancer.gov/about-cancer/treatment/types/biomarker-testing-cancer-treatment. Accessed August 20, 2022.