



A Patient's Guide

Understanding Tumor Markers for Breast and Colorectal Cancers



Recommendations of
the American Society
of Clinical Oncology



The American Society of Clinical Oncology (ASCO) is the world's leading professional society representing physicians from nearly 100 countries who treat people with cancer. ASCO's more than 18,000 members set the standard for patient care worldwide and lead the fight for more effective cancer treatments, increased funding for clinical and translational research, and, ultimately, cures for the many different cancers that strike 1.2 million Americans every year.

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A Patient's Guide to Understanding Tumor Markers for Breast and Colorectal Cancers

Introduction

The American Society of Clinical Oncology (ASCO) includes over 18,000 oncologists worldwide, and is a respected authority on the practice of clinical oncology, the care of people with cancer. To help doctors give their cancer patients the best possible care, ASCO asks its medical experts to review the latest research on issues in cancer care and develops recommendations called clinical practice guidelines.

To help patients understand their cancer care, ASCO has created this patient guide, based on what ASCO's experts ask your doctors to keep in mind when using tumor markers in breast and colorectal cancer. We hope it will help you learn about tumor markers and how they are used in diagnosing, treating, and following cancer.

As you read this guide, please keep in mind the following:

- Every person treated for cancer is different. These recommendations are not meant to replace your or your doctors' judgment. The final decisions you and your doctors make will be based on your individual circumstances.
- These recommendations do not apply to clinical trials (research studies), and many of the tumor markers here continue to be studied in clinical trials. Although ASCO does not recommend many of the markers listed here, it is often because there is not enough information to provide such recommendations, not because they are useless or harmful. Therefore, you may see these markers mentioned in other places as part of a research study as scientists seek to answer questions about the use of tumor markers.
- While tumor markers can sometimes help determine if cancer has come back (recurred), there is often no evidence that finding cancer early can either extend life or help people have a better quality of life. ASCO only recommends the use of a tumor marker when it has proven useful in prolonging life or improving quality of life.

About tumor markers

How are tumors usually detected, diagnosed, and treated?

A tumor is an abnormal mass of tissue that starts when cells grow unregulated by the signals that normally control cell growth and death. Tumors can be either benign (not cancer) or malignant (cancer). Malignant tumors can spread to surrounding tissues or other parts of the body, a process called metastasis.

When doctors think a person might have cancer, they may perform x-rays, magnetic resonance imaging (MRI), computed tomography (CT) scans, or laboratory tests. Your doctor may also do a biopsy, a procedure where a surgeon removes part of a tumor and checks it under a microscope for cancer cells.



What is a tumor marker?

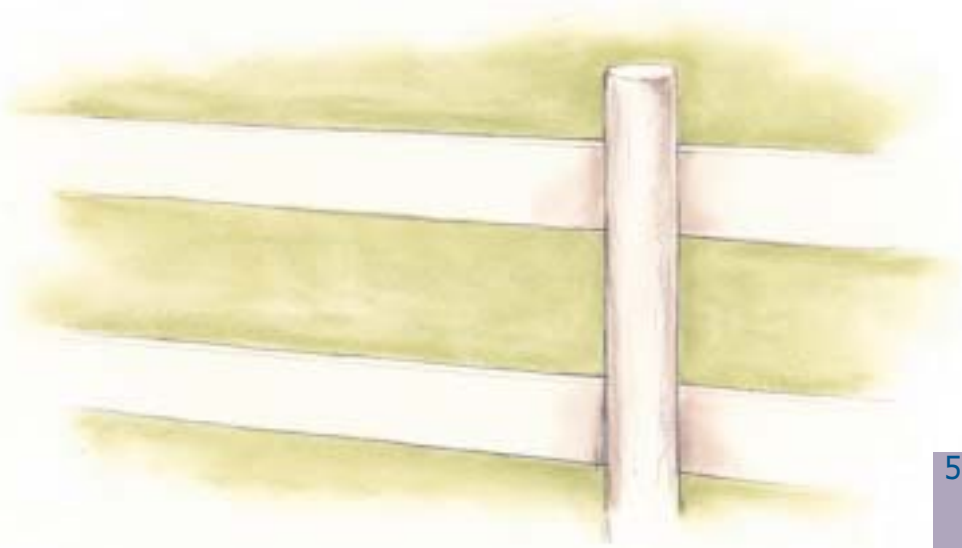
A tumor marker (also called a serum marker or biomarker) is a substance found in higher than normal amounts in the blood, urine, or body tissues of people with certain kinds of cancer.

Tumor markers are produced either by the tumor or by the body as a result of cancer or other conditions. To check the level of a tumor marker, the doctor takes a sample of blood, urine, or the tumor, and sends it to a laboratory for testing.

One day, we hope to use blood tests to detect and diagnose all cancers. We cannot yet do that, because:

- tumor markers can be high in people without cancer but with benign conditions, or can be present at some level in all people
- tumor markers are not higher in every person with cancer, especially in the early stages of disease
- many tumor markers are not specific to a certain type of cancer

But when used along with x-rays or other tests, higher than normal levels of tumor markers can help doctors diagnose and follow some types of cancer. If you have any tumor markers tested, your doctor will review the results of these and other tests with you, and will plan your treatment based on all available information.



How are tumor markers used?

ASCO decided to describe each tumor marker in terms of how it can help in the *screening, diagnosis, prognosis, monitoring, and surveillance* of cancer. Each is explained below. Your doctor can tell you more about tumor markers, and can help decide the best use of tumor markers for you.

Screening (Finding cancer early)

Since treatment is more likely to be successful if cancer is found before it spreads, we are looking for ways to use tumor markers to screen large numbers of healthy people or people at higher risk to try and detect cancer early. Doctors still recommend other, non-tumor marker screening tests for people at increased risk, such as mammography for breast cancer or colonoscopy for colorectal cancer.

Diagnosis (Is it really cancer?)

Doctors make a diagnosis using different sources of information, such as location of the tumor, symptoms and lab test results. Having a correct diagnosis helps doctors to plan the best treatment. Tumor markers may sometimes help diagnose some cancers by showing if a tumor is benign or malignant.

Prognosis (How will the cancer behave?)

Prognosis predicts how the cancer will behave and how it will respond to treatment. Prognosis involves staging, or finding out if the disease has spread to other parts of the body. Doctors can sometimes use tumor marker levels to help stage a disease and plan the best treatment.

Monitoring (How is the treatment working?)

Measuring tumor marker levels during treatment may help monitor, or watch, a tumor's response to treatment. A falling level of a tumor marker may mean that the treatment is working, while a rising level may mean that the cancer is growing. It is important to remember that tumor marker levels are just one piece of information and need to be considered in light of a patient's entire situation.

Predicting Response (Will a drug be effective?)

Markers associated with tumor cells, such as hormone receptors and HER-2, can identify cancers that are more likely to respond to certain treatments.

Surveillance (Will I need more treatment?)

After treatment has ended, patients receive follow-up care, or surveillance. Tumor markers may help predict if a tumor will come back.

What Should I Ask My Doctor About Tumor Markers?

Knowing as much about your cancer as possible can help you can make decisions about your care and treatment. If you have questions about tumor markers, be sure to ask your doctor, and keep asking until you understand. These questions might help you plan your meeting with your doctor:

- What tumor marker tests do you recommend for me? Which ones have you already performed?
- How are these tests performed? How often should I have them?
- Do I have abnormal levels of any tumor markers?
- If I do have abnormal levels of a tumor marker, what does that mean? How will it affect my treatment?
- How will you use tumor markers in my follow-up care?

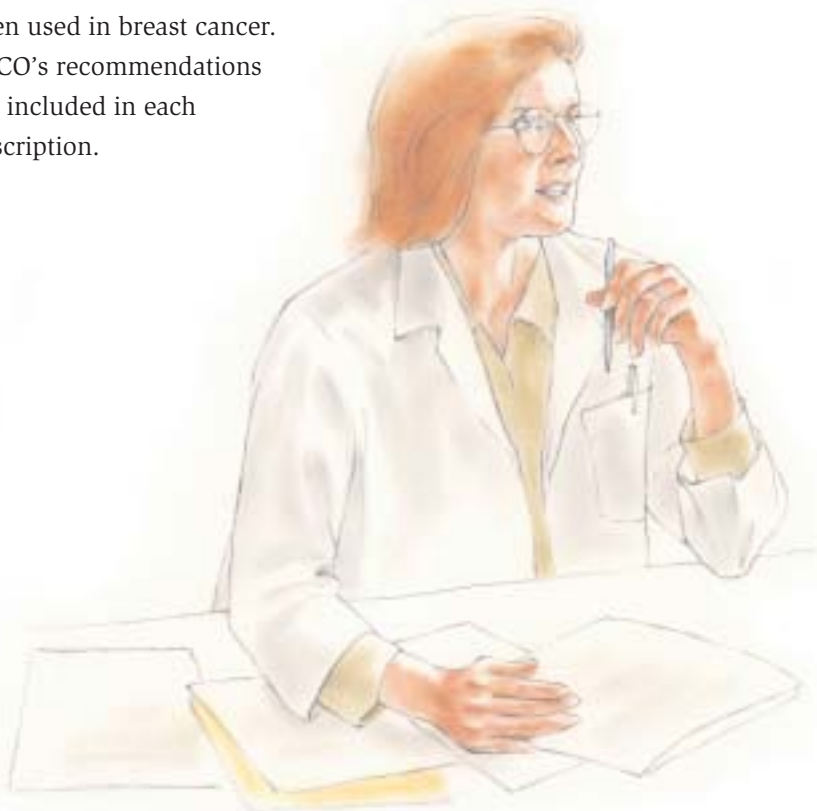
Tumor Markers for Breast and Colorectal Cancer

A panel of experts met in 1996 to develop the guidelines you will find below, then again in 2000 to update them. Of the tumor markers listed here, CEA, DNA ploidy, and p53 have been used in both breast and colorectal cancers.

Tumor Markers for Breast Cancer

Breast cancer is the second most common cancer in women and the second leading cause of cancer death among women. If breast cancer is found early, treatment is more likely to be successful. The best way to find breast cancer early is by having regular mammograms and clinical breast examinations, and by doing breast self-examination.

The tumor markers listed below have been used in breast cancer. ASCO's recommendations are included in each description.



HER-2/neu (c-erbB-2): This marker is found in some breast cancer cells, and may help indicate how a woman will respond to different types of treatment. *ASCO recommends the use of c-erbB-2 for the diagnosis and prognosis of breast cancer.*

- *Every patient with breast cancer should receive a test for HER-2/neu either at time of diagnosis or if cancer has come back (recurrence).*
- *HER-2/neu levels can identify women who are likely to benefit from trastuzumab (Herceptin) treatment or anthracycline-based treatments (adriamycin, doxorubicin, epirubicin).*
- *HER-2/neu levels should not be used to predict the risk of breast cancer recurrence.*



Tumor Markers for Breast Cancer, con't

Steroid Hormone Receptors: In both pre- and postmenopausal women, levels of steroid receptors (**estrogen** and **progesterone**) can predict which women are likely to benefit from hormone treatment. *ASCO recommends the use of steroid hormone receptors in the diagnosis, prognosis, and treatment planning for women with breast cancer. Levels of estrogen and progesterone should not be used alone in predicting breast cancer recurrence, but should be used along with other data such as the size of the tumor and the presence of cancer cells in lymph nodes.*

CA 15-3 (or CA 27.29): Levels of CA 15-3 can increase as a tumor grows. Very high levels of CA 15-3 may indicate advanced disease or metastatic cancer. *ASCO does not recommend CA 15-3 as a tumor marker for screening, prognosis, or predicting recurrence of breast cancer. A rising CA 15-3 level can detect recurrence after primary treatment, but it is not yet clear if using this test affects survival or quality of life for women with breast cancer. There can also be false positives (positive results in women with no cancer). CA 15-3 or CA 27.29 levels may indicate response to or failure of treatment in some women with breast cancer. Sometimes this can be helpful if other tests are not straightforward.*

Carcinoembryonic antigen (CEA): Cancer cells produce CEA in large amounts, but it can also be found in the blood of healthy people. *ASCO does not recommend CEA as a tumor marker for breast cancer. Routine use of CEA for monitoring response of metastatic disease to treatment is not recommended, but if no other test is available, a rising CEA level may indicate that treatment is not working.*

DNA Ploidy: DNA (deoxyribonucleic acid, found in all cells) contains a genetic code that controls cell growth and function.

A DNA ploidy test can measure DNA in tumor cells. *ASCO does not recommend the use of DNA ploidy as a tumor marker for breast cancer. There has not been enough research to justify recommending the use of this tumor marker to determine prognosis or treatment plans in women with breast cancer.*

p53: p53 is a tumor suppressor gene that is mutated, or changed, in more than 50 percent of tumors. When it is mutated, p53 can no longer stop cells from dividing, and they can form tumors.

ASCO does not recommend the use of p53 as a tumor marker for breast cancer. Studying p53 has helped researchers understand how tumors form, but measuring p53 levels in cancer patients has not yet been shown to predict differences in survival or quality of life. More research is needed before p53 can be recommended.

Cathepsin-D: High levels of this enzyme may indicate breast cancer. *ASCO does not recommend the use of cathepsin-D as a tumor marker for breast cancer. There is not enough information to recommend using cathepsin-D levels to make treatment decisions for patients with primary or metastatic breast cancers.*

Tumor Markers for Colorectal Cancer

Colorectal cancer is the second leading cause of cancer death in the United States for men and women combined. Regular screening can help prevent colorectal cancer by detecting pre-cancerous polyps (masses of tissue that can form in the colon). Removing these polyps can prevent colorectal cancer from developing. Talk with your doctor about colorectal cancer screening and which test is right for you.

The tumor markers listed below have been used in colorectal cancer. ASCO recommendations are included in each description.

Carcinoembryonic antigen (CEA): Cancer cells produce CEA in large amounts, but it is also found in the blood of healthy people. CEA is measured to help monitor colorectal cancer, especially when cancer has spread outside of the colon. Other types of cancer, as well as certain non-cancerous conditions such as inflammatory bowel disease, pancreatitis, and liver disease can also cause high levels of CEA. *ASCO recommends the use of CEA to help predict the risk of recurrence, help detect recurrence, and help determine the response to or failure of treatment for metastatic or recurrent disease.*

Lipid-associated sialic acid (LASA): A LASA test measures the amount of sialic acid in blood, and can be high in patients with many different cancers. LASA levels may also be higher in people with other, non-cancerous conditions. *ASCO does not recommend LASA as a tumor marker for colorectal cancer. LASA has not been shown to improve screening, diagnosis, prognosis, or monitoring recurrence of metastatic colorectal cancer.*

CA 19-9: The CA 19-9 test is now used as a tumor marker for pancreatic cancer. CA 19-9 is also produced by other intestinal tumors as well as colon, ovary, and lung cancers. *ASCO does not recommend CA 19-9 as a tumor marker for colorectal cancer. CA 19-9 is not used for screening of colorectal cancers because of high false-positive rates (positive results in cancer-free people). CA 19-9 has not been shown to improve the management of colorectal cancers, and does not add more information than is provided by the CEA tumor marker.*

DNA Ploidy: DNA (deoxyribonucleic acid, found in all cells) contains a genetic code that controls cell growth and function. A DNA ploidy test can measure DNA in tumor cells. *ASCO does not recommend the use of DNA ploidy as a tumor marker for colorectal cancer. A DNA ploidy test does not offer any extra information to what the standard tumor staging process offers. It should only be ordered as part of a research trial.*

p53: p53 is a tumor suppressor gene that is mutated in more than 50 percent of tumors. When mutated, p53 can no longer stop cells from dividing, and they can form tumors. *ASCO does not recommend the use of p53 as a tumor marker for colorectal cancer. While studying p53 has helped researchers understand the process of tumor formation, measuring p53 levels in cancer patients has not yet been shown to help predict differences in survival or quality of life. More research is needed before p53 can be recommended.*

ras: The ras oncogene is a gene that, if it changes (mutates), can play a part in the growth of cancer. It can be altered in polyps or cancers of the colon. *ASCO does not recommend ras as a tumor marker for colorectal cancer. There has not been enough research to justify the use of ras in the treatment of colorectal cancer.*

What about tumor markers for other cancers?

Right now, ASCO only has guidelines for using tumor markers for breast and colorectal cancers. Future guidelines may address their use for other cancers such as ovarian cancer, testicular cancer, or multiple myeloma. To see all of ASCO's recommendations, please visit our website at <http://www.asco.org>.

Where can I get the original Clinical Practice Guidelines?

The full text of all ASCO's Clinical Practice Guidelines are available on ASCO's website at <http://www.asco.org>.

Where can I find more information on cancer?

More information is also available online on ASCO's patient information website, **People Living with Cancer**, at <http://www.peoplelivingwithcancer.org>.



Summary of test recommendations

ASCO Recommendations

Yes, means the test is recommended for the specific use

No, means the test is NOT recommended for the specific use

Tumor Markers in Breast Cancer

<i>Specific Use</i>	<i>c-erb B-2</i>	<i>Steroid Hormones</i>	<i>Ca 15-3</i>	<i>CEA</i>	<i>DNA ploidy</i>	<i>p53</i>	<i>Cathespin -D</i>
<i>Screening</i>	No	No	No	No	No	No	No
<i>Diagnosis</i>	Yes	Yes	No	No	No	No	No
<i>Prognosis</i>	Yes	Yes	No	No	No	No	No
<i>Monitoring</i>	No	Yes	No	No	No	No	No
<i>Surveillance</i>	No	Yes	No	No	No	No	No

Tumor Markers in Colorectal Cancer

<i>Specific Use</i>	<i>CEA</i>	<i>LASA</i>	<i>Ca 19-9</i>	<i>DNA ploidy</i>	<i>p53</i>	<i>ras</i>
<i>Screening</i>	No	No	No	No	No	No
<i>Diagnosis</i>	No	No	No	No	No	No
<i>Prognosis</i>	Yes	No	No	No	No	No
<i>Monitoring</i>	Yes	No	No	No	No	No
<i>Surveillance</i>	No	No	No	No	No	No

Resources

Many organizations offer support to patients with cancer and their families. Ask your doctor or call your local hospital to find out about such groups in your community. In addition, these organizations can provide information or educational materials about cancer.

Cancer Care, Inc.

275 Seventh Avenue
New York, NY 10001
800-813-HOPE
www.cancercare.org

Colon Cancer Alliance

175 Ninth Avenue
New York, NY 10111
212-627-7451
Helpline: 877-422-2030
www.ccalliance.org

National Cancer Institute (National Institutes of Health)

NCI Public Inquiries Office
Building 31, Room 10A31
31 Center Drive, MSC 2580
Bethesda, MD 20892-2580
800-4-CANCER
www.cancer.gov

National Coalition for Cancer Survivorship

1010 Wayne Avenue, Suite 770
Silver Spring, MD 20910
301-650-9127
www.cansearch.org

The Susan G. Komen Breast Cancer Foundation

5005 LBJ Freeway, Suite 250
Dallas, TX 75244
972- 855-1600
www.komen.org

The ASCO Foundation

Our Promise to the Future

In 1999, the ASCO Foundation, a not-for-profit, charitable trust dedicated to furthering clinical cancer research and education was established. The Foundation works to advance careers in clinical cancer research and to communicate important advances in the treatment of cancer to oncologists via a broad range of educational programs.

The ASCO Foundation also provides an opportunity for cancer survivors, family members, and friends of the cancer community to contribute to the Foundation's efforts to improve the treatment and care of people living with cancer.

For more information about the ASCO Foundation, please contact

ASCO Foundation

American Society of Clinical Oncology

1900 Duke Street

Suite 200

Alexandria, Virginia 22314

Phone: (703) 299-0150





American Society of Clinical Oncology

1900 Duke Street

Suite 200

Alexandria, VA 22314

(703) 299-0150

www.asco.org

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