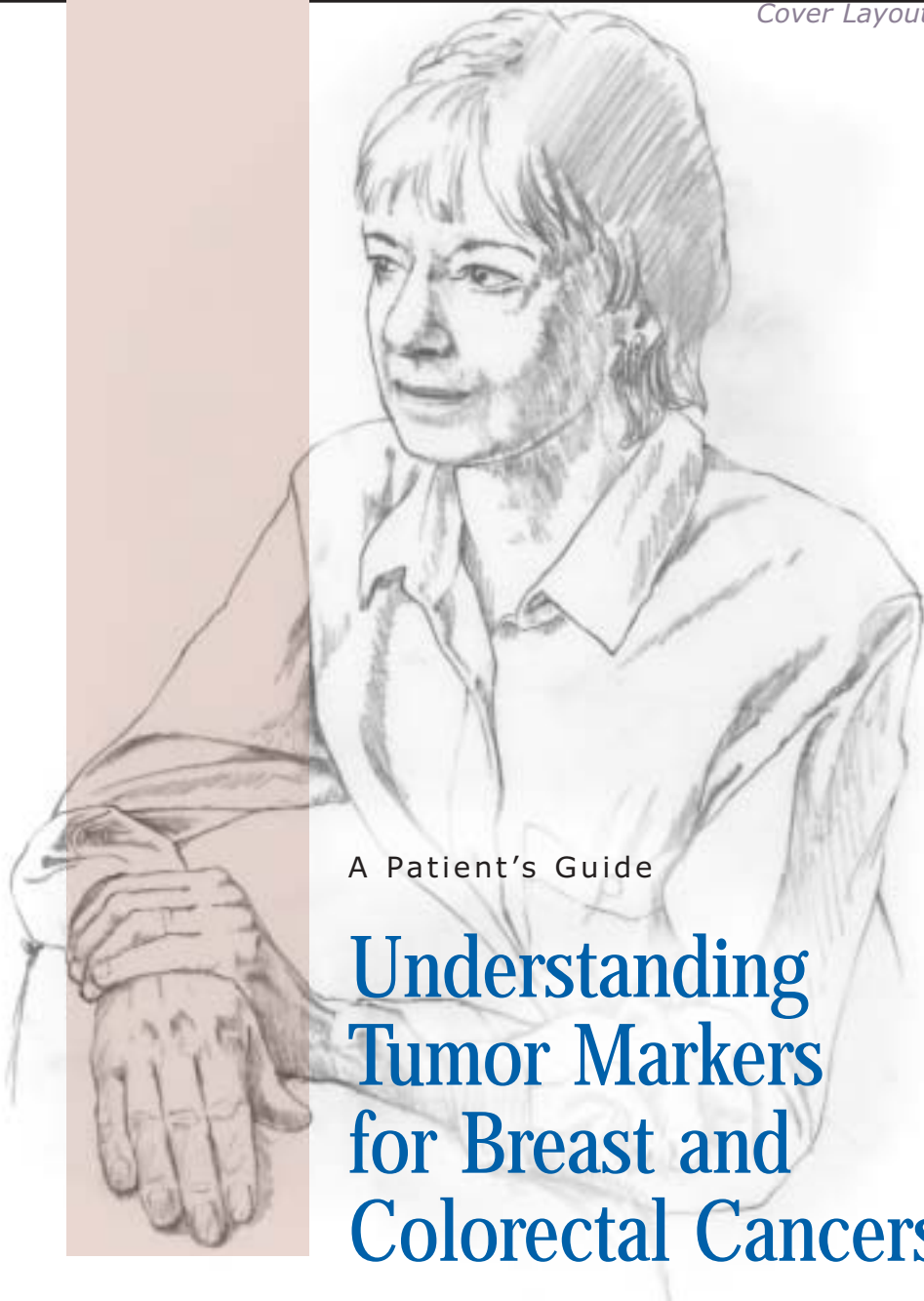


A Patient's Guide

Understanding Tumor Markers for Breast and Colorectal Cancers



Recommendations of
the American Society
of Clinical Oncology



A Patient's Guide

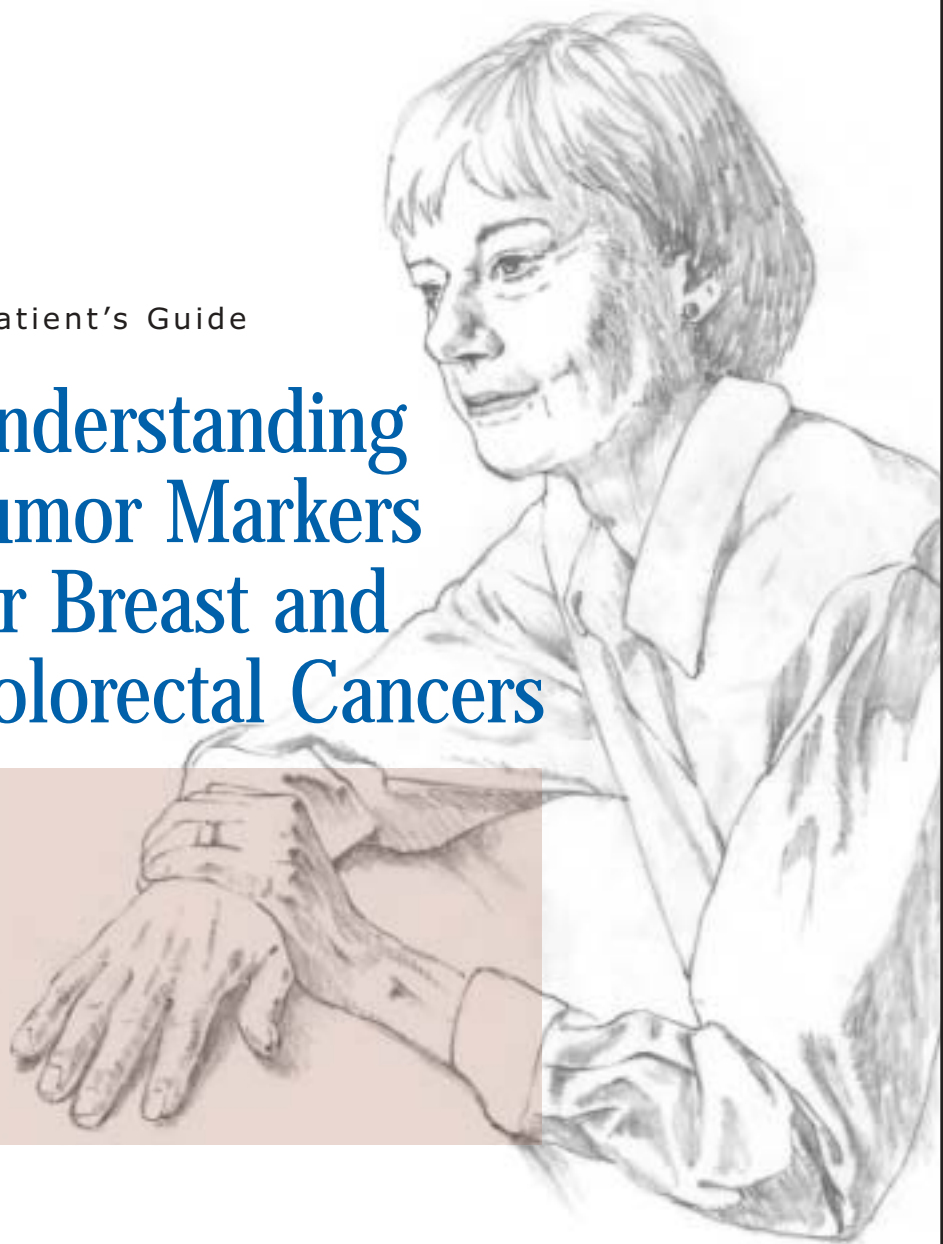
Understanding Tumor Markers for Breast and Colorectal Cancers

Recommendations of
the American Society
of Clinical Oncology



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.

A Patient's Guide to

Understanding Tumor Markers for Breast and Colorectal Cancers

Recommendations of the
American Society of Clinical Oncology (ASCO)

Table of Contents

Introduction	3
What are tumor markers?	4
How are tumor markers used?	6
Tumor Markers for Breast Cancer	8
Tumor Markers for Colorectal Cancer	12
What about tumor markers for other cancers?	14
Where can I get the original clinical practice guidelines?	14
Where can I find more information on cancer?	14
Resources	16

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

Introduction

ASCO is the authority on the practice of clinical oncology, or 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 asks 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 tell if cancer has come back (recurred), there is often no evidence that by finding cancer early we can either extend life or help patients have a better quality of life. ASCO only recommends the use of a tumor marker when it has proven useful in changing the outcome of cancer.

About tumor markers

How are tumors usually detected, diagnosed, and treated?

A tumor is an abnormal mass of tissue that is caused by fast and irregular cell growth. 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 patient might have cancer, they may perform x-rays, MRI, 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.



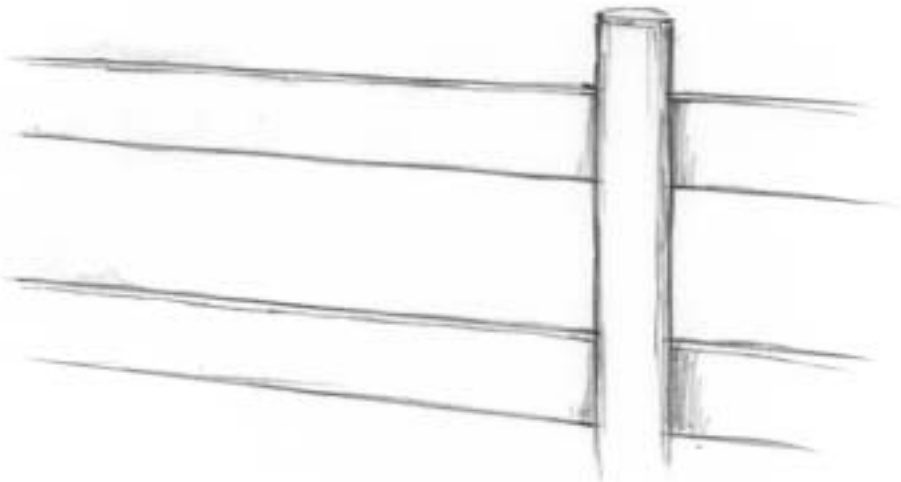
What is a tumor marker?

A tumor marker (also called 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 benign conditions. To detect the level of a tumor marker, the doctor takes a sample of blood or urine and sends it to a laboratory for testing.

One day, we hope to use a single blood test 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
- 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, measuring higher than normal levels of tumor markers can help diagnose and follow some types of cancer. Your doctors will review the results of your tumor marker tests 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 by 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?)

A diagnosis identifies a disease by its location, symptoms and lab test results. Having a correct diagnosis helps doctors to plan the best treatment. Tumor markers may help diagnose some cancers by showing if a tumor is benign or malignant.

Prognosis (How will the cancer behave?)

Prognosis is a prediction of 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 low level of a tumor marker may mean that the treatment is working, while a high level may mean that the cancer is growing. Doctors may also use tumor markers to watch certain non-cancerous conditions to see if cancer develops.

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 disease as possible can help you 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 high levels of any tumor markers?
- If I do have a high level 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 first in 1996, then again in 2000, to develop and then update the recommendations you will find below. 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 every month.

The tumor markers listed below have been used in breast cancer. ASCO's recommendations are included in each description. A symbol in the margin means that ASCO recommends the use of this tumor marker.



(c-erbB-2 (HER-2/neu): This marker is found in some breast cancer cells, and may indicate how a woman will respond to chemotherapy. *ASCO recommends the use of c-erbB2 for in the diagnosis and prognosis of breast cancer.*

- *Every patient with breast cancer should receive a test for c-erbB-2 either at time of diagnosis or recurrence (when cancer has come back).*
- *c-erbB-2 levels can identify patients who should begin trastuzumab (Herceptin) treatment or anthracycline-based chemotherapies (adriamycin, doxorubicin, cerubine, daunorubicin, idamycin, idarubicin).*
- *c-erbB-2 levels should not be used to identify patients who should begin taxane-based treatments (Taxol or Taxotere), or to predict recurrence of breast cancer.*



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 a patient's response to primary treatment or treatment for metastatic breast cancer. *ASCO recommends the use of steroid hormone receptors in the diagnosis, prognosis, monitoring or surveillance of breast cancer. Levels of estrogen and progesterone should not be used alone in predicting breast cancer recurrence.*

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 breast cancer. Although a rising CA 15-3 level can detect recurrence after primary treatment, it is not yet clear if using this test actually impacts survival or quality of life for breast cancer patients. There are also high **false-positive** (positive results in cancer-free women) rates when using CA 15-3 in screening and diagnosis of breast cancer. But, if no other test is available, CA 15-3 or CA 27.29 levels may indicate that treatment has failed.*

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 has failed.*

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 breast cancer patients.*

p53: p53 is a tumor suppressor gene that is mutated in more than 50% of tumors. When mutated, p53 can no longer stop cells from entering the cell division cycle, and cells divide uncontrollably to form tumors. *ASCO does not recommend the use of p53 as a tumor marker for breast cancer. While studying p53 has helped researchers to 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.*

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. A symbol in the margin means that ASCO recommends the use of this tumor marker.

(***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 the disease has spread. 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 in the prognosis and monitoring of colorectal cancer.

Lipid-associated sialic acid (LASA): A LASA test measures the amount of sialic acid in blood, which can be high in patients with many different cancers. LASA levels may also be higher in patients 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 currently offer any additional information than the standard tumor staging process and should only be ordered as part of a research trial.*

p53: p53 is a tumor suppressor gene that is mutated in more than 50% of tumors. When mutated, p53 can no longer stop cells from entering the cell division cycle, and cells divide uncontrollably to 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 (a gene that can play a part in the growth of cancer if it changes) can be altered in polyps or carcinomas 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. To see ASCO's recommendations on other aspects of cancer care, please visit our web site 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 web site at <http://www.asco.org>.

Where can I find more information on cancer?

More information is also available online on ASCO's patient information web site, 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 B2</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

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.cancercares.org

Colon Cancer Alliance

175 Ninth Avenue
New York, NY 10111
212-439-1101
www.ccalliance.org

National Cancer Institute (National Institutes of Health)

Office of Communication
Building 31, Room 10A24
9000 Rockville Pike
Bethesda, MD 20892
800-4-CANCER
www.cancer.gov

National Coalition for Cancer Survivorship

1010 Wayne Avenue, Suite 595
Silver Spring, MD 20910
301-650-8868
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

Supporting Clinical Cancer Research and Education Around the World

The ASCO Foundation is a nonprofit corporation based in Alexandria, Virginia, dedicated to furthering clinical cancer research and education. The Foundation provides an added mechanism for private fund-raising in support of the broad range of ASCO programs, with special emphasis on the advancement of careers in clinical cancer research through the Society's Fellowship Grants Program. The Foundation's ultimate goal is to support the development of the next generation's leaders in the field of clinical oncology.

The ASCO Foundation has received a generous contribution from its charter sponsor, Ortho Biotech Inc., but it still needs your help to fund these important research and education programs.

For more information, or to make a contribution to the ASCO Foundation, please contact

American Society of Clinical Oncology

ASCO Foundation

225 Reinekers Lane

Suite 650

Alexandria, Virginia 22314

Phone: (888) 651-3038 or (703) 299-0150



American Society of Clinical Oncology

225 Reinekers Lane

Suite 650

Alexandria, VA 22314

(888) 651-3038 or (703) 299-0150

www.asco.org