



CANCERcare
Connect[®]

Treatment Update on Gastrointestinal Stromal Tumors

Presented by

Michael C. Heinrich, MD

Oregon Health Sciences University Cancer Institute

George D. Demetri, MD

Ludwig Center at Dana-Farber/Harvard Cancer Center

Carolyn Messner, DSW

CancerCare

Learn about:

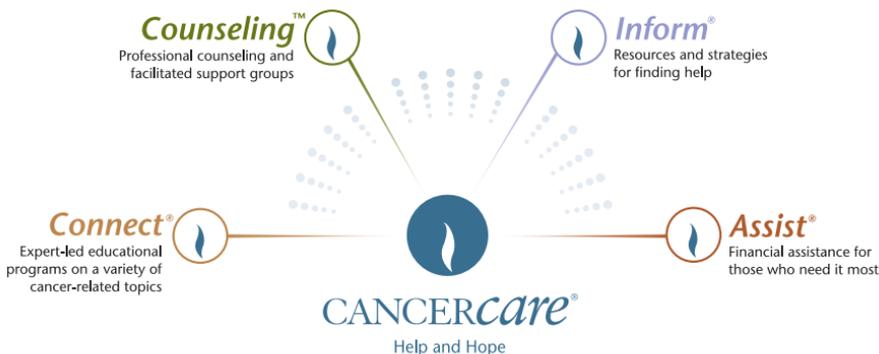
- Diagnosing GIST
- Current treatments
- New drugs in development
- Coping with pain and other symptoms



CANCERcare[®]

Help and Hope

The *CANCERcare*® Constellation of Services



CancerCare's services are provided free of charge to anyone affected by cancer

1-800-813-HOPE (4673) • www.cancercares.org

CancerCare is a national nonprofit organization that provides free professional support services to anyone affected by cancer: people with cancer, caregivers, children, loved ones, and the bereaved. CancerCare programs—including counseling, education, financial assistance, and practical help—are provided by trained oncology social workers and are completely free of charge. Founded in 1944, CancerCare now provides individual help to more than 91,000 people each year, and an additional 1.6 million people visit our websites, www.cancercares.org and www.lungcancer.org, to gain information and resources.

Contacting CancerCare

National Office

CancerCare
275 Seventh Avenue
New York, NY 10001
E-mail: teled@cancercares.org

Administration

Tel: 212-712-8400
Fax: 212-712-8495
E-mail: info@cancercares.org
Website: www.cancercares.org

Services

Tel: 212-712-8080
1-800-813-HOPE (4673)

If you are a health care professional interested in ordering free copies of this booklet for your patients, please use the online order form on our website, www.cancercares.org, or call 1-800-813-HOPE (4673).

Treatment Update on Gastrointestinal Stromal Tumors

Presented by

Michael C. Heinrich, MD

Professor of Medicine

Division of Hematology and Medical Oncology

Oregon Health Sciences University Cancer Institute

Portland, Oregon

George D. Demetri, MD

Director, Ludwig Center at Dana-Farber/Harvard Cancer Center

Boston, Massachusetts

Executive Director, Clinical and Translational Research

Ludwig Institute for Cancer Research

New York, NY, and Zurich, Switzerland

Carolyn Messner, DSW

Director of Education & Training

CancerCare

The information in this booklet is based on the CancerCare Connect® Telephone Education Workshop “Treatment Update on GIST (Gastrointestinal Stromal Tumors),” which took place in January 2007. The workshop was conducted by CancerCare in partnership with the American Cancer Society, American Society of Clinical Oncology, Association of Clinicians for the Underserved, Association of Oncology Social Work, GIST Cancer Research Fund, GIST Support International, Intercultural Cancer Council, Life Raft Group, Multinational Association of Supportive Care in Cancer, National Center for Frontier Communities, The National Coalition for Cancer Survivorship, and The Wellness Community.

INTRODUCTION

page 2

FREQUENTLY ASKED QUESTIONS

page 13

GLOSSARY (definitions of blue boldfaced words in the text)

page 15

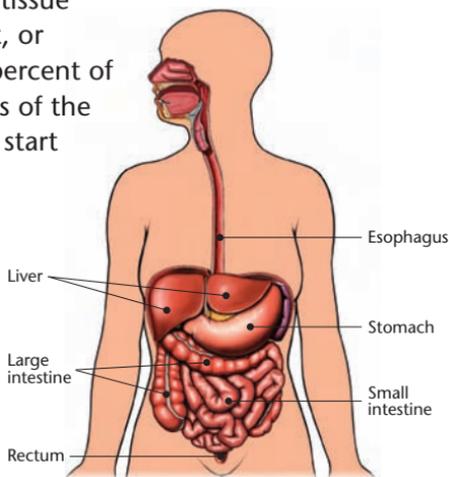
RESOURCES

page 16

This patient booklet was made possible by an educational grant from Pfizer Oncology.

The development of new drugs has revolutionized GIST treatment.

Each year about 5,000 people in the United States are diagnosed with a **gastrointestinal stromal tumor (GIST)**. GIST belongs to a class of cancers called **soft tissue sarcomas**. Soft tissue sarcomas are a diverse group of diseases that originate in a soft tissue of the body, such as muscle, fat, or blood vessels. About 60 to 70 percent of GISTs arise in the muscular walls of the stomach, and 20 to 30 percent start in the small intestine. Rarely, GIST may arise in the large intestine, the esophagus, or the anal region. Not all GISTs are aggressive tumors. Some can be removed by surgery, with a very low chance they will return. But some GISTs may come back after they are removed, especially tumors that were larger than two inches in diameter. They can also spread to other parts of the body, particularly the liver.



Treatments for GIST

Unlike other types of cancer, GISTs cannot be treated effectively with standard chemotherapy or radiation. Usually, doctors treat GISTs with surgery and drugs belonging to a class of medications called **targeted treatments**. These “smart

Symptoms of GIST

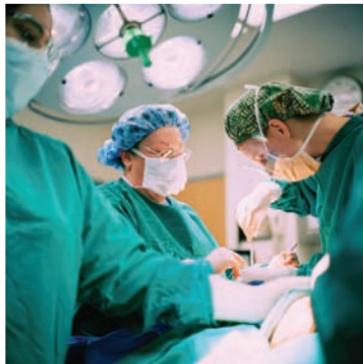
Many patients, especially those with smaller GISTs, may have no symptoms. However, large, aggressive GISTs may cause some of the following symptoms:

- Pain or discomfort in the abdomen, the area of the body that contains the stomach, intestines, and other organs
- Nausea and vomiting
- Blood in the stool or vomiting blood
- Fatigue due to low red blood cell counts (anemia)
- Diarrhea
- Weight loss

drugs” target cell mechanisms that promote the uncontrolled growth of cancer cells. Rather than killing both healthy and unhealthy cells, as chemotherapy does, targeted treatments attack cancer cells primarily. In recent years, targeted drugs have revolutionized GIST treatment, giving new hope to people with this cancer and their loved ones.

SURGERY

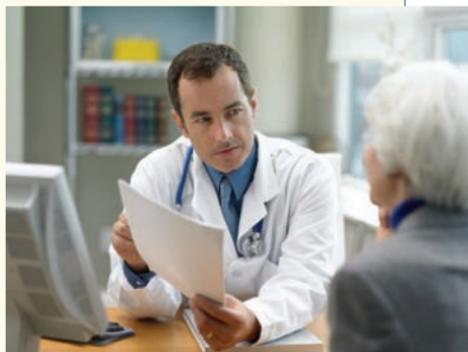
It is important to note that surgery remains the treatment of choice for GISTs that have not spread from the place they started. In some cases, if the disease has spread to other parts of the abdomen, surgery may also be performed, usually after a targeted treatment. The surgeon tries to remove the whole tumor to reduce the chances that it will come back and to keep it from blocking the digestive system or causing other problems. To get rid of the whole tumor, part of the affected organ, such as the stomach, may have to be removed as well.



Finding a GIST Expert

Gastrointestinal stromal tumors are rare, and not every doctor has seen many people with them. If you are told you may have a GIST, it is vital that you take steps to ensure the diagnosis is correct:

- Find out how many cases of GIST your health care team has treated. Because GIST is so rare, some doctors see only one case of GIST every other year, while others see hundreds each year. It's best if your doctor and pathologist are familiar with treating GIST.
- Get a referral for treatment at a center that specializes in GIST. Major academic centers, such as the Dana-Farber Cancer Institute in Boston, the University of Oregon Health Sciences Center in Portland, Fox Chase Cancer Center in Philadelphia, Memorial Sloan-Kettering Cancer Center in New York City, and M. D. Anderson Cancer Center in Houston, have all conducted research on GIST.
- If a GIST treatment center is too far from your home for regular visits, travel once for a consultation. You may wish to go to one of these centers for an informational visit that will help you choose the best possible health care team, or for a crucial second opinion.



Once the tumor is removed, it is examined under a microscope by a **pathologist**, an expert in identifying the nature, origin, progress, and cause of disease. Doctors use information from this examination to help them judge how aggressive the disease is likely to be and how likely it is to come back or spread.

TARGETED TREATMENTS

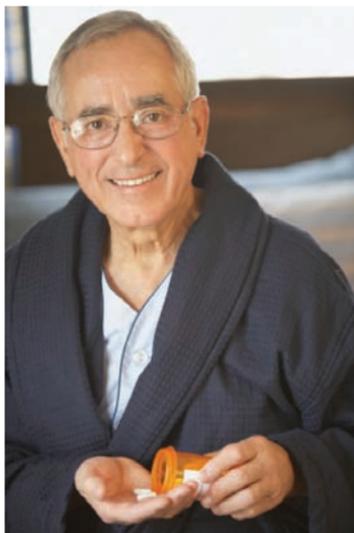
Imatinib (Gleevec)

Before the year 2000, the only treatment option for GISTs was surgery. But studies started that year showed that imatinib shrank tumors in approximately two-thirds of people with GISTs. What's more, the tumors stopped growing in another 15 percent of patients who were treated with imatinib.

Studies also showed that most people with GIST feel better and live longer when they are treated with the drug. Imatinib works by preventing uncontrollably active **receptors** on the surface of cancer cells from sending signals to encourage the cells to grow and multiply.

These findings on imatinib had a tremendous impact on GIST treatment. This research was among the first and most important demonstrations of the potential of new, targeted treatments. The discovery energized the entire field of cancer research.

Today, imatinib is used as a first treatment in patients for whom surgery is not an option. It may also be recommended prior to surgery to shrink a tumor that is very large or has spread into nearby organs.



However, imatinib does not appear to be a cure for GIST after the disease has recurred or spread. It also works better at controlling the growth of some types of tumors than others.

To try to control GIST, imatinib must be taken long term. Stopping the drug can lead to a rapid regrowth of the tumor. Also, in more than half the people who take imatinib for two years, the GISTs begin growing again. Researchers suspect that

once cancer cells are exposed to the drug for a period of time, they are able to adapt (that is, they develop a **resistance** to it) and continue growing. These things are important to discuss with your doctor when considering imatinib treatment.

Sunitinib (Sutent)

When GIST begins growing despite imatinib treatment, there are still other targeted treatment options. Some people may benefit from surgery to remove the resistant tumor and a continuation of imatinib. Others may benefit from switching to another targeted treatment, called sunitinib (Sutent). In 2006, the U.S. Food and Drug Administration (FDA) approved sunitinib for the treatment of GIST after imatinib stopped working. Sunitinib targets several mechanisms that are responsible for the



abnormal growth of cancer cells, cutting off their blood supply and blocking their ability to grow.

NEW TREATMENT OPTIONS ON THE HORIZON

Eventually, some GISTs become resistant to both imatinib and sunitinib. That is why a tremendous amount of research is under way now to find new drug options for people with this form of cancer. The following is a short list of selected new drugs that are currently being tested in clinical trials:

Nilotinib (Tasigna) This drug and some related compounds are designed to block the switches that are responsible for the growth of GIST cells.

Flavoperidol This drug works by interfering with a GIST cell's growth mechanisms, causing the cell to die.

The Importance of Clinical Trials

The progress that has been made in treating GIST has been made possible because researchers have banded together to test new drugs such as imatinib and sunitinib. Without these trials, doctors would not have these powerful tools to help people with GIST. The GIST community—patients, their loved ones, and health care providers—has joined together to support these clinical trials and propel research on the disease forward.

Clinical trials are the standard by which we measure the worth of new medications and the quality of life for people with all types of cancers as they go through treatment. For all of these reasons, doctors and scientists urge patients to take part in well-designed clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things you should know:

- Often, patients who take part in clinical trials gain access to and benefit from new treatments not available to the general public.
- Before you participate in a trial, you will be fully informed as to the risks and benefits of the trial.
- No patient receives a placebo, an inactive treatment, if there is a standard treatment available for the disease. Most trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Perifosine This drug appears to block several growth mechanisms in cancer cells. Perifosine may shrink or slow the growth of cancer cells.

Take Your Medication Every Day

We know that GISTs regrow when people stop taking imatinib. Yet, many people with GIST sometimes forget to take their prescribed doses of this medication. In fact, research has shown that, on average, people with GIST may take only 75 to 80 percent of their prescribed doses.

If you are being treated with imatinib, the most important thing you can do for yourself is to take the prescribed dose of the medication every day. Talk with your doctor about any problems you may have taking your medication every day.

CancerCare® and the National Institutes of Health suggest these tips to help you stick to your drug treatment plan:

- **Get it in writing.** When you start taking imatinib, have your doctor provide written instructions that you can take home and review.
- **Fit the drug into your usual routine.** For instance, if your doctor asks you to take your pill once a day, you might want to take it when you brush your teeth each morning, at bedtime, or with a meal. (Check with your doctor about taking imatinib with food, especially grapefruits and grapefruit juice.)
- **Consider using a pill sorter** (available at drug stores) to sort an entire week's worth of medications. Some even come



with alarms to remind you to take your pills.

- **Know what to do if you miss a dose.** Experts recommend that you take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular pill schedule. Do not take a double dose to make up for a missed one.
- **If you have trouble swallowing imatinib tablets,** you may place all of the tablets that you need for one dose into a glass of water or apple juice. Use a little less than 2 ounces of liquid for each 100 mg tablet and a little less than 4 ounces of liquid for each 400 mg tablet. Stir with a spoon until the tablets crumble completely and drink the mixture immediately. Note: if your doctor has told you to take 800 mg of imatinib, you should take two of the 400 mg tablets. Do not take 8 of the 100 mg tablets. The tablet coating contains iron, and you will receive too much iron if you take 8 of the 100 mg tablets.
- **Know what to expect.** So that you're not taken by surprise, you should know that imatinib can cause certain side effects such as diarrhea, loss of appetite, or teary eyes, for example. Some side effects can be more serious, such as swelling of the hands and feet or shortness of breath. Call your doctor immediately if you experience any unusual symptoms. Do not try to treat these side effects on your own.
- **Do not stop taking imatinib without talking to your doctor.**

Sirolimus (rapamycin, Rapamune), AP23573, Everolimus (RAD001), Temsirolimus (CCI-779) Each of these drugs, now in clinical trials, can block a substance that signals cancer cells to grow. Many of these drugs are being tested in combination with either imatinib or sunitinib in GISTs and other tumors to see if their combined use is more effective than one drug alone.

IPI-504 This drug blocks a key substance inside cancer cells that is responsible for their growth.

Coping With Pain and Other Symptoms

If you are experiencing pain or any other symptoms as you are being treated for GIST, it's important to let your doctor know. GIST experts—physicians and the teams of nurses and other specialists who work with them—are skilled in managing pain and side effects.

Often, the pain is caused by the tumor pressing on nerves or surrounding tissues. In those cases, doctors have found that one of the best ways to relieve pain is to treat the tumor. Pain can also be a side effect of treatment.

No matter what kind of symptoms you are having, a useful way to communicate your experience is by keeping a symptom and medication diary or log.

When you write down your experience, you won't forget it. Specific information will help your medical team provide the best possible treatment. These are some of the things to record in your diary each day:

- What medicines you are taking and when



- What kind of symptoms you are experiencing
- Where in your body you feel your symptoms
- When the symptoms occur
- How long they last
- What makes them worse
- Whether anything, such as heat, ice, or medicine, relieves the symptoms
- Length of time the symptom-relieving method works and how much relief it provides
- How the symptoms are affecting your everyday life—whether they keep you from sleeping, eating, walking, working, or exercising

Your Support Team

When you are diagnosed with GIST, you're faced with a series of choices that will have a major effect on your life, and maybe you're not sure where to turn. Of course, your most important resources are your health care team, family members, and friends. It is very important to develop good communication with them. You can also turn to these resources:

Oncology social workers and nurse practitioners are specially trained to help you find out more about your treatment options, learn how to navigate the health care system, and get the best care possible, including finding GIST experts. Often, when people are coping with cancer, they need someone to talk with who can help them and their families sort through the complex emotions and issues that arise. For instance, some people with GIST need extra help coping with pain and communicating with their doctor or nurse about this. Oncology social workers and nurse practitioners can provide emotional support, help you cope with treatment and its side effects, and guide you to resources. CancerCare® offers free

counseling from professional oncology social workers on staff.

Support groups can reduce the feeling that you are going through cancer alone. These groups provide reassurance, suggestions, insight—a safe haven where you can share similar concerns with your peers in a supportive environment. At CancerCare®, people with cancer and their families can take part in support groups in person, online, or on the telephone.

Financial help is offered by a number of organizations, including CancerCare, to help cover the cost of transportation to treatment, child care, or help needed around the home. CancerCare can also refer you to other resources in your community that can provide assistance.



Frequently Asked Questions

Q I'm taking Gleevec and I'm wondering about its interaction with other drugs, herbs, vitamins, or minerals that might make it less effective.

A It's certainly important to let your doctor know if you're taking any of these substances, and in what dose. There are some medications that can affect the amount of imatinib in a person's blood. In particular, drugs used to treat epilepsy can cause a person's blood levels of imatinib to drop rapidly, making treatment less effective.

Q My dad is having surgery to remove a GIST, and his doctor has given him the option of starting treatment with imatinib immediately afterward and staying on it for a year. Will this keep his tumor from coming back or spreading?

A Every individual is different, but we do know from a recent clinical trial that patients who had surgery to remove a GIST had a lower recurrence rate when they took imatinib for one year than those who were given an inactive treatment—that is, a placebo. The results of that study have not yet been published in a scientific journal, but clinical trials are continuing. One question researchers want to answer is whether to recommend continuing imatinib after one year. It's best for you and your father to discuss this in detail with his oncologist.

Q How many second opinions should I get before undergoing treatment for GIST?

A You don't need to get an endless number of opinions. One opinion from an expert might be good enough, if you feel comfortable that it's the "right" opinion, or you might wish to get a second opinion. You should be confident that the doctor has a lot of experience in treating patients with GIST and that his or her style and your personality and needs are a good fit. If you have to travel to get a second opinion, you can have a summary of the consultation sent to your local doctor so you can have the option to receive your care closer to your home. You may also choose to take part in a clinical trial to test some new drugs. This is something to discuss with an expert team at a cancer center that sees a lot of GIST patients. (See "Finding a GIST Expert" on page 4.)

Glossary

gastrointestinal stromal tumor (GIST) A tumor belonging to a class of cancers called soft tissue sarcomas. Soft tissue sarcomas originate in a soft tissue of the body, such as muscle, fat, or tendons.

pathologist A medical specialist who is trained to correctly identify the nature, origin, progress, and cause of disease.

receptors On each cell's surface, the job of receptors is to find and catch specific substances (such as hormones) released by other cells. Once these substances attach to the receptors, the receptors send signals that trigger mechanisms in the cell, causing it to change, grow, and divide.

resistance When a tumor adapts (that is, becomes resistant to) a drug, after being exposed to it for a period of time. Once a tumor develops resistance to a particular drug, it may grow back, despite continued treatment with the drug.

soft tissue sarcomas A diverse group of diseases that originate in a soft tissue of the body such as muscle, fat, or blood vessels.

targeted treatments Treatments that attack cancer cells, primarily, sparing normal, healthy tissues. Targeted treatments tend to cause fewer and less severe side effects than conventional chemotherapy.

Resources

CancerCare

Services: 1-800-813-HOPE (4673)
www.cancercares.org

American Cancer Society

1-800-227-2345 ■ www.cancer.org

People Living With Cancer

(patient website of the American Society of Clinical Oncology)
1-888-651-3038 ■ www.plwc.org

GIST Support International

215-340-9374 ■ www.gistsupport.org

Life Raft Group

973-837-9092
www.liferaftgroup.org

The National Coalition for Cancer Survivorship

1-877-622-7937 ■ www.canceradvocacy.org

National Cancer Institute

Cancer Information Service
1-800-422-6237 ■ www.cancer.gov

The Wellness Community

1-888-793-9355
www.thewellnesscommunity.org

To find out about clinical trials:

Coalition of Cancer Cooperative Groups

1-877-520-4457 ■ www.CancerTrialsHelp.org

National Cancer Institute

1-800-422-6237 ■ www.cancer.gov/clinicaltrials

Book:

100 Questions & Answers About Gastrointestinal Stromal Tumor (GIST) by Ronald P. DeMatteo, MD, Marina Symcox, PhD, and George D. Demetri, MD (Jones and Bartlett Publishers, Inc., Sudbury, Mass., 2006)



CANCER*care*[®]

The information presented in this patient booklet is provided for your general information only. It is not intended as medical advice and should not be relied upon as a substitute for consultations with qualified health professionals who are aware of your specific situation. We encourage you to take information and questions back to your individual health care provider as a way of creating a dialogue and partnership about your cancer and your treatment.

All people depicted in the photographs in this booklet are models and are used for illustrative purposes only. Page 2: medical illustration copyright © 2007 Nucleus Medical Art, all rights reserved. www.nucleusinc.com.

This booklet was edited and produced by Elsevier Oncology.

© 2007 Cancer Care, Inc. All rights reserved.



From the moment of diagnosis, let the hope begin.

When Fran was diagnosed with cancer, she knew that she and her daughter, Rachel, would need support. Both found help and hope with *CancerCare*.

Since 1944, our professional oncology social workers have provided **free** counseling, education and practical help for anyone touched by cancer. *CancerCare* is with you every step of the way.

If we can help you and your family, please call us at 1-800-813-HOPE (4673) or visit www.cancercares.org.



CANCERcare[®]
Help and Hope

1-800-813-HOPE (4673)
www.cancercares.org

©CancerCare 2005