TREATMENT UPDATE:

Gastrointestinal Stromal Tumors

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Toll-free 800-813-HOPE (4673)
Fax 212-712-8495
Email info@cancercare.org
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Treatment Update: Gastrointestinal Stromal Tumors

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EDITOR

Suzanne George, MD
Clinical Director, Center for Sarcoma and Bone Oncology,
Senior Physician, Dana-Farber Cancer Institute,
Associate Professor of Medicine, Harvard Medical School

All people depicted in the photographs in this booklet are models, used for illustrative purposes only.

GIST (gastrointestinal stromal tumors) is a rare form of cancer, with approximately 5,000 cases diagnosed in the United States each year. GIST is most commonly found in people over the age of 50.

Soft tissue sarcomas are cancers of the connective tissues that hold organs together. GIST is a soft tissue sarcoma that can start in almost any part of the digestive system, most commonly in the stomach or small intestine.

Diagnosis

Diagnostic tests used if GIST is suspected may include:

- **Physical examination.** A thorough physical exam will allow the doctor to better understand signs and symptoms, including any pain that is being experienced.
- **Imaging tests.** Ultrasound, PET scans, CT scans and/or MRIs are used to view the areas of the body that might be of concern and are helpful in diagnosing GIST and other soft tissue sarcomas.
- **Biopsy.** Using a hollow needle, tissue samples from the tumor will be removed. This is most often done by either an interventional radiologist or a gastroenterologist depending on the location of the tumor. The sample is then tested to determine if cancer cells are present.

Additional tests may be recommended once a diagnosis of GIST has been made, to determine if the cancer has spread to other parts of the body (metastasized). When GIST metastasizes, it is usually to the liver or to the lining of the abdomen or pelvis (the peritoneum).

Genomic testing to evaluate the genes in the tumor is often performed to determine the presence and type of mutations in the GIST.

Treatment Options

How GIST is treated depends on its original location in the digestive system, whether or not it has spread to other locations (metastasized) and the type of genetic mutation it exhibits.

The best treatment approach is often guided by an interdisciplinary team composed of medical oncologists, radiologists, surgeons and nurses.

Surgery

Surgery is the primary approach in the treatment of localized (non-metastatic) GIST. The goal of surgery is to completely remove the tumor in one piece without hurting nerves, organs or other important body structures. Whether the surgery is done through a large incision or laparoscopically (smaller incision) depends on the location of the tumor.

The need for adjuvant (post-surgery) treatment is determined based on the risk of the GIST recurring. Factors include where the tumor originated, its size and its mitotic rate (the proportion of cells in an analyzed section of cancer tissue that is undergoing mitosis, a type of cell division).

Targeted Therapy

Targeted therapies focus on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth, taking advantage of what researchers have learned in recent years about how tumors grow.

Approximately 80 percent of GIST cases have a mutation of the KIT gene. KIT specifies the genetic code for a type of protein called a tyrosine kinase. When mutated, KIT essentially stays in the "on" position and sends signals into the GIST cells instructing them to grow and divide.

GIST is treated with medications called tyrosine kinase inhibitors (TKIs) which specifically block, or inhibit, KIT, slowing GIST cell growth. There are four TKIs currently approved by the U.S. Food and Drug Administration (FDA) for the treatment of GIST:

- **Imatinib (Gleevec).** First approved in 2002, imatinib is typically the drug used to treat high-risk GIST post-surgery (adjuvant therapy). In addition, imatinib is the frontline (initial) drug used to treat patients with metastatic GIST. It can also be used prior to surgery (neo-adjuvant therapy) to shrink the size the tumor, making surgery an easier process and increasing its chances of success.
- **Sunitinib (Sutent).** The FDA approved sunitinib in 2006 for the treatment of people with metastatic GIST who are intolerant to (can't take) imatinib or for whom imatinib is no longer working.
- **Regorafenib (Stivarga).** In 2013, regorafenib was approved for the treatment of people with metastatic GIST who are intolerant to imatinib and sunitinib or for whom imatinib and sunitinib are no longer working.
- **Ripretinib (Qinlock).** In May 2020, the FDA approved ripretinib for the treatment of people with metastatic GIST who have received prior treatment with at least three TKIs, including imatinib.

Approximately 10 percent of GIST cases have a mutation of the PDGFRA gene, which provides instructions for making a protein called platelet-derived growth factor receptor alpha. In January 2020, the FDA approved avapritinib (Ayvakit) for the treatment of metastatic GIST with a specific gene mutation in exon 18 of PDGFRA. The most common mutation in this location is known as PDGFRA D842V. Avapritinib is the only known drug that has shown clinical activity against this uncommon mutation.

Ablation Therapy

Ablation therapy is a treatment that uses a locally-delivered energy source to destroy cancer cells. It can be used in cases of GIST that have spread to the liver. The types of ablation therapy most commonly used are:

- **Radiofrequency ablation (RFA) and microwave ablation (MWA),** in which the doctor uses an imaging technique, such as an ultrasound or CT scan, to guide a needle into the tumor. High-frequency electrical currents (in RFA) or microwaves (in MWA) are passed through the needle, creating a small region of heat that destroys the tumor.
- **Ethanol ablation,** in which concentrated alcohol is injected directly into the tumor to kill cancer cells.
- **Cryotherapy,** an approach that involves using a thin metal probe to freeze the tumor and kill cancer cells.

Embolization

GIST that has spread to the liver can be treated with a minimally-invasive procedure called transarterial embolization (TAE). In TAE, an interventional radiologist injects tiny particles made of gelatin sponges or beads into a catheter (small plastic tube) that has been placed into the hepatic artery. This kills tumors by blocking their blood supply.

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in 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 that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all patients experience all side effects, and patients may experience side effects not listed here.

Side Effects of Targeted Therapy

Side effects of targeted therapies depend on the specific treatment being used and can include fluid retention, liver problems, heart problems, rashes, high blood pressure, increased risk of bleeding, cognitive difficulties, and problems with blood clotting and wound healing.

Side Effects of Ablation Therapy

Possible side effects of ablation therapy in the treatment of GIST include abdominal pain, liver infection and bleeding into the abdomen.

Side Effects of Embolization

Possible side effects of embolization include abdominal pain, fever, liver infection, gallbladder inflammation, blood clots in the liver's main blood vessels and a reduction in overall liver function.

General Side Effects

Some side effects may occur across treatment approaches. This section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

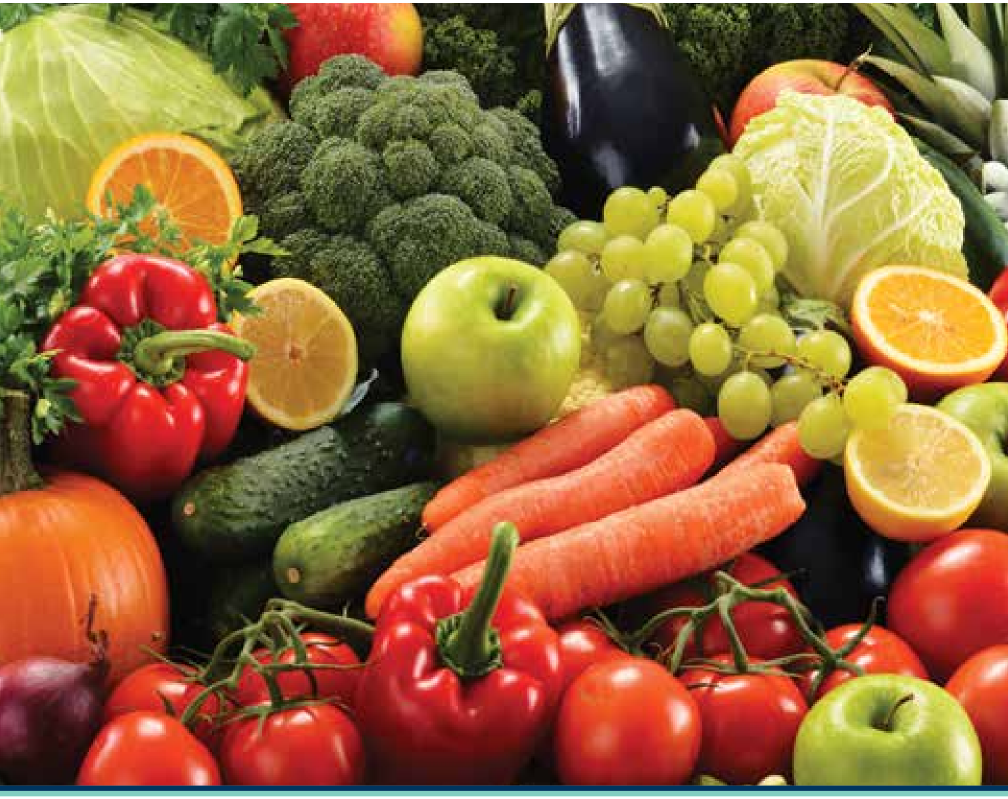
- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Constipation

- As hydration is important to avoid constipation, make sure to drink plenty of fluids. Also, limit your intake of caffeine and alcoholic beverages, as they can cause dehydration.
- Include foods high in fiber in your daily diet, such as fruit (especially pears and prunes), vegetables and cereals. If your health care team approves, you may want to add synthetic fiber to your diet, such as Metamucil, Citrucel or FiberCon.
- Be as physically active as you can, after checking with your health care team on the level of physical activity that is right for you.
- If your doctor has prescribed a “bowel regimen,” make sure to follow it exactly.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.



Managing Loss of Appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. Here are a few tips that may help reduce fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

There are also prescription medications that may help. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis or depression. Be sure to ask your doctor if they think any of these conditions may be contributing to your fatigue.

It can also be beneficial to speak with an oncology social worker or oncology nurse to help manage your fatigue. These professionals can work with you to manage any emotional or practical concerns that may be causing symptoms and help you find ways to cope.

Managing Flu-Like Symptoms

The fever and aches that may occur with treatment can be managed with a combination of rest and medication. Acetaminophen (such as Tylenol) is often a doctor's first choice to treat these symptoms. Nonsteroidal anti-inflammatory drugs (NSAIDs) can also help, but should be taken only if recommended by your doctor, as they can cause other side effects. NSAIDs include aspirin, ibuprofen (Motrin and others) and naproxen (Naprelan, Midol, Aleve and others).

Communicating With Your Health Care Team

As you manage your cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and the members of your health care team, including doctors, nurses, nurse practitioners, physician assistants, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with cancer and treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, you should ask your most important questions first, and be as specific as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person who accompanies you can serve as a second set of ears. They may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, like a tablet or smartphone, ask if you can use it to take notes. Writing notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have, or any pain you are experiencing, so that they can consult with your primary care physician or your specialist if needed.
- Ask your oncologist to send a summary of your visits to your primary care physician and all doctors involved in your care.

Remember, there is no such thing as over-communication.

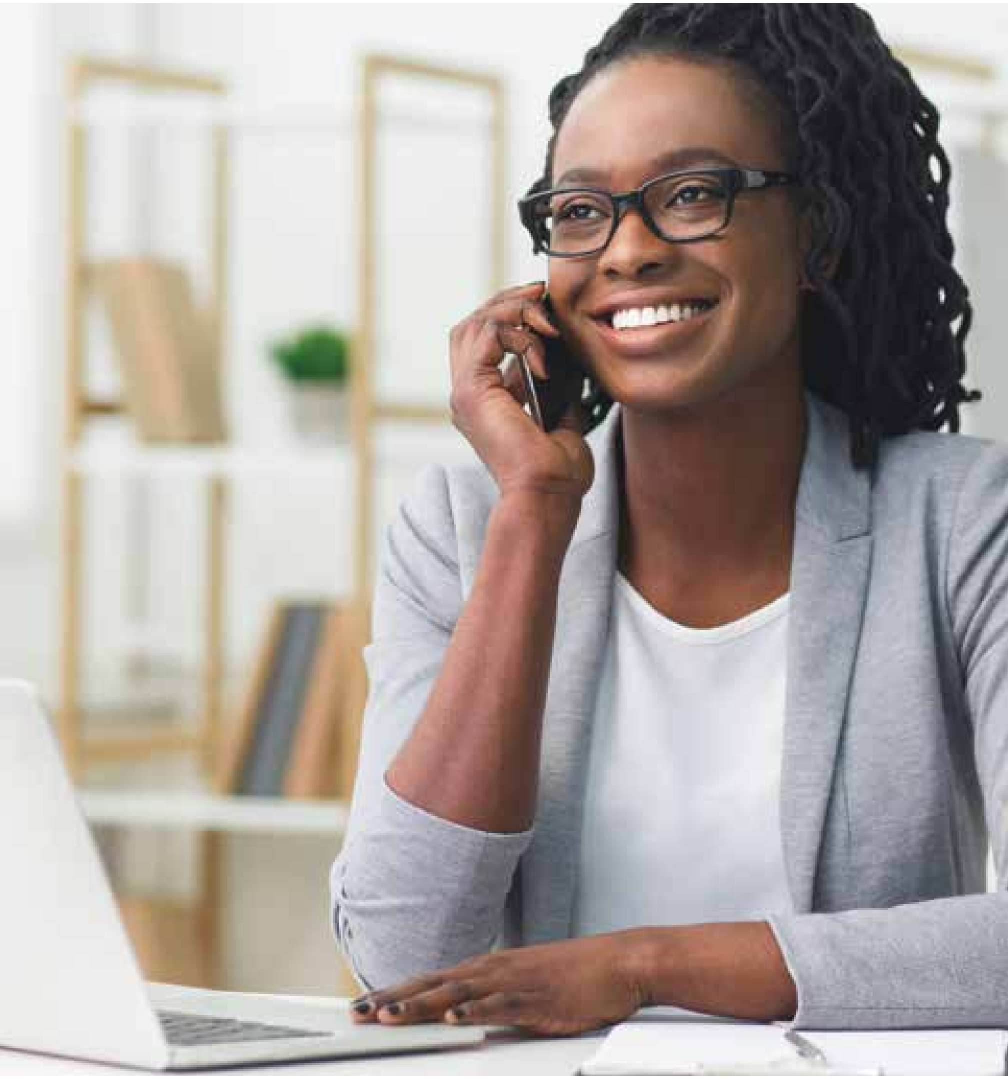
Cancer*Care*'s Free Support Services and Programs

It can be very difficult to receive a diagnosis of cancer, and adjusting to the necessary changes in your life can be challenging.

Cancer*Care*® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and offer information on support groups and other resources.

To learn more about how Cancer*Care* helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.



MORE ABOUT GASTROINTESTINAL STROMAL TUMORS

Frequently Asked Questions

Q: Does it matter at what hospital or health care facility my treatment takes place?

A: GIST is rare, and experts at sarcoma treatment centers have the latest information and extensive experience in diagnosing and treating this type of cancer. A list of some of these centers can be found on the Sarcoma Alliance website, www.sarcomaalliance.org. Your doctor may also be able to refer you to a nearby sarcoma treatment center.

Q: I've heard the term "precision medicine." What does that mean?

A: Each tumor has its own biological makeup, based on the genes found in its cells. An important area of cancer research is understanding this biology. With this information, it's possible for doctors to know whether a particular tumor is likely to respond to a specific treatment, allowing them to suggest the right treatment for each person's tumor. This approach is known as precision (or personalized) medicine.

To better understand the biological makeup of a person's tumor, doctors look for tumor "markers" in cell genes. Markers can predict whether a given treatment will be effective against a tumor and whether there is a high risk of the tumor coming back. Tumor markers and genetic traits are an important step on the road toward precision medicine, and they are being actively studied in clinical trials for GIST and other types of cancer.

Q: What follow-up care should I expect after my treatment regimen is completed?

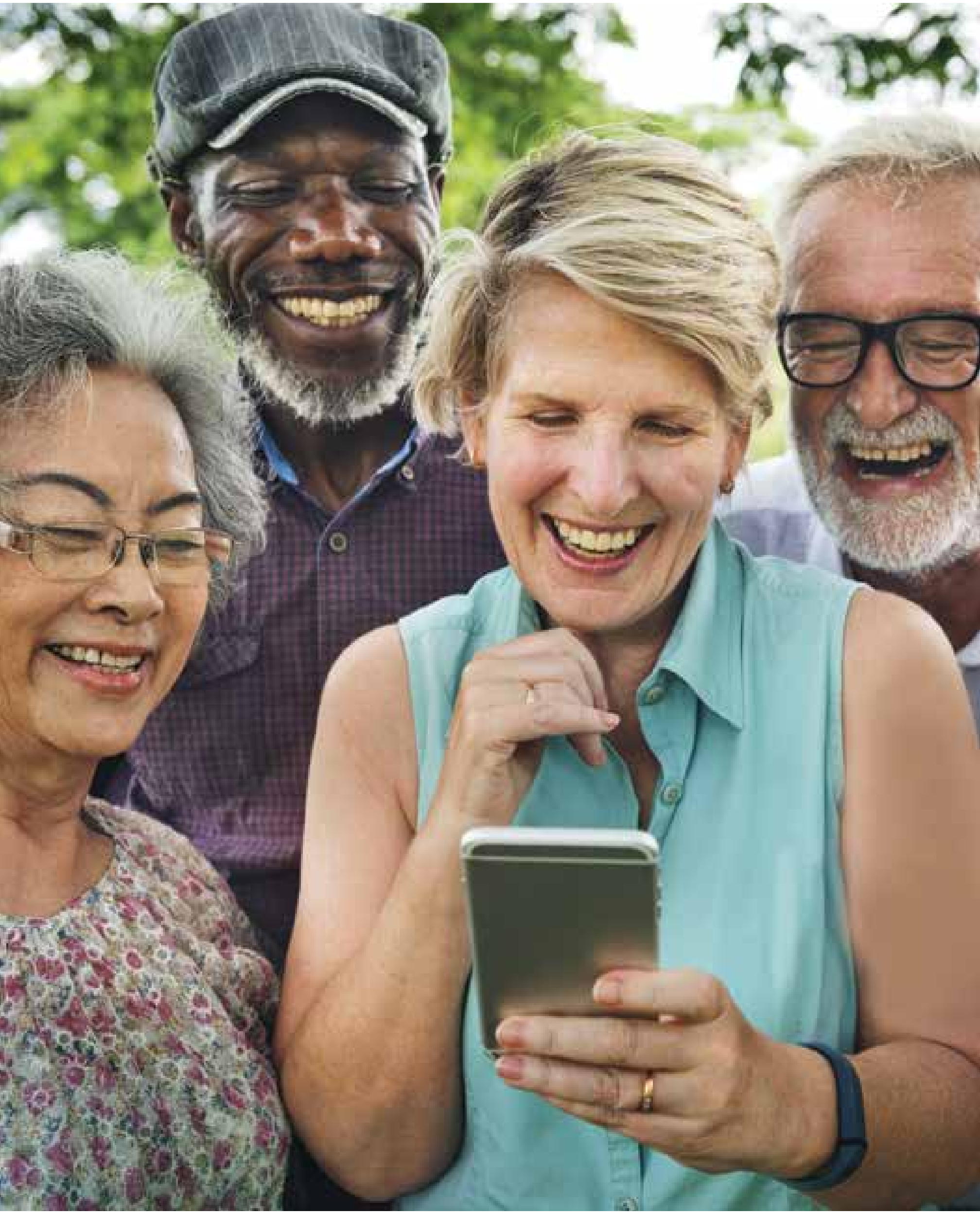
A: Follow-up care is very important for people who have been treated for GIST, as there is always a chance that the GIST could recur (come back), even a number of years after treatment. Typically, your doctor will want to see you every 3 to 6 months for up to 5 years, and once a year after that. However, this schedule may vary depending on your individual circumstances. Your follow-up care will likely include physical examinations and medical tests.

Q: What is a treatment summary and why is important?

A: Keeping your own records up-to-date in the form of a treatment summary can be helpful, as it allows you and your family members to have instant access to the specifics of your cancer diagnosis and treatment. A treatment summary should include:

- Your name and date of birth
- Date of diagnosis
- Prescribed therapy/therapies, including dates started and stopped and dosages when appropriate
- Dates and types of baseline and post-diagnosis testing and the results of these tests
- Other medications and supplements you are taking
- Names, affiliations and contact information of all members of your health care team

Ask the members of your health care team what they suggest be included. Take your personal record with you when you visit any doctor, not just your oncologist.



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