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TREATMENT UPDATE

Sarcoma

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For the best care, consult sarcoma experts experienced in diagnosing and treating this rare type of cancer.

Sarcoma is a cancer of the bone or connective tissues, which include bone, fat, muscle, blood vessels, nerves, deep skin tissue, and cartilage. Sarcoma is rare, affecting less than one percent of adults with cancer. However, 15 percent of children with cancer have sarcoma. Sarcoma can be divided into two types: soft tissue and bone.

One of the biggest challenges that doctors and patients face is trying to figure out exactly which bone and soft-tissue



tumors are sarcomas and which are benign (not cancerous) growths. That is why it is so important for people with sarcoma to seek advice at sarcoma treatment centers. Experts at these centers have a lot of experience in diagnosing and treating this type of cancer. The Sarcoma Alliance posts a list of some of these centers on its website, www.sarcomaalliance.org. You can also ask your doctor to refer you to a sarcoma treatment center.

Types of Sarcoma

Some of the most common types of sarcoma include:

- **Angiosarcoma**, which develops in the lining of the blood vessels.
- **Chondrosarcoma**, which forms in cartilage.
- **Ewing's sarcoma**, which forms in soft tissue and bone.
- **Fibrosarcoma**, which develops in the connective tissue holding bone, muscles, and organs in place.
- **Gastrointestinal stromal tumor (GIST)**, which forms in the stomach or intestines.
- **Leiomyosarcoma**, which develops in smooth muscle tissue.
- **Liposarcoma**, which develops in fat tissue.
- **Malignant peripheral nerve sheath tumor**, which occurs in the cells that surround nerves.
- **Osteosarcoma**, which affects bone.
- **Rhabdomyosarcoma**, which forms in a type of muscle called striated muscle.
- **Synovial sarcoma**, which can develop anywhere in the body.

Diagnosing Sarcoma

Sarcoma often does not cause symptoms until the cancer has become advanced. Most primary care doctors don't see many cases of sarcoma during their careers. That makes diagnosing these tumors particularly difficult.

Generally, anyone who has a mass or lump that doesn't go away and gets bigger or causes pain or other symptoms should consider a biopsy. A biopsy is a procedure in which some tissue from the mass is removed in order to examine it under a microscope. A biopsy is the only way to find out whether a tumor is benign or malignant (cancerous) and, for sarcoma, what type of sarcoma it is. Doctors use three different types of biopsy techniques to diagnose sarcoma:

Percutaneous biopsy The simplest and easiest biopsy technique is to put a small hollow needle through the skin into the tumor. The needle is used to withdraw cells or a small piece of tissue, which is examined under a microscope. Generally, percutaneous biopsy is the preferred technique because it is simple and 95 percent accurate in diagnosing sarcoma. However, fine-needle aspiration (FNA), a type of percutaneous biopsy used to detect many types of cancer, does not provide adequate information to diagnose sarcoma. FNA is probably not the best method to choose if a sarcoma is suspected.

Excisional biopsy For this procedure, a surgeon cuts through the skin to remove the entire mass that is suspected of being cancerous. This type of biopsy should never be done if a sarcoma is suspected. Removing the entire tumor before a diagnosis is made may affect the choice of the best surgical approach to use in treating a sarcoma.



Incisional biopsy This technique is similar to excisional biopsy, except that only a small part of the tumor is removed for examination. Both incisional and excisional biopsy techniques are surgical procedures that are done while a patient is under local or general anesthesia. Generally, these types of biopsies are only performed when a percutaneous biopsy is not possible.

Once a sample has been taken, it has to be examined by a pathologist—a doctor who examines biopsied cells and tissues to check for cancer and other conditions. Because sarcomas are so rare, it's very important to have the biopsy material reviewed by a pathologist who has a lot of experience diagnosing sarcoma. Whenever possible, this examination should be done before the patient receives any type of treatment.

Treatments for Sarcoma

If you are diagnosed with sarcoma, one of the most important things you can do is work with a medical team that specializes in treating sarcoma. Ask your doctor to refer you to a sarcoma treatment center with health care professionals who see hundreds of patients with sarcoma each year and who use a team approach to treating this cancer. If you prefer to keep working with your current oncologist, he or she can consult or work with a specialist team to make sure you get the best care possible.

A localized sarcoma (one that has not spread to other parts of the body) is usually treated with surgery to remove the tumor. Radiation is often added to surgery. This combination has proved more effective than surgery alone, especially for deep tumors that are larger than five centimeters (about two inches) or those that cannot be removed with clean margins. A margin is the edge or border of the tumor tissue removed during cancer surgery. The margin is described as “clean” when there are no cancer cells at the edge of the tissue, suggesting that all of the cancer has been removed. Other treatments include chemotherapy, which is used to treat only certain types of sarcoma, and newer targeted treatments, described on pages 11–13.

Surgery

Important advances in the surgical treatment of sarcoma have been made during the past three decades. In the past, people with sarcoma in the arms or legs usually had to undergo amputation—surgical removal—of those limbs as part of treatment. Now, sarcoma usually can be treated with limb-sparing surgery. With this newer technique, sarcoma is

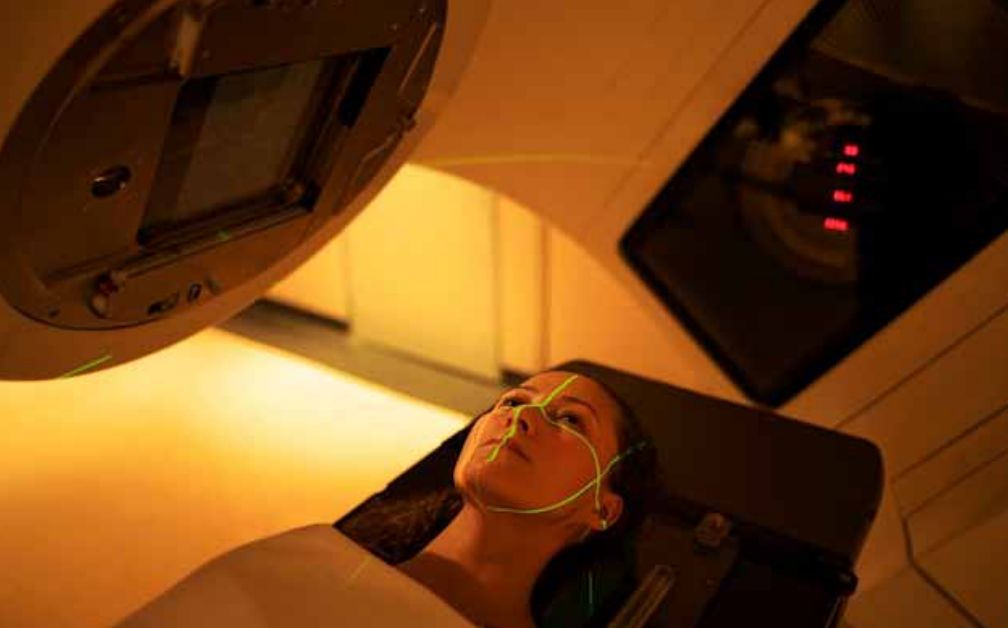
surgically removed in a way that preserves the use of the arm or the leg. The development of limb-sparing surgery has led to a dramatic drop in amputation rates among people with sarcoma, from about 50 percent in the past to less than five percent today.

Another surgical advance that has made a tremendous difference for people with sarcoma is the use of microvascular surgical techniques. When a sarcoma is removed, surgeons sometimes have to take a large amount of skin and muscle around the tumor as well, to make sure that all the cancer cells are taken away. But removing this tissue may cause changes to the appearance or full use of the arm, leg, or other area where the tumor had been. Microvascular surgical techniques allow surgeons to transfer muscle and skin from other parts of the body to the surgical site. This procedure helps the wound to heal properly and the surrounding area to maintain its function.

Radiation

For many types of sarcoma, combining surgery with radiation treatment has proved more effective than surgery alone. There are several kinds of radiation techniques. In some cases, radiation is given after the tumor is surgically removed. Radiation treatments usually begin about four to six weeks after surgery and last for five to six-and-a-half weeks. Another option is to give radiation first and then do surgery about four to eight weeks after radiation treatment is finished.

Either approach has its advantages and disadvantages. For example, when radiation is given before surgery, doctors can usually give a lower dose to a smaller area. Giving radiation treatment before surgery also causes fewer long-term side effects than radiation given after surgery.



Should a patient have surgery first, it's best to let the surgical wound heal before radiation treatment is given. Radiation can affect the ability of some normal tissues to heal after surgery. Side effects from radiation can include fibrosis, a condition in which the tissues can become very firm and inflexible, and edema, or swelling of the tissues, which can also become a long-term treatment side effect. Each person should discuss the sequence of surgery and radiation treatment with his or her medical team.

Radiation treatments can be delivered in several different ways. The most common is a type called external-beam radiation, in which the radiation is delivered to the tumor from a machine outside the body. Another option, called brachytherapy, uses radioactive material sealed in needles, seeds, or wires. These devices are placed directly into or near a tumor after surgery. A third option is a technique called IMRT, in which thin beams of radiation of different strengths are aimed at the tumor from many angles. This type of

radiation treatment reduces the damage to healthy tissue near the tumor. A fourth option is proton-beam radiation, which protects the spinal cord and nerves when treating sarcomas of the head and neck, for example. It's important for patients to discuss their options with their medical team. Which radiation technique doctors recommend depends on the type of sarcoma, its location, and other factors.

Whether surgery alone or surgery combined with radiation is used, the goal of treatment is to remove the entire sarcoma with a margin of normal tissue around it while preserving as much function as possible. Occasionally, a sarcoma cannot be removed without either amputating a limb or causing a major decrease in its use. In such situations, radiation treatment alone is sometimes used to shrink the tumor and help control the cancer while preserving limb function.

Chemotherapy

Chemotherapy is used to treat at least three types of sarcoma, all of which tend to occur in children under the age of 18: osteosarcoma (bone sarcoma), Ewing's sarcoma (bone and soft-tissue sarcoma), and rhabdomyosarcoma (muscle sarcoma). Radiation may be combined with chemotherapy for effective treatment of sarcoma. Chemotherapy alone usually is less effective at treating other types of sarcoma.

There are a number of clinical trials under way to find out whether new medications might improve treatment in both children and adults. For example, one trial is studying young patients with soft-tissue sarcoma. Sometimes after surgery, the tumor may not need more treatment unless it continues to grow. Researchers in the Children's Oncology Group are trying to learn whether observing the patient and giving no further treatment unless needed works as well

as giving radiation and chemotherapy after surgery. In this study, researchers combine ifosfamide (Ifex and others) and doxorubicin, two standard chemotherapy drugs that are widely used.

Although there are more side effects when taking these two drugs together, the combination may prove to be a better treatment than doxorubicin alone. In Europe, researchers have conducted a study to find out whether the benefits outweigh the risks for people who take ifosfamide and doxorubicin together, rather than one at a time. The results will be available soon.

Other clinical trials are testing whether newer versions of ifosfamide-like drugs might be more effective. A clinical trial called PICASSO 3 is studying palifosfamide plus doxorubicin as front-line treatment for adults with metastatic (cancer that has spread) soft-tissue sarcoma. Half of the patients in this worldwide study will receive palifosfamide plus doxorubicin. The other half will receive doxorubicin plus placebo (an inactive substance). This will test whether the new drug, palifosfamide, might be more beneficial than doxorubicin alone.

A similar clinical trial will combine another new drug, called TH-302, with doxorubicin to find out whether that combination is better than doxorubicin alone. The people taking part in this study are adults with advanced soft-tissue sarcoma.

Because palifosfamide and TH-302 are not yet approved by the U.S. Food and Drug Administration (FDA), only people who enroll in the clinical trials can receive them.

Two large clinical trials for people with advanced liposarcomas or leiomyosarcomas are now under way. The patients taking part have sarcomas that continue to grow,

even though they have received standard chemotherapy. One study is comparing the effectiveness of trabectedin (Yondelis) to dacarbazine (DTIC). A second clinical trial is comparing eribulin (Halaven) with dacarbazine. Eribulin has already been approved by the FDA for breast cancer treatment.

Targeted Treatments

Targeted treatments attack specific molecules and cell mechanisms thought to be important for cancer cell survival and growth. This specific targeting helps to spare healthy tissues and cause less severe side effects.

In 2002, the first successful targeted treatment for sarcoma, the drug imatinib (Gleevec), was approved by the FDA for use in people with a rare type of sarcoma in the upper digestive tract called gastrointestinal stromal tumor (GIST). In clinical trials, imatinib shrank or controlled the growth of tumors in



The Importance of Clinical Trials

There is no question that clinical trials have led to advances in cancer treatments, creating a brighter future for people with cancer.

Clinical trials are the standard by which we measure the worth of new treatments and their effect on quality of life as patients go through these treatments. For this reason, doctors and scientists urge patients 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 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 of the risks and benefits of the trial.
- 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.

nearly nine out of 10 people with GIST. This medication works by preventing the transmission of signals to cancer cells to grow and multiply. But after about two years of taking the drug, at least half the patients' tumors became resistant to imatinib, continuing to grow despite treatment with the drug.

Other clinical trials showed that a second targeted treatment called sunitinib (Sutent) could help many patients if imatinib

no longer worked for them. Sunitinib cuts off the blood supply of cancer cells and blocks their ability to grow. It was approved by the FDA in 2006 for the treatment of GIST.

Since then, researchers have continued to search for more ways to treat advanced GIST if the tumor resists both imatinib and sunitinib. Your doctor can talk with you about the newest drug treatments available through clinical trials at specialized GIST treatment centers.

Studies now show that taking imatinib after GIST surgery can benefit many patients who have a high risk of the tumor returning or spreading.

Pain and Symptom Management

Sarcoma and its treatments can cause a number of side effects. A key to managing these side effects is to be aware of them and to talk with your health care team if they arise. For example, it is important to discuss with your health care providers any pain you experience before, during, and after treatment. The type of pain may vary, and different strategies are used to manage different types of pain. It's helpful to score pain on a scale of zero to 10, where zero is no pain and 10 is the worst pain. By tracking the pain, you and your doctor can tell whether the recommended pain management techniques and treatments are working.

In addition, it's important to talk with your health care team about any quality-of-life concerns. As mentioned, sarcomas can occur just about anywhere in the body, and treatment strategies vary from person to person. For example, if a sarcoma or its treatment affects your ability to walk, it's important to discuss this with your health care team. Your doctor can then include rehabilitation specialists in your care plan.

Your Support Team

When you are diagnosed with sarcoma, you are faced with a series of choices that will have a major effect on your life, and maybe you're not sure where to turn. But help is available.

Your health care team, family members, and friends will likely be an invaluable source of support at this time. You can also turn to these resources:

Oncology social workers provide emotional and practical support for people living with cancer and their loved ones. These professionals can help you cope with the challenges of a sarcoma diagnosis and guide you to resources. CancerCare® offers free counseling from oncology social workers who understand the challenges faced by people with sarcoma.

Support groups provide a caring environment in which you can share your concerns with others in similar circumstances. Support group members come together to help one another, providing insights and suggestions on ways to cope. At CancerCare, people with sarcoma and their families can take part in support groups in person, online, or on the telephone. All our groups are led by professional oncology social workers.

Financial help is offered by a number of organizations, including CancerCare, to help cover cancer-related costs such as transportation to treatment, child care, and home care. CancerCare also provides referrals to other organizations that offer assistance.

To learn more about how we help, call 800-813-HOPE (4673) or visit www.cancercares.org.

MORE ABOUT SARCOMA

Frequently Asked Questions

Q. My husband has a soft-tissue sarcoma. Are there any clinical trials that might be good for him?

A. First, be sure that he gets an accurate diagnosis from a sarcoma center and an expert opinion on treatment options. It may be that your husband has a good chance of doing well with standard treatments. If your oncologist believes that standard treatments will not be enough, he or she will likely give you information about clinical trials your husband may be eligible for. You can also get information about clinical trials from organizations such as the National Cancer Institute. Any information you find should be



discussed with your husband's oncologist, who is familiar with the specifics of your husband's sarcoma and can discuss with you particular clinical trials that might be appropriate for him.

Q. I just read a newspaper article about a new treatment for sarcoma. How can I tell whether it's a breakthrough treatment or something that's been hyped?

A. Your oncologist has access to scientific information about sarcoma and its current treatments. He or she can answer your questions about the merit of what you have read or heard. It is also helpful to look for additional information from professional groups such as the National Cancer Institute's Cancer Information Service, the American Society of Clinical Oncology, or the other organizations listed throughout this booklet and on the resource list on page 17. If the information is difficult to understand, you can take it to your oncologist. He or she can help you understand it and determine whether it is useful for you or your loved one.

Resources

CancerCare

1-800-813-HOPE (4673)

www.cancercares.org

American Cancer Society

1-800-227-2345

www.cancer.org

Cancer.Net

Patient information from the American Society of Clinical Oncology

1-888-651-3038

www.cancer.net

National Cancer Institute

Cancer Information Service

1-800-422-6237

www.cancer.gov

National Coalition for Cancer Survivorship

See especially the Cancer Survival Toolbox®

1-888-650-9127

www.canceradvocacy.org

National Organization for Rare Disorders

1-203-744-0100

www.rarediseases.org

Sarcoma Alliance

1-415-381-7236

www.sarcomaalliance.org

Sarcoma Foundation of America

1-301-253-8687

www.curesarcoma.org

TO FIND OUT ABOUT CLINICAL TRIALS:

Coalition of Cancer Cooperative Groups

www.CancerTrialsHelp.org

National Institutes of Health

www.cancer.gov/clinicaltrials

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