

Melanoma

Treatment Guidelines for Patients

Version IV/January 2008



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The mutual goal of the National Comprehensive Cancer Network® (NCCN®) and the American Cancer Society (ACS) partnership is to give patients and the general public state-of-the-art cancer treatment information in a language that is easy to understand. This information, based on the NCCN's Clinical Practice Guidelines, is meant to help you talk with your doctor about your treatment. These guidelines do not replace your doctor's expertise and clinical judgment. Each patient's situation must be evaluated individually. It is important to discuss the guidelines and all information about treatment options with your doctor.

The NCCN Clinical Practice Guidelines are developed for health professionals by a diverse panel of experts. These guidelines are a statement of the authors' consensus regarding the scientific evidence and their views of currently accepted approaches to treatment. The NCCN guidelines are updated as new information becomes available. The patient information version is updated accordingly and is available on-line through the NCCN and the ACS Web sites. To be sure you have the most recent version, contact the NCCN at 1-888-909-NCCN or the ACS at 1-800-ACS-2345.

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Introduction

This booklet was written to give patients information about the way melanoma is treated at the nation's leading cancer centers. Originally developed for cancer specialists by the National Comprehensive Cancer Network (NCCN), these treatment guidelines have now been written in an easier-to-understand version by the American Cancer Society (ACS). To get more copies of these guidelines, call the ACS at 1-800-ACS-2345 or the NCCN at 1-888-909-NCCN, or visit these organizations' Web sites at www.cancer.org (ACS) and www.nccn.org (NCCN).

Since 1995, doctors have looked to the NCCN for advice on treating cancer. The NCCN Clinical Practice Guidelines were developed by a diverse panel of experts from 21 of the nation's leading cancer centers.

For more than 90 years, the public has relied on the American Cancer Society for information about cancer. The Society's books, brochures, and Web pages provide comprehensive, current, and understandable information to hundreds of thousands of patients, their families, and friends. This collaboration between the NCCN and ACS provides an authoritative and understandable source of cancer treatment information for the general public. These patient guidelines will help you better understand how to make decisions about your cancer care that are important to you.

These patient guidelines will help you better understand your cancer treatment options. We urge you to discuss them with your doctor. After reading these guidelines, you might start by asking the following questions:

- What is my cancer's stage?
- Where is my cancer located?
- How far has my cancer spread?
- How does the stage influence my outlook for cure and survival and my treatment options?
- What treatment options do I have?
- What are the risks or side effects associated with each of my treatment options, and how are they likely to affect my quality of life?
- What should I do to be ready for treatment, reduce side effects of treatment, and hasten my recovery?
- When will I be able to return to normal activities?
- Are there any clinical trials that I should consider?

In addition to these questions, be sure to write down some of your own. For instance, you might want more information about how long it will take you to recover from surgery so you can plan your work schedule. Or you may want to ask about clinical trials.

Making decisions about melanoma treatment

The American Cancer Society estimates that around 60,000 new melanomas are diagnosed in the United States each year. The number of new melanomas diagnosed in the US every year is increasing. Since 1973, the incidence rate for melanoma (the number of new melanomas diagnosed per 100,000 people each year) has more than doubled and the mortality rate for melanoma (the number of

deaths from melanoma per 100,000 people each year) has increased. The good news is that melanoma mortality rates have only slightly increased during the past 10 years.

Although melanoma is a serious disease, it can be treated and cured. It is important that you receive care from a team of health care professionals who are experienced in treating melanoma. This team may include a dermatologist, surgeon, medical oncologist, radiation oncologist, pathologist, nurse, radiologist, and social worker — often along with your primary care doctor.

The information in this booklet is intended to help you understand your options for treatment of melanoma so that you and your cancer care team can work together to decide which treatment is best for you.

On the pages after the general information about melanoma, you will find flowcharts that doctors call “Decision Trees.” The charts represent different stages of melanoma. Each one shows you step-by-step how you and your doctor can arrive at the choices you need to make about your treatment.

To reach an informed decision, you need to understand some of the medical terms that your doctors use. You may feel you’re on familiar ground already, or perhaps you need to refer to the various sections listed in the table of contents. In this booklet you will find not only background information on melanoma, but also explanations of melanoma stages, work-up (evaluation), and treatments — all categories used in the flowcharts.

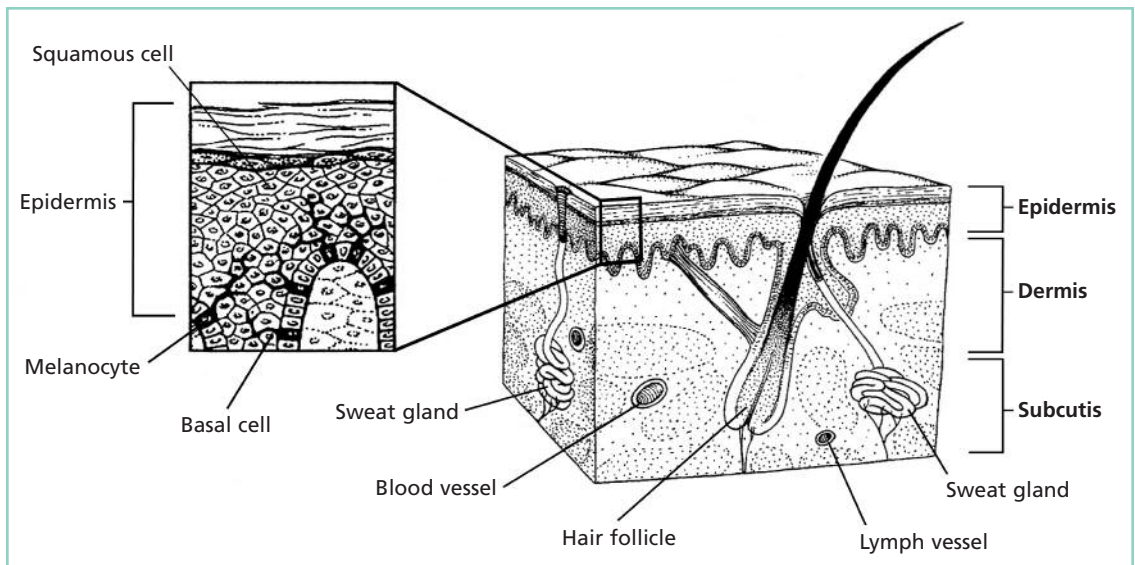


Figure 1. The layers of the skin

About the skin

The skin has 3 layers: epidermis, dermis, and subcutis (see Figure 1). The top layer is the epidermis. The epidermis is very thin, averaging only 0.2 mm (about $\frac{1}{100}$ of an inch). It protects the deeper layers of skin and the organs of the body from the environment.

The outermost part of the epidermis is called the stratum corneum, or horny layer. It is made up of dead cells of the epidermis that are continually shedding. Below the stratum corneum are layers of living cells called squamous cells. These cells form an important protein called keratin. Keratin is part of the skin's ability to protect the rest of the body. The lowest part of the epidermis, the basal layer, is formed by basal cells. These cells continually divide to form new cells to replace the older ones that wear off the skin's surface.

Melanoma comes from cells called melanocytes that are also present in the epidermis. These skin cells produce the protective pigment called melanin. Melanin gives a tan or brown color to the skin and helps protect the deeper layers of the skin from the harmful effects of the sun. The basal lamina separates the epidermis from the deeper layers of skin.

The middle layer of the skin is called the dermis. The dermis is much thicker than the epidermis. It contains hair follicles, sweat glands, blood vessels, and nerves that are held in place by a protein called collagen. Collagen, which is made by skin cells called fibroblasts, gives the skin its resilience and strength.

Below the skin is the subcutis. The subcutis and the lowest part of the dermis form a network of collagen and fat cells. The subcutis

conserves heat and has a shock-absorbing effect that helps protect the body's organs from injury.

Types of skin cancer

Skin cancers are divided into 2 general types: melanoma and non-melanoma. Non-melanoma skin cancers (usually basal cell and squamous cell cancers) are the most common cancers of the skin. They are called non-melanoma skin cancer because they develop from skin cells other than melanocytes. Because they rarely spread elsewhere in the body, they are treated differently.

Melanoma is a cancer that begins in the melanocytes, the cells that produce the skin coloring or pigment known as melanin. Because most melanoma cells still produce melanin, melanoma tumors are often brown or black. Although melanoma is much less common than basal cell and squamous cell cancers, it can be more dangerous. Melanoma, like basal cell and squamous cell cancers, is almost always curable in its early stages. But, melanoma is much more likely than basal or squamous cell cancer to spread to other parts of the body.

Melanomas can occur anywhere on the skin, but are more likely to develop in certain locations. The trunk is the more common site in men. In women, the legs are more commonly affected. Having darkly pigmented skin lowers the risk of being diagnosed with melanoma, but it is not a guarantee that you will not develop melanoma. Anyone, including people with dark skin, can develop this

cancer on the palms of the hands, soles of the feet, and under the nails. Melanomas of the palms, soles, and nails represent about half of all melanomas in African Americans but fewer than 10% of melanomas in whites.

Tests and exams for melanoma diagnosis and work-up (evaluation)

How is melanoma diagnosed?

Any new skin wound (lesion), or change, spot, or growth on your skin could be melanoma. Your doctor will examine it and other tests will be used to find out whether it is melanoma, non-melanoma, or some other skin condition. An exact diagnosis can only be made by a biopsy of the skin

History and physical examination

Usually the first step is for your doctor to take your medical history which will include questions about your symptoms and risk factors. The doctor will ask when the skin lesion first appeared and whether it has changed in size or appearance. You may also be asked about past exposures to known causes of melanoma and whether anyone in your family has had melanoma.

During the physical examination, your doctor will note the size, shape, color, and texture of the area in question and look for any bleeding or scaling. The rest of your body will be checked for spots and moles that may be related to melanoma. The doctor will also examine lymph nodes near the abnormal area of skin. Lymph nodes, also called lymph glands, are small bean-shaped collections of

immune system tissue that are found along lymphatic vessels. Enlarged lymph nodes may suggest the spread of a melanoma to these structures.

If your doctor is not a specialist in skin disorders (a dermatologist), you may be sent to one for further evaluation and a biopsy.

Types of skin biopsy

If the doctor thinks a melanoma might be present, he or she will take a sample of skin from the suspicious area to be looked at under a microscope. This is called a skin biopsy. There are different ways to take the sample of your skin. The choice depends on the size of the affected area and its location on your body. Any biopsy is likely to leave a scar. Because different methods produce different types of scars, you should ask the doctor about biopsies and scarring before the procedure is done. Skin biopsies are done using a local anesthetic. Which means only the involved area will be numbed with medicine. When this is done you will likely feel a small needle stick and a little burning with some pressure for less than a minute.

All skin biopsy samples are looked at under a microscope. The skin sample is sent to a pathologist, a doctor who has been specially trained in the microscopic examination and diagnosis of tissue samples. Often, the skin sample is sent to a dermatopathologist, a dermatologist or pathologist who has had extra training in making diagnoses from skin samples and may be more experienced with certain skin cancers than a general pathologist. He or she will determine if the cells look dysplastic, that is, abnormal, or if they look like they may become cancerous.

Incisional and excisional biopsies

An incisional biopsy removes only a part of the tumor. If the entire tumor is removed, it is called an excisional biopsy. A narrow rim of normal skin (called the margin) is taken with this biopsy for further examination, and the edges of the wound are sewn together. Both types of biopsies can be done using local anesthesia. Excisional biopsy is the method usually preferred when melanoma is suspected.

Punch biopsy

A punch biopsy removes a small sample of skin. The doctor uses a punch biopsy tool that looks like a tiny, round cookie cutter. Once the skin is numbed with a local anesthetic, the doctor rotates the punch biopsy tool on the surface of the skin until it cuts through all the layers of the skin, including the epidermis, dermis, and the upper parts of the subcutis. Punch biopsy may be appropriate for areas such as the palm, sole, finger, toe, face, ear, or for very large lesions.

Shave biopsy

After numbing the area with a local anesthetic, the doctor “shaves” off the top layers of the skin (the epidermis and part of the dermis) with a surgical blade. A shave biopsy is useful in diagnosing many types of skin diseases and in treating benign (non-cancerous) moles. However, if an invasive melanoma is suspected, a shave biopsy sample may not be deep enough to precisely measure its thickness or depth of invasion. If melanoma is suspected, a shave biopsy is usually not done.

Blood tests

There are no specific blood tests for melanoma, but sometimes a blood test for LDH (lactate dehydrogenase) levels might be helpful. LDH is an enzyme found in the blood that may be elevated when a lot of cancer cells are present or when the liver has been damaged by cancer. Blood LDH levels can be a marker for widespread melanoma. LDH levels are seldom elevated when the melanoma is first diagnosed.

Imaging tests

These tests use x-rays, magnetic fields, or radioactive substances to create pictures of the inside of the body to look at the extent of spread of the cancer. Imaging tests such as computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, and positron emission tomography (PET) scans may be used to see whether the melanoma has spread to other organs or to lymph nodes deep inside the body. These tests may not always be needed and are used mostly for patients with known or suspected metastases (spread).

Chest x-ray

A chest x-ray may be taken to find out whether the melanoma has spread (metastasized) to the lungs. A chest x-ray is sometimes not needed for patients with very early (thin) melanoma.

Computed tomography

The CT (computed tomography) scan is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking 1 picture, like a usual chest x-ray, a CT

scanner takes many pictures as it rotates around you. You will need to lie still on a table while this is being done. A computer then combines these pictures into an image of a slice of your body. The machine produces multiple images of the part of your body that is being studied.

Often after the first set of pictures is taken, you will get an intravenous (IV) injection of a special dye (called a radiocontrast agent) that helps better outline structures in your body. A second set of pictures is then taken. The dye can cause some people get hives or, rarely, more serious allergic reactions like trouble breathing and low blood pressure can occur. Be sure to tell the doctor, before you get this scan, if you have ever had a reaction to any contrast material used for x-rays. The CT may show melanoma that has spread to your lungs or liver and can help find enlarged lymph nodes that might contain cancer.

Magnetic resonance imaging

MRI (magnetic resonance imaging) scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into very detailed cross-sectional images of parts of the body. A contrast material might be injected just as with CT scans. (Please see the discussion above.) MRI can be very useful for looking for tumors in the brain and spinal cord.

Positron emission tomography

PET (positron emission tomography) scans use glucose (a form of sugar) that contains a

radioactive atom. Cancer cells absorb large amounts of the radioactive sugar because of their high rate of metabolism. The sugar is injected into a vein and after a certain amount of time you are put into the PET machine where a special camera can detect the radioactivity. A PET scan may supplement the results of the CT and MRI scans. Sometimes a PET scan will be combined with a CT scan. This is called a PET/CT scan. In general, scans with radioactive compounds are easy to take. There are usually no side effects, and you are exposed to only a tiny amount of radioactive material.

Procedures and tests to find metastases (spread)

Sentinel lymph node mapping and biopsy

This has become a standard procedure for finding melanoma that has spread to nearby lymph nodes. Sentinel lymph node mapping can find the lymph nodes that drain lymph fluid from the area of the skin where the melanoma started. If the melanoma has spread, these lymph nodes are usually the first place it will go. That is why these lymph nodes are called sentinel nodes (sentinel means to watch over the tumor, so to speak).

To map the sentinel lymph node, some time before surgery the doctor injects a small amount of radioactive material into the melanoma. By checking various lymph node areas with a radioactivity detection device like a Geiger counter, the doctor can see what group of lymph nodes the melanoma is most likely to travel to. Then the doctor injects a small amount of a harmless blue dye into the site of the melanoma. After about an hour, a

surgeon makes a small incision in the identified lymph node area. The lymph nodes can then be checked to find which one has turned blue or become radioactive. When the sentinel node has been found, it is removed and looked at under a microscope. If melanoma cells are found in this lymph node, the remaining lymph nodes in this area are surgically removed and also checked for cancer. This is called lymph node dissection. If the sentinel node does not contain melanoma cells, no more lymph node surgery is needed.

If a lymph node near a melanoma is abnormally large, a fine needle aspiration or surgical biopsy of that lymph node is done and the sentinel node procedure may not be needed.

Fine needle aspiration biopsy

A fine needle aspiration (FNA) biopsy uses a syringe with a very thin needle to remove cells from a mass. A local anesthetic is sometimes used to numb the area. This test rarely causes much discomfort and does not leave a scar. FNA may be used to biopsy enlarged lymph nodes near a melanoma to find out if the cancer has metastasized (spread). Sometimes the doctor will look at a CT scan or ultrasound to guide the needle into a mass.

Surgical (excisional) lymph node biopsy:

In this procedure, an abnormally large lymph node is removed surgically through a small skin incision. A local anesthetic is generally used. This technique is often done if a lymph node's size suggests spread of melanoma, but the FNA did not find any melanoma cells.

Diagnosis of metastatic melanoma

Although many melanomas are completely cured, some melanomas spread so quickly that a patient can have metastases to the lymph nodes, lungs, brain, gastrointestinal (GI) tract, or liver while the original melanoma is still small. On the other hand, melanoma that has spread to other parts of the body sometimes may not be found until long after the original melanoma was removed from the skin.

When it has spread like this, the metastatic melanoma in certain organs might be confused with a cancer starting in that organ. For example, melanoma that has spread to the lungs might be confused with a primary lung cancer (cancer that starts in the lungs). Special tests can be done on biopsy samples to tell whether it is a melanoma or some other kind of cancer. This is important because different cancers are treated differently.

Examination of the skin biopsy

It is important to measure the thickness of a melanoma under a microscope because this is believed to be one of the best ways to determine the prognosis (or outlook for survival).

The pathologist examining the skin biopsy specimen measures the thickness of the melanoma under the microscope with a device called a micrometer, which is like a very small ruler. This technique is called the Breslow measurement. The thinner the melanoma, the better the prognosis. In general, melanomas less than 1 millimeter (mm) in depth (about $\frac{1}{25}$ of an inch) have a very small chance of spreading. As the melanoma becomes thicker, it has a greater chance of

spreading. The thickness of the melanoma also guides the choice of treatment.

Another system describes the thickness of a melanoma in relation to its penetration into the skin instead of actually measuring it. The Clark level of a melanoma uses a scale of Roman numerals I to V to describe thickness (with higher numbers indicating a deeper melanoma). The Clark level Roman numerals should not be confused with the stage grouping Roman numerals.

- Clark level I: the melanoma stays in the epidermis
- Clark level II: the melanoma has begun to penetrate to the upper dermis
- Clark level III: the melanoma involves most of the upper dermis
- Clark level IV: the melanoma has penetrated to the lower dermis
- Clark level V: the melanoma has penetrated very deeply, to the subcutis

In the newest classification, the Breslow measurement of thickness has become more useful than the Clark level of penetration as the first prognostic factor. This is because the thickness measurement is easier and depends less on the pathologist's judgment. But sometimes the Clark level tells us that a melanoma is more advanced than we may think it is from the Breslow measurement. Therefore, both systems are often used to help stage a melanoma.

In either system, the melanoma has a worse prognosis if the pathologist says it is ulcerated. (This means the layer of skin covering the melanoma is absent).

Melanoma stages

Staging is a process of describing how far a cancer has spread. This includes describing the size of the skin tumor and whether it has spread to any other organs. A staging system is a standard way for your health care team to summarize the extent of your cancer.

The American Joint Committee on Cancer (AJCC) staging system is used most often to describe the extent of melanoma. In this system, each cancer is given a T category, an N category, and an M category.

- The T category is based on the tumor's thickness and whether it is ulcerated (there is no layer of skin covering the melanoma).
- The N category reflects whether the melanoma has spread to lymph nodes near the melanoma. The N category also reflects whether the melanoma cancer cells are beginning to spread and are found in lymphatic channels connecting to the lymph nodes.
- The M category indicates whether there is spread (metastases) to distant organs.

In TNM staging, information about the tumor, lymph nodes, and metastasis is combined to assign a stage according to a process called stage grouping. The stage is then described using 0 and Roman numerals from I to IV.

Several tests and procedures are used to gather information about a melanoma and whether it has spread to lymph nodes and distant organs. This information is used to assign T, N, and M categories and a grouped stage.

Descriptions of grouped stages

The stages used in these guidelines are as follows:

Stage 0: The melanoma is in situ, meaning that it involves the epidermis but has not spread to the dermis. This is also called Clark level I.

Stage IA: The melanoma is less than or equal to 1.0 mm or about $\frac{1}{25}$ inch in thickness and no ulceration is present. Using the Clark system, this can be level II or III. It appears to be localized in the skin and has not been found in lymph nodes or distant organs.

Stage IB: The melanoma is less than or equal to 1.0 mm in thickness and is ulcerated, *or* Clark IV or V, *or* it is between 1.01 and 2.0 mm and is not ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs.

Stage IIA: The melanoma is between 1.01 mm and 2.0 mm in thickness and is ulcerated, *or* it is between 2.01 and 4.0 mm and is not ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs.

Stage IIB: The melanoma is between 2.01 mm and 4.0 mm in thickness and is ulcerated, *or* it is thicker than 4.0 mm and is not ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs.

Stage IIC: The melanoma is thicker than 4.0 mm and is ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs.

Stage III: The melanoma has spread to the lymph nodes nearest the affected skin area. There is no distant spread.

Stage IV: The melanoma has spread beyond the original area of skin and the nearby lymph nodes to other organs, such as the lung, liver, or brain, or to distant areas of the skin or lymph nodes.

Types of treatment for melanoma

After the diagnostic tests are done, your cancer care team will recommend one or more treatment options. Consider the options without feeling rushed. If there is anything you do not understand, ask to have it explained. The choice of treatment depends largely on the thickness of the primary tumor and the stage of the disease.

Types of surgery for melanoma

Wide local excision

When the diagnosis of melanoma is established by biopsy, a wide local excision is done to decrease the chance of local recurrence. More tissue is removed around the melanoma site, and the tissue from the final excision is examined to make sure that no cancer cells remain in the skin. The size of the margin removed (the edge of healthy tissue around the melanoma) depends on the thickness of the tumor.

Tumor thickness	Recommended margins
In situ	0.5 cm (1 inch = 2.54 cm)
Less than 1 mm	1 cm
1 to 2 mm	1 to 2 cm
2 to 4 mm	2 cm
Over 4 mm	At least 2 cm

If the melanoma is on a finger or toe, the treatment may be to amputate as much of that digit as is necessary to get clear margins.

Lymph node evaluation

After the diagnosis of melanoma is made, the doctor will examine the lymph nodes nearest the melanoma. If the lymph nodes are not enlarged, then a sentinel node biopsy procedure may be done. Sentinel lymph node biopsy is usually recommended if the melanoma is more than 1 mm thick, but may be considered for thinner melanomas. If the sentinel lymph node does not show cancer, then it is unlikely that the melanoma has spread to the lymph nodes and there is no need for a lymph node dissection. If the sentinel lymph node is positive, removal of the remaining lymph nodes is usually advised.

If the regional lymph nodes feel hard or large, and FNA or biopsy shows metastatic melanoma, a lymph node dissection may be done. This procedure removes most of the lymph nodes in that area. They will be examined under a microscope to see how many lymph nodes contain cancer.

Lymph node removal can cause some side effects that may be permanent. The most troublesome is called lymphedema. Lymph nodes in the groin or under the arm help

drain fluid from the limbs. Without them, fluid may back up and cause swelling in the leg or arm. Most patients do not get lymphedema. Elastic stockings or sleeves can help some people with this condition. Sometimes special devices that squeeze the limbs are used and may be helpful. The side effects, along with the discomfort from the surgery itself, are why this procedure is not done unless the doctor thinks it is necessary. Discuss risks of the possible side effects and ways to prevent them with your doctor.

Surgery for Metastatic Melanoma

Once melanoma has spread from the skin to distant organs (such as the lungs or brain), the cancer is unlikely to be curable by surgery. Even when only 1 or 2 metastases are found by imaging studies such as CT or MRI scans, other areas of metastasis are likely to be present that are too small to be found by these scans. Surgery is sometimes done in these cases. If one or even a few metastases are present and can be completely removed, surgery may help some patients live longer. Also, removing a metastasis that is causing symptoms may help improve the patient's quality of life.

Immunotherapy

Immunotherapy enhances and encourages a patient's immune system to recognize and destroy cancer cells more effectively. Several types of immunotherapy are used to treat patients with melanoma. Some are being studied as adjuvant therapy. Adjuvant therapy is treatment given after surgery that is intended to destroy any cancer cells that may not have been removed by the surgery.

Bacille Calmette-Guerin

Immunotherapy with BCG (Bacille Calmette-Guerin) is used for the treatment of advanced or recurrent melanoma. BCG vaccine contains an inactivated form of the bacteria that causes tuberculosis and is used to immunize people against tuberculosis. BCG has also been shown to boost the immune system of patients with melanoma. It is given by direct injection into the melanoma lesions (this is called intralesional therapy).

Cytokine therapy

Cytokines are proteins that activate the immune system in a general way. Cytokine therapy is a type of immunotherapy. Two cytokines, interferon-alpha and interleukin-2 (IL-2), can help boost immunity in patients with melanoma. Both drugs can help shrink metastatic (stage III and IV) melanoma in about 10% to 20% of patients. IL-2 is given as an intravenous (IV) injection. For advanced or recurrent melanoma IL-2 is injected directly into the melanoma lesion (intralesional therapy). Side effects of cytokine therapy may include fever, chills, aches, depression, and severe tiredness. Interleukin-2, particularly in high doses, can cause fluid to collect in the body, so the person swells up and can feel quite sick. Some patients may need to be hospitalized because of this problem.

Interferon therapy

Interferons are immune substances produced naturally by the body in response to infection. A man-made version of interferon (alfa-2b) can be administered systemically by intravenous (IV) injection or under the skin (subcutaneous injection). Interferons can be used as adjuvant

therapy (additional therapy following initial treatment). Side effects include fever, chills, aches and severe tiredness. Interferons can also have an effect on the heart and liver. Patients should be treated by an oncologist who is experienced with this therapy. Interferons given to patients with stage III melanoma following surgery can delay the recurrence of melanoma, but may not prolong patients' lives. Your decisions about adjuvant therapy should take into account the potential benefits and side effects of this treatment.

Vaccine therapy

Melanoma vaccines are experimental therapies that are being tested in patients with stage III or stage IV melanoma. Anti-melanoma vaccines are, in some ways, like the vaccines used to prevent diseases caused by viruses such as polio, measles, and mumps. Anti-virus vaccines usually contain weakened or killed viruses or parts of a virus that cannot cause the disease. The vaccine stimulates the body's immune system to destroy the more harmful type of virus. In the same way, weakened melanoma cells or parts of melanoma cells called antigens can be injected into a patient in an attempt to stimulate the body's immune system to destroy melanoma cells. Usually, the melanoma cells are mixed with substances that help stimulate the body's immune system.

Chemotherapy for melanoma

Chemotherapy is systemic therapy using anti-cancer drugs. The drugs are usually injected into a vein or given by mouth. These medicines travel through the bloodstream to all parts of the body, where they attack cancer cells that

have already spread beyond the skin to lymph nodes and other organs.

Chemotherapy drugs kill cancer cells but also kill some normal cells, such as the blood-producing cells of the bone marrow, the cells lining the gastrointestinal (GI) tract, and cells of hair follicles. Short-term side effects of systemic chemotherapy might include nausea and vomiting, loss of appetite, hair loss, and mouth sores.

Because chemotherapy can kill normal blood cells, patients may have low blood cell counts, which can result in:

- an increased chance of infection (due to a shortage of white blood cells)
- bleeding or bruising after minor cuts or injuries (due to a shortage of blood platelets)
- fatigue (often due to low red blood cell counts, but also can be caused by the chemotherapy alone)

Most side effects disappear once treatment is stopped. There are treatments for many of the short-term side effects of chemotherapy, so be sure to discuss side effects with your cancer care team. For example, anti-nausea drugs can be given to prevent or reduce nausea and vomiting.

Only a few chemotherapy drugs are used for stage IV melanoma. Although chemotherapy is usually not as effective in melanoma as in some other types of cancer, it may relieve symptoms or extend the survival time of some patients with stage IV melanoma.

The preferred treatment for advanced or metastatic melanoma is participation in a clinical trial. As another option, patients with

advanced melanoma can be treated with high-dose interleukin-2, or with the chemotherapy drugs dacarbazine (DTIC) or temozolomide either alone or combined with other drugs like, cisplatin and vinblastine. Chemotherapy may also be given in combination with interferon alfa and/or interleukin-2.

Hyperthermic isolated limb perfusion is a type of chemotherapy sometimes used for treating metastatic melanomas confined to the arm or leg. This method temporarily separates the circulation of the involved limb from the rest of the body and injects high doses of chemotherapy into the artery feeding the limb. This allows high doses to be given to the area of the tumor without exposing internal organs to these doses that would otherwise cause severe side effects. Usually the fluid is warmed to 102° to 104° F. Melphalan is the drug most often used in this procedure. Limb perfusion is done to help control disease in the affected extremity but it is not thought to improve survival time.

Radiation therapy

Radiation therapy uses high-energy rays or particles to kill cancer cells. External beam radiation therapy focuses radiation from outside the body on the skin tumor. This type of radiation therapy is used for treating some patients with melanoma.

Radiation therapy is not commonly used to treat the primary tumors of melanoma (the original melanoma that developed on the skin). But it may be considered in some patients whose melanoma has come back (recurred).

CO2 laser ablation

This treatment may be used in some patients with several small nodules of metastatic melanomas that have spread along the skin. The CO2 laser is a type of laser used for skin problems. It emits a very high energy beam that destroys superficial (shallow) skin lesions.

Supportive care

Most of this document discusses ways to cure people with melanoma or to help them live longer by removing or destroying melanoma cancer cells. But, another important goal is to help you feel as well as you can and to continue to do the things in life that you want to do. This is called supportive care. Don't hesitate to discuss your symptoms or how you are feeling with your cancer care team. There are effective and safe ways to treat symptoms you may be having, as well as most of the side effects caused by treatment for melanoma.

Pain is often a concern for patients with advanced cancer. Growth of the cancer around certain nerves may cause severe pain. It is important that patients not hesitate to tell their doctors if they have pain. For most patients, treatment with morphine or other opioids (prescription medicines that are the strongest pain relievers available) will reduce the pain considerably. For more information on the treatment of cancer pain, please contact the ACS or NCCN to request a copy of the *Cancer Pain Treatment Guidelines for Patients*.

Complementary and alternative therapies

Complementary and alternative medicines are a group of different types of health care practices, systems, and products that are not part of your usual medical treatment. They may include Chinese herbs, special supplements, acupuncture, massage, and a host of other types of treatment. You may hear about different treatments from your family and friends. People may offer all sorts of things, such as vitamins, herbs, stress reduction, and more as a treatment for your cancer or to help you feel better. Some of these treatments are harmless in certain situations, while others have been shown to cause harm. Most of them are of unproven benefit.

The American Cancer Society defines complementary medicine or methods as those that are used in addition to your regular medical care. If these treatments are carefully managed, they may add to your comfort and well-being. Alternative therapies are defined as those that are used instead of your regular medical care. Some of them have been proven harmful, but are still promoted as "cures." If you choose to use these alternatives, they may reduce your chance of fighting your cancer by delaying or replacing regular cancer treatment.

There is a great deal of interest today in complementary and alternative treatments for cancer. Many are being studied to find out if they are truly helpful to people with cancer. Before changing your treatment or adding any of these methods, it is best to discuss this openly with your doctor or nurse. Some methods can be safely used along with standard medical treatment. But others can interfere

with standard treatment or cause serious side effects. That is why it's important to talk with your doctor. More information about complementary and alternative methods of cancer treatment is available through the American Cancer Society's toll-free number at 1-800-ACS-2345 or on our Web site at www.cancer.org.

About Clinical Trials

All drugs used to treat cancer or other diseases must undergo clinical trials in order to determine their safety and effectiveness before the Food and Drug Administration (FDA) can approve them for use. Treatments used in clinical trials are often found to have real benefits. Researchers conduct studies of new treatments to answer the following questions:

- Is the treatment helpful?
- How does this new type of treatment work?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Do the benefits outweigh the risks, including side effects?
- Which patients will the treatment most likely help?

During cancer treatment, the doctor may suggest taking part in a clinical trial. Scientists conduct clinical trials only when they believe that the treatment being studied may be better than other treatments.

All patients in a clinical trial are closely watched by a team of experts to monitor their progress very carefully. The study is done to find out if the new treatment will work better than the standard treatment and if the side effects are worse or less. The new treatment may have some side effects, which the doctor will discuss with the patient before the clinical trial is started.

Deciding to Enter a Clinical Trial

Taking part in any clinical trial is completely voluntary. Doctors and nurses explain the study in detail and provide a consent form to read and sign. This form states that the patient understands the risks and wants to participate. Even after signing the form and the trial begins, the patient may leave the study at any time, for any reason.

Taking part in the study will not keep anyone from getting other medical care they may need. Patients should always check with their health insurance company to find out whether it will cover the costs of taking part in a clinical trial.

Participating in a clinical trial evaluating new, improved methods for treating cancer may help the patient directly, and it may help other people with cancer in the future. For these reasons, members of the National Comprehensive Cancer Network and the American Cancer Society encourage participation in clinical trials.

How can I find out more about clinical trials that might be right for me?

The American Cancer Society offers a clinical trials matching service that will help you find a clinical trials that is right for you. You can reach this service at 1-800-303-5691 or our Web site <http://clinicaltrials.cancer.org>. Based on the information you give about your cancer type, stage, and previous treatments, this service compiles a list of clinical trials that match your medical needs. The service will also ask where you live and whether you are willing to travel so that it can look for a treatment center you can get to.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinical_trials/.

More information about clinical trials is available through the American Cancer Society's toll-free number at 1-800-ACS-2345 or on our Web site at www.cancer.org.

Other things to consider during and after treatment

During and after treatment for your melanoma you may be able to speed up your recovery and improve your quality of life by taking an active role. Learn about the benefits and disadvantages of each of your treatment options and ask questions of your cancer care team if there is anything you do not understand. Learn about and look out for side effects of treatment and report these promptly to your

cancer care team so that they can take steps to reduce them.

Remember that your body is as unique as your personality and your fingerprints. Although understanding your cancer's stage and learning about your treatment options can help predict what health problems you may face, no one can say for sure how you will respond to cancer or its treatment.

You may have special strengths such as a history of excellent nutrition and physical activity, a strong family support system, or a deep faith, and these strengths may make a difference in how you respond to cancer treatment. There are also experienced professionals in mental health services, social work services, and pastoral services who may assist you and your family in coping with your illness.

You can help in your own recovery from cancer by making healthy lifestyle choices. If you use tobacco, stop now. Quitting will improve your overall health, and the full return of the sense of smell may help you enjoy a healthy diet. If you use alcohol, limit how much you drink. Have no more than 1 drink per day if you are a woman or 2 drinks per day if you are a man. Good nutrition can help you get better during and after treatment. Eat a nutritious and balanced diet, with plenty of fruits, vegetables, and whole grain foods. If you are having eating problems, ask your cancer care team if you may benefit from talking with a dietician.

If you are in treatment for cancer, be aware of the battle that is going on in your body. Radiation therapy and chemotherapy all add to the fatigue caused by the disease itself. To help you with the fatigue, plan your daily

activities around when you feel your best. Get plenty of sleep at night. Ask your cancer care team about a daily exercise program to help you feel better.

A cancer diagnosis and its treatment are major life challenges, with an impact on you and everyone who cares for you. Before you get to the point where you feel overwhelmed, consider attending a meeting of a local support group. If you need assistance in other ways, contact your hospital's social service department or the American Cancer Society.

Protecting your skin from sun exposure

Everyone needs to protect his or her skin from the harmful effects of the sun. Sunlight contains ultraviolet radiation (UV), which can damage the genes in your skin cells. Tanning lamps and booths are another source of ultraviolet radiation. Excessive exposure to light from these sources can increase the risk of skin cancer, including melanoma. The amount of UV exposure depends on the intensity of the radiation, length of time the skin was exposed, and whether the skin was protected with clothing and sunscreen.

The most important ways to protect your skin is by avoiding being outdoors in intense sunlight too long and to protect your skin whenever you are outdoors. You can continue your usual outdoor activities and protect your skin at the same time by doing the following:

Seeking shade: The simplest and most effective way to limit exposure to ultraviolet

(UV) light is to avoid being outdoors in sunlight too long. This is most important in the middle of the day when UV light is most intense. Seek shade under a tree or umbrella whenever possible.

Protecting your skin with clothing: You can protect most of your skin with clothing, including a shirt with long sleeves and a hat with a broad brim. Tightly woven and dark colored fabrics generally provide the best sun protection.

Using sunscreen: Sunscreens with an SPF of 15 or more should be used on areas of skin exposed to the sun, particularly when the sunlight is strong. Always follow directions when putting on sunscreen. You should apply sunscreen before you go outside, use it thickly on all sun-exposed skin, and reapply it every 2 hours. A 1-ounce application (a palmful of sunscreen) is recommended. Many sunscreens wear off with sweating and swimming and must be reapplied for maximum effectiveness. Use sunscreen even on hazy days or days with light or broken cloud cover because the UV light still comes through.

Sunscreen should not be used to gain extra sun exposure time. Sunscreen will not prevent melanoma; it just reduces the amount of UV light exposure. Researchers have found that many people use sunscreens so that they can stay out in the sun longer. But, by extending their time in the sun, they end up receiving the same amount of UV light exposure as if they hadn't used sunscreen at all. All excessive sun exposure is unhealthy. Sunscreen should not be used to allow a person more time in the sun.

Wearing sunglasses: Wrap-around sunglasses with 99% to 100% UV absorption provide the best protection for the eyes and the skin area around the eyes.

Avoiding other sources of UV light: The use of tanning beds and sun lamps is not safe. The UV radiation they deliver can damage your skin. Their use may increase your risk of developing melanoma.

Checking your skin

As part of your follow-up care, your doctor may talk to you about checking your skin on a regular basis. You should know the pattern of your existing moles, blemishes, freckles, and other marks on your skin so that you'll notice any changes. Self-examination is best done in front of a full-length mirror. A hand-held mirror can be used for areas that are hard to see.

It is important to know the difference between a normal mole (sometimes called a *nevus*) and a melanoma. A normal mole is generally an evenly colored brown, tan, or

black spot on the skin. It can be either flat or raised. It can be round or oval. Moles are generally less than 6 mm ($\frac{1}{4}$ inch) in diameter (about the width of a pencil eraser). A mole can be present at birth, or it can appear during childhood or young adulthood. Several moles can appear at the same time, especially on areas of the skin exposed to the sun. Moles may fade away in older people.

A spouse or other partner may be able to help you with these examinations, especially for those hard-to-see areas, like the back of your thighs and buttocks. All areas should be inspected, including the palms and soles, the lower back, and the back of the legs. Friends and family members can also help by pointing out areas of skin that look different. Be sure to show your doctor any spots that concern you. Your doctor will also examine your skin on your follow-up visits.

Spots on the skin that are changing in size, shape, or color should be evaluated as soon as possible. Any unusual sore, lump, blemish, marking, or change in the way an area of the skin looks or feels should be looked at by your doctor.

Work-up (evaluation) and treatment guidelines

Decision trees

The Decision Trees (or flow charts) on the following pages represent treatment options for melanoma based on how thick it is and how far it has spread. Each one shows you step-by-step how you and your doctor can arrive at the choices you need to make about your treatment.

Keep in mind that this information is not meant to be used without the expertise of your own doctor, who is familiar with your situation, medical history, and personal preferences.

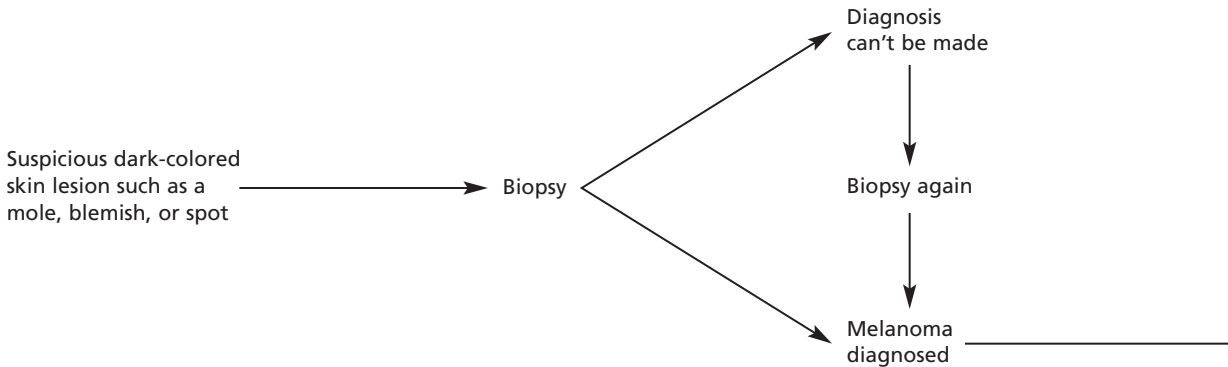
You may even want to review this booklet with your doctor, who can show you which of the Decision Trees apply to you. Ask your doctor about the specific stage your disease is in (i.e., **tumor**, **nodes**, **metastasis**) which refers to how deeply the melanoma is extending into the underlying skin and whether it has spread beyond the skin. This information will also help you know which Decision Trees apply to you. We've left some blank spaces in the Decision Trees for you or your doctor to add notes about the treatments. You also might use this space to write down some questions to ask your doctors about the treatments.

People with any stage of melanoma have the option of participating in a clinical trial. Taking part in that type of study does not prevent you from getting other medical care you may need.

The NCCN guidelines are updated as new significant information become available. To be sure you have the most recent version, consult the Web sites of the ACS (www.cancer.org) or NCCN (www.nccn.org). You may also call the NCCN at 1-888-909-NCCN or the ACS at 1-800-ACS-2345 for the most recent information on these guidelines. If you have questions about your cancer or cancer treatment, please call the ACS any day at any time at 1-800-ACS-2345.

Clinical presentation

Diagnosis

**Work-up (evaluation) of melanoma**

This Decision Tree begins when you or your doctor finds an abnormal looking skin growth or spot (called a skin lesion). If the lesion looks suspicious for melanoma the first step is a biopsy. The whole lesion, if possible, should be removed, along with 1 to 3 mm (about $\frac{1}{25}$ to $\frac{2}{25}$ inch) of surrounding normal skin (called the margin). If this is not possible, then the thickest part of the lesion should be removed, including the full depth of the lesion.

Any further testing is based on what the skin lesion looks like under the microscope. Sometimes the first biopsy is not adequate for complete evaluation and a second biopsy might be recommended. A pathologist (a doctor who specializes in examining tissue samples) who is experienced with skin tumors will examine the specimen to determine if it is a melanoma. He or she will do all of the following:

Work-up (evaluation) of melanoma

Pathology evaluation and report

The pathology report should identify:

- Breslow scale – a measurement of thickness
- Clark level – describes how deep the melanoma cells have grown
- Whether there is ulceration
- Whether there is cancer at the edges (margins) of the biopsy
- Whether there are separate clusters of melanoma cells in the skin near the biopsy site

Preliminary work-up

The doctor will do:

- Complete history (including asking about any family history of melanoma)
- Physical examination, especially of the entire skin, lymph node areas near the melanoma, and organs

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- measure the thickness of the lesion (Breslow scale);
- note how deeply it grows into the underlying normal tissue (Clark level);
- check whether the top of the lesion has ulcerated (determine if the epidermis or outer layer of the skin is no longer present)
- look for cancer at the edges of the biopsy
- look for clusters of melanoma cells in the skin near the biopsy site (this is called satellitosis)

If the diagnosis of melanoma is confirmed, you should have a complete history and physical examination. Your doctor will ask if any members of your family have been diagnosed with melanoma. The physical examination will include a thorough inspection of all of your skin; looking for any enlarged lymph nodes, particularly near the melanoma; and looking for enlarged organs. These evaluations will give information about the specific stage of your melanoma and the best treatment plan.

Clinical stage

Initial work-up

Stage 0
In situ

No further tests needed

Stage IA – low risk:
(less than or equal to 1 mm thick, Clark level II or III, no ulceration)

Further imaging by CT scan, PET scan, or MRI if having symptoms or signs of spread

Stage IB – intermediate to high risk:
(less than or equal to 1 mm thick, with ulceration, or Clark level IV or V)

OR

Stage II – intermediate to high risk:
(more than 1 mm thick with or without ulceration, with no lymph node spread)

- Chest x-ray (optional)
- Further imaging by CT scan, PET scan, or MRI if having symptoms or signs of spread (especially for Stage IIB and IIC)

Discuss the value of sentinel lymph node biopsy with the doctor

Work-up and treatment of lower stage melanoma (in situ, and stages I and II)

If your melanoma is stage 0 (in situ), meaning that it has not spread beyond the outer layer of the skin, no further tests are needed. The only treatment should be a wider excision of the melanoma and of the surrounding area. About 0.5 cm (½ inch) of extra skin (margin)

should be removed. Sentinel node biopsy is not needed. No adjuvant (additional) treatment is recommended.

If your melanoma is stage I or II, imaging tests such as a CT, PET scan, or MRI may be advised if you are having symptoms or if your physical exam suggests that melanoma may have spread beyond the skin. A chest x-ray may be recommended for stage IB or stage II

Work-up and treatment of lower stage melanoma (in situ, and stages I and II)

Primary (main) treatment

Adjuvant (additional) treatment

Wide excision of tumor with removal of an extra 0.5 cm (1/2 inch) of surrounding normal skin

Wide excision (with or without sentinel node biopsy) with the removal of an extra 1 to 2 cm of surrounding normal skin for 1 to 2 mm thick lesions

Wide excision with the removal of an extra 1 to 2 cm of surrounding normal skin for 1 to 2 mm thick lesions, and sentinel node biopsy

See the Decision Tree for follow-up (page 34)

If lesion is stage IA

If lesion is stage IB or II

- If lesion is less than 4 mm thick: Observation*, or Clinical trial
- If lesion is more than 4 mm thick: Clinical trial, or Interferon injections, or Observation*

Sentinel node does not contain cancer

If lesion is stage IB or II

If lesion is stage IA

See the Decision Tree for follow-up (page 34)

Sentinel node contains cancer

See Decision Tree for stage III treatment (page 30)

* Observation means close follow-up with no treatment

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melanomas. The next step is wide excision of the melanoma, which will include removal of 1 to 2 cm of surrounding normal skin depending on the thickness of the melanoma.

Your doctor may also recommend a biopsy of 1 or more sentinel nodes when the excision

is done in order to help determine your future risk of recurrence and to help guide treatment decisions. Although a sentinel node biopsy is an option if you have Stage IA disease, it is considered more strongly for stage IB and stage II disease. This is because

spread to the lymph nodes is more likely with higher stage disease. Further treatment decisions will depend on whether or not the sentinel lymph node biopsy is done, and if so, whether or not melanoma cells are found in the lymph nodes.

If you have stage IA disease (low risk) and did not have a sentinel node biopsy, or if the

sentinel node biopsy result is negative, no further treatment with close follow-up is usually recommended.

If you have stage IB or stage II disease, further treatment may be recommended even if the sentinel lymph node biopsy result is negative, since people with these disease stages have a higher risk of recurrence. Because it is

NOTES

Work-up and treatment of lower stage melanoma (in situ, and stages I and II) (continued)

not certain what treatment is best, no further treatment with very close follow-up is one option. Another option you might consider is entering a clinical trial. If your melanoma is thicker than 4 mm, treatment with interferon injections may be recommended.

For both stage I and stage II disease, if the lymph nodes were found to contain melanoma,

then the patients will be treated as if they have stage III disease, which is described in the Decision Tree starting on page 30.

The follow-up plan after initial treatment of all stages of melanoma is outlined in the Decision Tree on page 34.

NOTES

Clinical or pathologic stage

Work-up

Stage III,
Sentinel node
contains melanoma

- Other imaging tests if needed to evaluate symptoms (CT with or without PET scan or MRI)
- Chest x-ray (optional)
- Blood LDH test (optional)

Stage III,
Lymph nodes enlarged
and contain melanoma

- Fine needle aspirate (FNA) biopsy (preferred) or lymph node biopsy
- Chest x-ray (optional)
- Blood LDH level (optional)
- CT scan of pelvis if groin lymph nodes are enlarged
- Other imaging tests if needed to evaluate symptoms (CT with or without PET scan or MRI)

**Stage III in-transit
Melanoma**

- FNA biopsy of skin lesion (preferred) or lymph node biopsy
- Chest x-ray (optional)
- Blood LDH level (optional)
- Other imaging tests if needed to evaluate symptoms (CT with or without PET scan or MRI)

**Stage IV,
Metastatic**

- FNA (preferred) or biopsy of the distant site
- Chest x-ray or chest CT
- Blood LDH level
- Consider abdominal/pelvic CT scan or head MRI and/or PET scan
- Other imaging tests if needed to evaluate symptoms

Work-up and treatment for higher stages of melanoma: stages III and IV

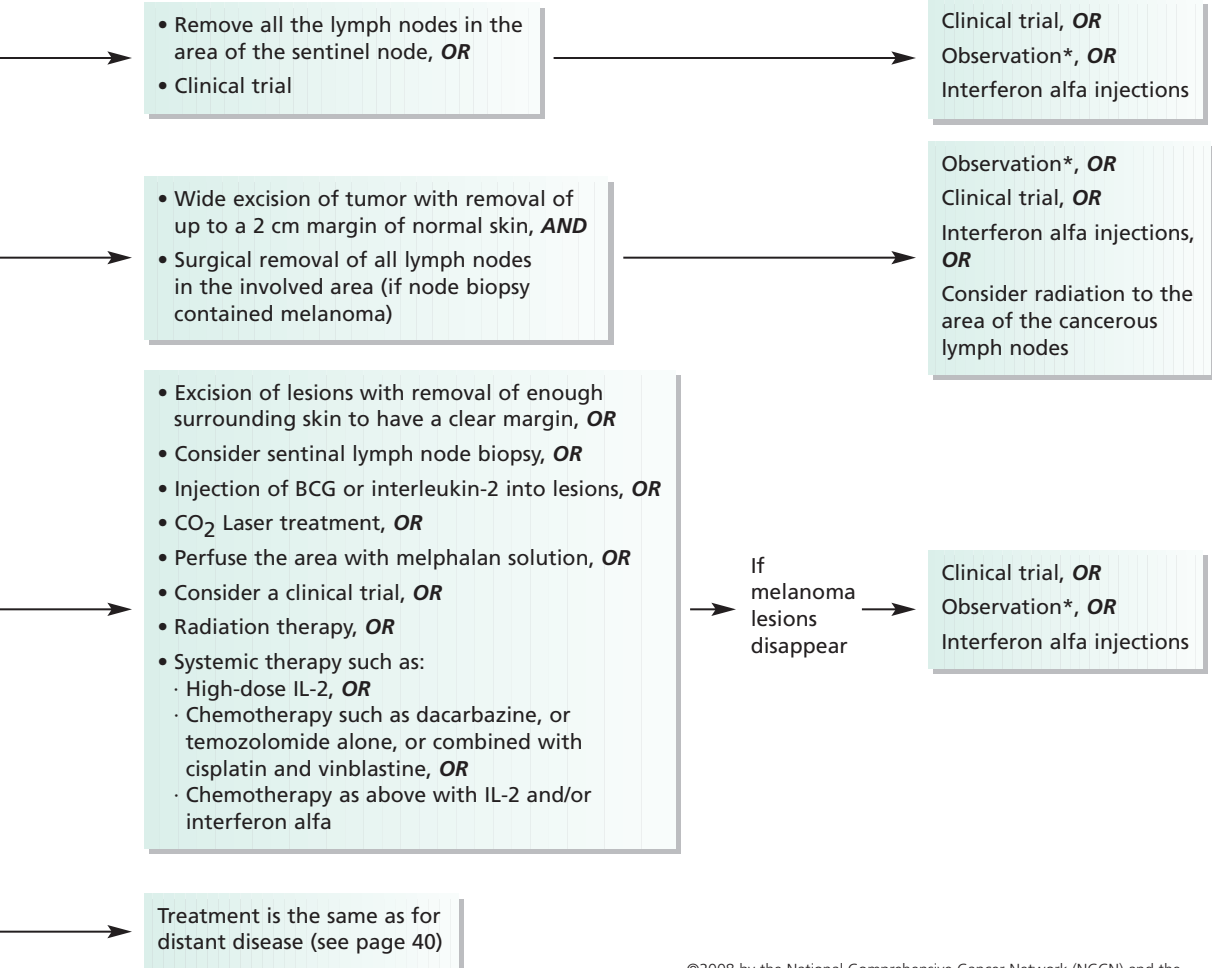
This Decision Tree describes treatment of advanced melanoma, defined as Stage III or IV.

Stage III describes any tumor with involvement of the lymph nodes, but without spread to distant sites. Lymph node spread is subdivided into minimal spread that can only be detected

Work-up and treatment of higher stage melanoma (stages III and IV)

Primary (main) treatment

Adjuvant (additional) treatment



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* *Observation means close follow-up with no treatment*

by looking at the sentinel lymph node biopsy under the microscope, or more advanced spread which is suspected on the basis of

enlarged lymph nodes found during a physical exam. Stage III in-transit melanoma describes a tumor with several nodules of melanoma

mainly found between the primary tumor and the lymph nodes. Additional imaging tests may be recommended for all types of stage III disease, depending on the physical exam and symptoms. Imaging tests may include CT scan, PET scan, MRI. Chest x-ray and blood tests, such as lactate dehydrogenase (LDH) levels are optional.

For stage III melanoma with minimal involvement of lymph nodes (based on the sentinel node biopsy), the recommended treatment is removal of all the lymph nodes in the area of the sentinel node. A clinical trial looking at alternatives to complete lymph node removal is another option.

When the lymph nodes are enlarged, a biopsy is first recommended. The preferred biopsy technique is a fine needle aspiration, where a needle is placed into the enlarged lymph nodes to remove a sample of cells. Alternatively, an excisional biopsy may be done where the physician uses a scalpel to

open the skin and remove a lymph node. Following the biopsy, a wide excision of the tumor with the removal of up to 2 cm of surrounding normal skin is recommended.

If the lymph node biopsy result was positive, all the lymph nodes in the involved area should be removed. Following the surgery, additional therapy may be recommended. Because it is not certain which treatment is best, you may not receive any further treatment but instead continue with the doctor closely watching you. Other options include entering a clinical trial or treatment with interferon injections. Finally, if the cancer was stage IIIC, radiation therapy to the area of cancerous lymph nodes is recommended either alone or combined with any of the above treatments.

Biopsy is the first step for stage III in-transit melanoma, to make sure that these nodules are melanoma. If possible, all tumor nodules should be removed along with

NOTES

Work-up and treatment of higher stage melanoma (stages III and IV) (continued)

enough surrounding normal skin. This may be combined with a sentinel node biopsy. If this is not possible, injections of Bacille Calmette-Guerin (BCG) vaccine or interleukin-2 (IL-2) directly into the melanoma is a treatment option. Tumor nodules also might be destroyed with laser therapy (discussed on page 17). If the melanoma is located on a limb, another possible treatment is to perfuse the area with a melphalan solution heated to 102° to 104° F, referred to as hyperthermic perfusion (discussed on page 16). Because it is not certain which treatment is best, you might want to consider entering a clinical trial. Other possible treatments are radiation therapy to the area, or systemic treatment, such as high-dose interleukin therapy, or chemotherapy with dacarbazine (DTIC) or temozolomide (either alone or combined with cisplatin and vinblastine), or chemotherapy combined with interleukin-2 (IL-2) and/or interferon alfa. If all the melanoma lesions

completely disappear with initial treatment, you can consider a clinical trial for ongoing treatment, careful observation by your doctor, or additional therapy with interferon injections.

Finally, if your melanoma is stage IV, meaning it has spread to distant sites, the first step should be a biopsy of one of those distant sites to confirm that it is truly a metastasis. The biopsy can be a fine needle aspiration or an excisional biopsy. Other tests that may be done are a chest x-ray and/or chest CT and blood LDH level. CT scans of the abdomen and pelvis, PET scans, or MRI of the brain may be considered, as well as other imaging tests depending on your symptoms or physical exam. Treatment for stage IV melanoma is described in the Decision Tree “Treatment of melanoma with distant metastasis” starting on page 40.

The follow-up plan after initial treatment of all stages of melanoma is outlined in the Decision Tree on page 34.

NOTES

Clinical or pathological stage

Follow-up

Stage 0
In situ

- Complete history and physical exam, with emphasis on skin and lymph nodes
- Complete skin exam every year
- Consider self-exam of all skin and lymph nodes near melanoma site monthly

Stage IA
1 mm or less thick,
no ulceration

- Complete history and physical exam, every 3 to 12 months, with emphasis on skin and lymph nodes
- Complete skin exam every year
- Consider self-exam of all skin and lymph nodes near melanoma site monthly

Stage IB to III
1 mm or thicker with
or without spread to
lymph nodes

- Complete history and physical exam, with emphasis on lymph nodes and skin, every 3 to 6 months for 3 years, then every 4 to 12 months for 2 years, and then every year
- Complete skin exam every year
- Chest x-ray every 3 to 12 months (optional)
- LDH level and blood counts every 3 to 12 months (optional)
- CT scans if symptoms or physical exam changes
- Consider self-exam of all skin and lymph nodes near melanoma site monthly

Follow-up after initial treatment of melanoma

All patients with treated melanoma, regardless of stage, should have a complete skin examination every year.

Patients with stage 0 melanoma need no follow-up other than routine medical history and physical exam, yearly skin exams by a physician, and monthly self-exams of the skin.

Patients with stage IA melanoma should also have a medical history and physical exam

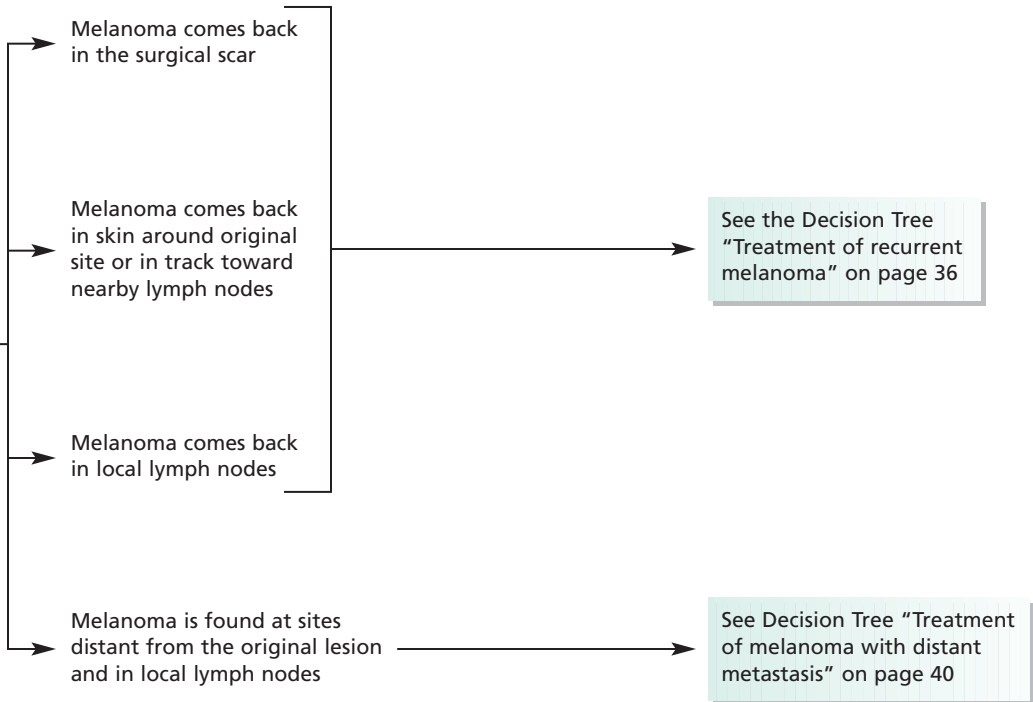
done at least yearly, with special attention paid to the skin and lymph nodes. Monthly self-exams of skin and lymph nodes should be considered.

If your melanoma was stage IB to III, thicker than 1 mm, and had or had not spread to your lymph nodes, a complete history and physical exam should be done every 3 to 6 months for 3 years, then every 4 to 12 months for 2 years, and then yearly. Chest x-rays and blood tests every 3 to 12 months are optional.

Follow-up after initial treatment of melanoma

Recurrence

(biopsy should be done if possible)



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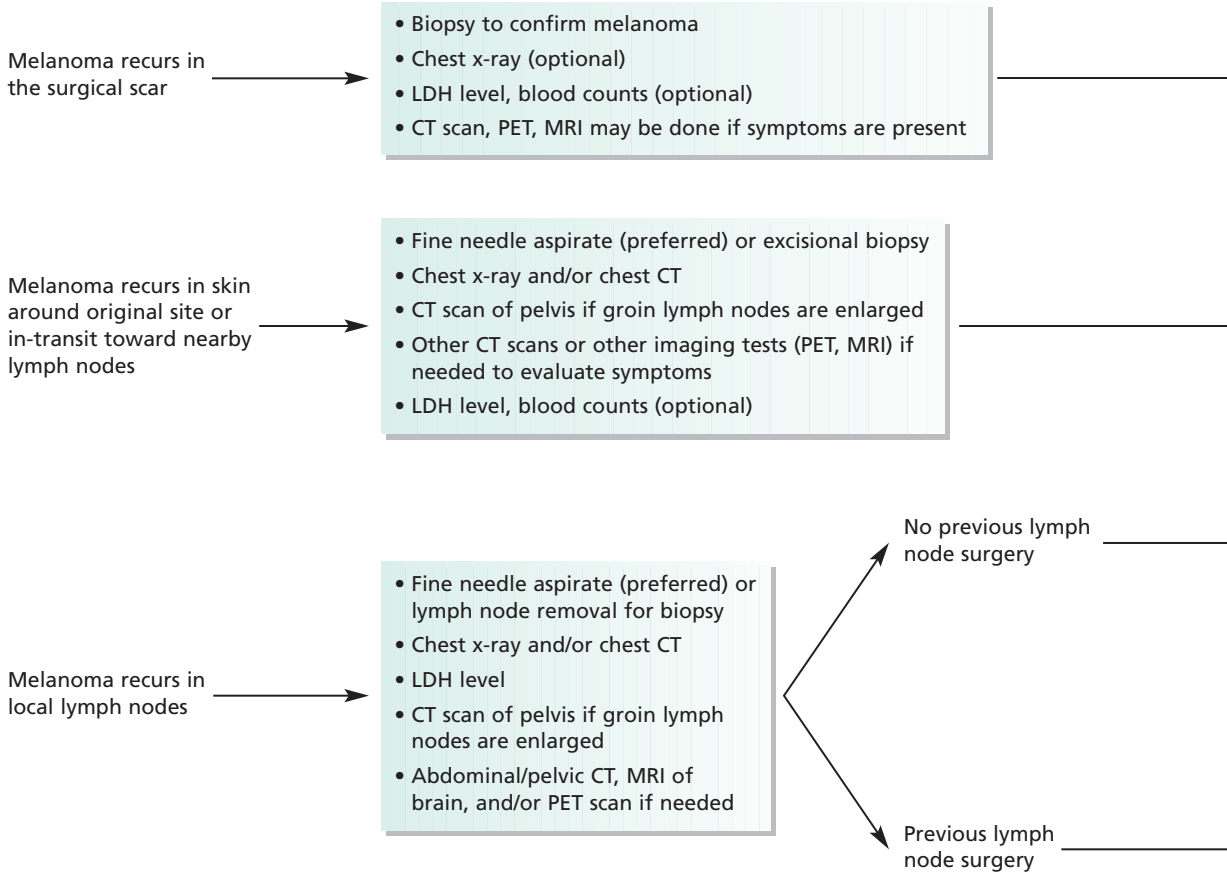
CT scans may be done if your symptoms or physical exam results change. You may also want to consider examining the skin and lymph nodes near the melanoma site monthly.

Any suspicious areas should be biopsied to check for recurrent melanoma. If the melanoma comes back in the scar or nearby

skin or lymph nodes, it should be evaluated as described in the Decision Tree "Treatment of recurrent melanoma" which starts on page 36. If it comes back in distant sites, its evaluation is described in the "Treatment of melanoma with distant metastasis" Decision Tree beginning on page 40.

Type of recurrence

Work-up



Treatment of recurrent melanoma

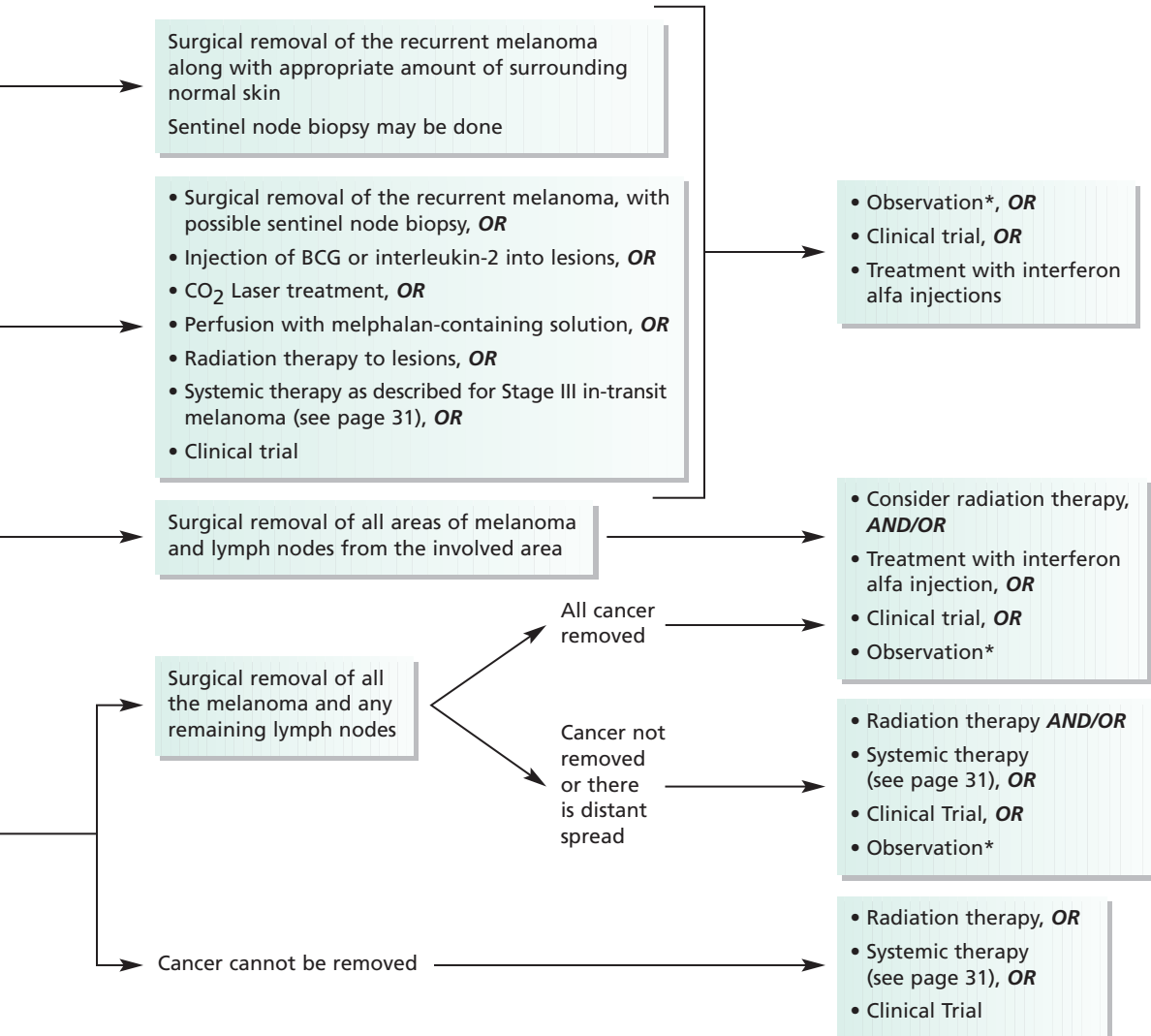
The work-up and treatment of recurrent melanoma is based on whether the melanoma has come back at the site of the original excision, near the original skin site, or in the lymph nodes. In all situations a biopsy should be done to make sure recurrent melanoma is

present. Additional imaging tests and blood tests depend on the site of recurrence, associated symptoms, and the physical exam.

If the melanoma recurs in the surgical scar, a chest x-ray, blood counts, and a test for blood lactate dehydrogenase (LDH) levels may be done along with CT scan, PET scan, or brain

Treatment of recurrent melanoma

Treatment of recurrence



* *Observation means close follow-up with no treatment*

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MRI, as needed to evaluate your symptoms. The melanoma should be surgically removed along with adequate surrounding normal skin. If the nearby lymph nodes have not been biopsied, a sentinel node biopsy may be recommended, based on the thickness of the recurrent melanoma.

The risk of spread to distant areas is higher if one or several nodules are present around the original site of the cancer or between it and the nearby lymph nodes (in-transit). Therefore, a chest x-ray, CT scan, PET scan, or brain MRI could be considered depending on your symptoms and physical exam, or for staging. Tests for blood LDH levels and blood counts are optional. If possible, all the in-transit metastases should be removed and a sentinel node biopsy should be considered at the same

time. If this is not possible, then one treatment option is to inject Bacille Calmette-Guerin (BCG) vaccine or interleukin-2 (IL-2) directly into the lesions. The lesions also might be destroyed with laser therapy (discussed on page 17).

Another possible treatment is to perfuse or infuse the area, if it is a limb, with a heated melphalan solution (discussed on page 16). Other possible treatments are radiation therapy to the area or systemic therapy, such as high dose interleukin-2 (IL-2) therapy or chemotherapy with dacarbazine (DTIC) or temozolomide (either alone or in combination with cisplatin and vinblastine), or chemotherapy in combination with interleukin-2 (IL-2) and/or interferon alfa. Because it is not certain which treatment is best, you might

NOTES

Treatment of recurrent melanoma (continued)

consider entering a clinical trial. After any one of these initial treatments, additional therapy may be recommended either in a clinical trial or with interferon injection.

When melanoma comes back in lymph nodes, a chest x-ray and/or a chest CT should be done. A blood test for LDH levels should also be done. A pelvic CT scan is recommended if the lymph nodes in the groin are enlarged. Other imaging tests may be considered depending on your symptoms. These include a CT scan of the abdomen and pelvis, an MRI of the brain, and/or a PET scan. If the lymph nodes had not been removed before, then as many as possible should be surgically removed along with any other melanoma in the area, if possible. If some lymph nodes were

removed, then all remaining lymph nodes should be removed.

Additional therapy is often recommended even if surgery removes all the melanoma. Options include radiation therapy to the node area and/or interferon alfa injections. Participation in a clinical trial or observation are other options.

If the melanoma cannot be removed completely, then radiation to destroy the remaining tumor cells and/or additional systemic treatment is recommended. A clinical trial or observation are other options.

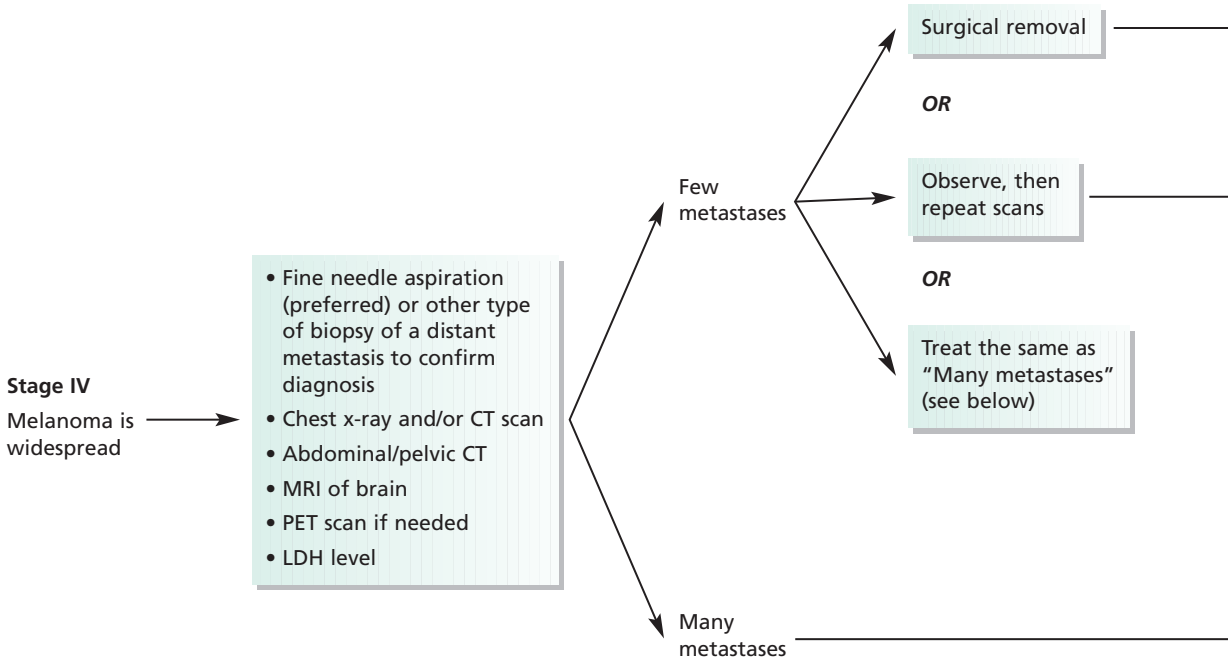
If the lymph nodes cannot be removed by surgery, then systemic therapy or radiation to relieve symptoms may be considered. Participation in a clinical trial is another option.

NOTES

Stage

Work-up

Treatment

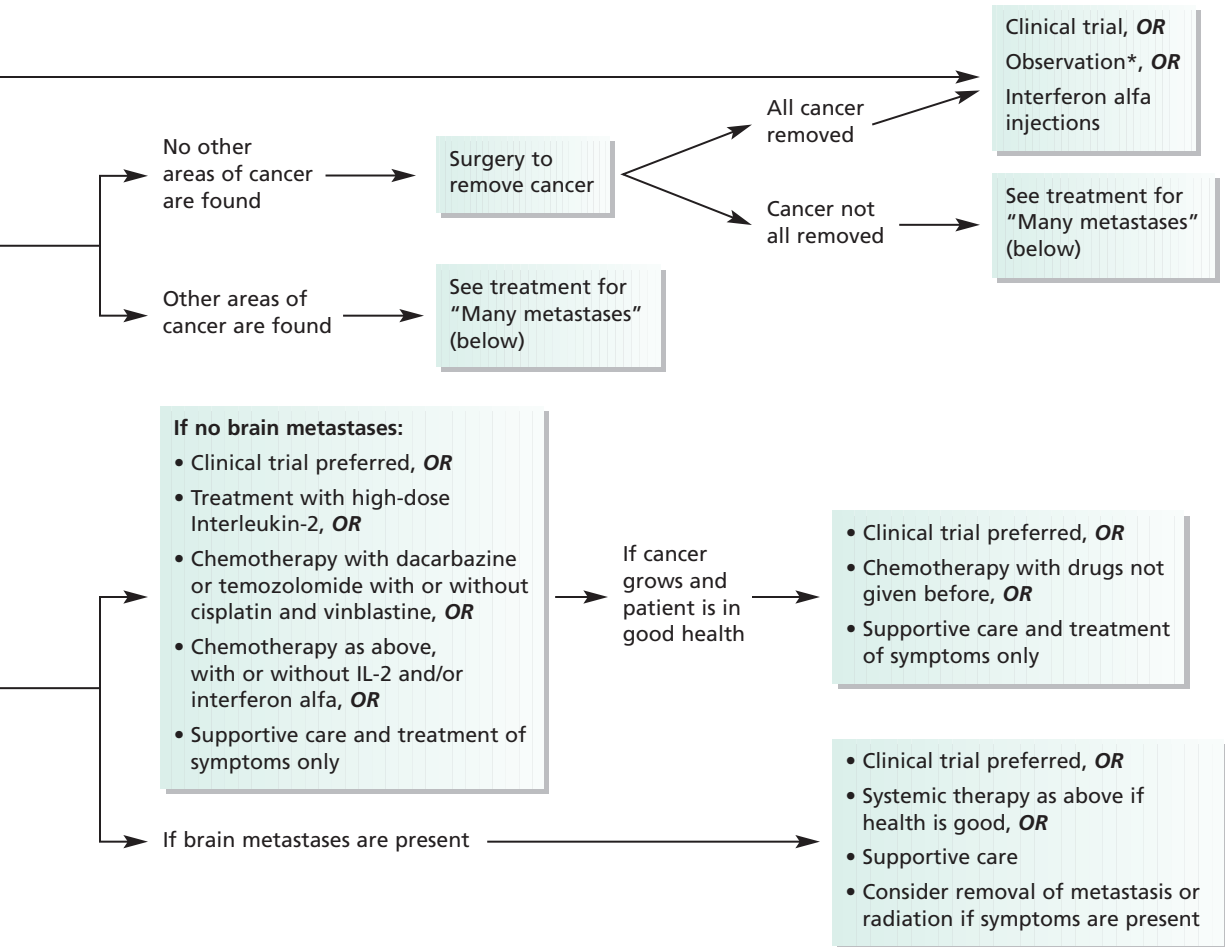


Treatment of melanoma with distant metastasis

Melanoma that has come back or is initially diagnosed in distant sites requires a biopsy to confirm the diagnosis. You should have a chest x-ray and/or a CT scan of your chest. Other imaging tests may be recommended depending on symptoms and physical exam, including a CT scan of the abdomen and pelvis, MRI of your brain, or a PET scan. A blood test of lactate dehydrogenase (LDH) levels should also be done.

If there are only a small number of metastases, several options may be considered. Surgery may be an option if the melanoma has not metastasized to other areas. Or, you can wait to see if any new metastases develop. If there are no new metastases and the tumor is not spreading quickly, surgery to remove the metastases can be considered. If there is no further evidence of cancer after surgery, options include participation in a clinical trial, or observation, or interferon injections. If the metastases cannot be removed completely or if new ones develop

Treatment of melanoma with distant metastasis



* *Observation means close follow-up with no treatment*

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during the waiting period, then the treatment will be as if there were many metastases.

If many areas of metastases are seen on imaging studies, surgery is usually not an

option. If the cancer has not spread to your brain, and you are in otherwise good health you may consider entering a clinical trial. Other options include systemic treatment

such as high-dose interleukin therapy, or chemotherapy with dacarbazine (DTIC) or temozolomide (either alone or combined with cisplatin and vinblastine), or chemotherapy in combination with interleukin-2 (IL-2) and/or interferon alfa. If the cancer grows during one of these treatments and your

health is fair to good, another one of these treatments may be offered. Another option is supportive care with treatment of symptoms or participation in a clinical trial.

If the MRI shows brain metastases, you may be offered the following options: a clinical trial; systemic treatment such as high dose

NOTES

Treatment of melanoma with distant metastasis (continued)

interleukin-2 therapy, chemotherapy with dacarbazine (DTIC) or temozolomide (either alone in combination with cisplatin and vinblastine); or chemotherapy in combination with interleukin-2 (IL-2) and/or interferon

alfa. Supportive care is another option. It may include surgery or radiation therapy to control the symptoms related to the metastases (for example, gastrointestinal bleeding, ulceration of metastases, or swollen lymph nodes).

NOTES

Current Cancer Treatment Guidelines for Patients

Advanced Cancer and Palliative Care Treatment Guidelines for Patients
(English and Spanish)

Bladder Cancer Treatment Guidelines for Patients (English and Spanish)

Breast Cancer Treatment Guidelines for Patients (English and Spanish)

Cancer Pain Treatment Guidelines for Patients (English and Spanish)

Cancer-Related Fatigue and Anemia Treatment Guidelines for Patients
(English and Spanish)

Colon and Rectal Cancer Treatment Guidelines for Patients (English and Spanish)

Distress Treatment Guidelines for Patients (English and Spanish)

Fever and Neutropenia Treatment Guidelines for Patients with Cancer
(English and Spanish)

Lung Cancer Treatment Guidelines for Patients (English and Spanish)

Melanoma Cancer Treatment Guidelines for Patients (English and Spanish)

Nausea and Vomiting Treatment Guidelines for Patients with Cancer
(English and Spanish)

Non-Hodgkin's Lymphoma Treatment Guidelines for Patients (English and Spanish)

Ovarian Cancer Treatment Guidelines for Patients (English and Spanish)

Prostate Cancer Treatment Guidelines for Patients (English and Spanish)

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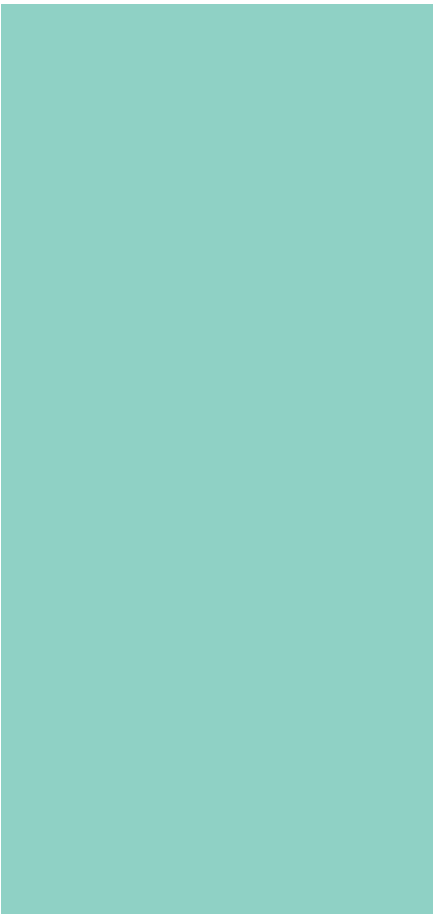
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