Melanoma Treatment Guidelines

There are different types of treatment for patients with melanoma.

Different types of treatment are available for patients with melanoma. Some treatments are standard (the currently used treatment), and some are being tested in clinical trials. A treatment clinical trial is a research study meant to help improve current treatments or obtain information on new treatments for patients with cancer. When clinical trials show that a new treatment is better than the standard treatment, the new treatment may become the standard treatment. Patients may want to think about taking part in a clinical trial. Some clinical trials are open only to patients who have not started treatment.

The following types of treatment are used:

Surgery

Surgery to remove the tumor is the primary treatment of all stages of melanoma. A wide local excision is used to remove the melanoma and some of the normal tissue around it. Skin grafting (taking skin from another part of the body to replace the skin that is removed) may be done to cover the wound caused by surgery.

Sometimes, it is important to know whether cancer has spread to the lymph nodes. Lymph node mapping and sentinel lymph node biopsy are done to check for cancer in the sentinel lymph node (the first lymph node in a group of lymph nodes to receive lymphatic drainage from the primary tumor). It is the first lymph node the cancer is likely to spread to from the primary tumor. A radioactive substance and/or blue dye is injected near the tumor. The substance or dye flows through the lymph ducts to the lymph nodes.

The first lymph node to receive the substance or dye is removed. A pathologist views the tissue under a microscope to look for cancer cells. If cancer cells are found, more lymph nodes will be removed, and tissue samples will be checked for signs of cancer. This is called a lymphadenectomy. Sometimes, a sentinel lymph node is found in more than one group of nodes.

After the doctor removes all the melanoma that can be seen at the time of the surgery, some patients may be given chemotherapy after surgery to kill any cancer cells that are left. Chemotherapy given after the surgery, to lower the risk that the cancer will come back, is called adjuvant therapy.

Surgery to remove cancer that has spread to the lymph nodes, lung, gastrointestinal (GI) tract, bone, or brain may be done to improve the patient's quality of life by controlling symptoms.

Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the cerebrospinal fluid, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy).

One type of regional chemotherapy is hyperthermic isolated limb perfusion. With this method, anticancer drugs go directly to the arm or leg the cancer is in. The flow of blood to and from the limb is temporarily stopped with a tourniquet. A warm solution with the anticancer drug is put directly into the blood of the limb. This gives a high dose of drugs to the area where the cancer is.

The way the chemotherapy is given depends on the type and stage of the cancer being treated.

Radiation therapy

Radiation therapy is a cancer treatment that uses high-energy X-rays or other types of radiation to kill cancer cells or keep them from growing. External radiation therapy uses a machine outside the body to send radiation toward the area of the body with cancer. External radiation therapy is used to treat melanoma and may also be used as palliative therapy to relieve symptoms and improve quality of life.

Immunotherapy

Immunotherapy is a treatment that uses the patient's immune system to fight cancer. Substances made by the body or made in a laboratory are used to boost, direct, or restore the body's natural defenses against cancer.

The following types of immunotherapy are being used in the treatment of melanoma:

- **Immune checkpoint inhibitor therapy:** Immune checkpoint inhibitors block proteins called checkpoints that are made by some types of immune system cells, such as T cells, and some cancer cells. These checkpoints help keep immune responses from being too strong and sometimes can keep T cells from killing cancer cells. When these checkpoints are blocked, T cells can kill cancer cells better. They are used to treat some patients with advanced melanoma or tumors that cannot be removed by surgery.

  There are two types of immune checkpoint inhibitor therapy:

  - **CTLA-4 inhibitor therapy:** CTLA-4 is a protein on the surface of T cells that helps keep the body's immune responses in check. When CTLA-4 attaches to another protein called B7 on a cancer cell, it stops the T cell from killing the cancer cell. CTLA-4 inhibitors attach to CTLA-4 and allow the T cells to kill cancer cells. Ipilimumab is a type of CTLA-4 inhibitor.

  - **PD-1 and PD-L1 inhibitor therapy:** PD-1 is a protein on the surface of T cells that helps keep the body's immune responses in check. PD-L1 is a protein found in some types of cancer cells. When PD-1 attaches to PD-L1, it stops the T cell from killing the cancer cell. PD-1 and PD-L1 inhibitors keep PD-1 and PD-L1 proteins from attaching to each other. This allows the T cells to kill cancer cells. Pembrolizumab and nivolumab are types of PD-1 inhibitors. Atezolizumab is a PD-L1 inhibitor that is being studied in combination with cobimetinib and vemurafenib.

- **Interleukin-2 (IL-2):** IL-2 boosts the growth and activity of many immune cells, especially lymphocytes (a type of white blood cell). Lymphocytes can attack and kill cancer cells.

- **Tumor necrosis factor (TNF) therapy:** TNF is a protein made by white blood cells in response to an antigen or infection. TNF is made in the laboratory and used as a treatment to kill cancer cells. It is being studied in the treatment of melanoma.

Targeted therapy

Targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells. The following types of targeted therapy are used or being studied in the treatment of melanoma:

- **Signal transduction inhibitor therapy:** Signal transduction inhibitors block signals that are passed from one molecule to another inside a cell. Blocking these signals may kill cancer cells. They are used to treat some patients with advanced melanoma or tumors that cannot be removed by surgery. Signal transduction inhibitors include:

  - BRAF inhibitors (dabrafenib, vemurafenib, encorafenib) that block the activity of proteins made by mutant *BRAF* genes; and

  - MEK inhibitors (trametinib, cobimetinib, binimetinib) that block proteins called MEK1 and MEK2 which affect the growth and survival of cancer cells.

Combinations of BRAF inhibitors and MEK inhibitors used to treat melanoma include:

- Dabrafenib plus trametinib.
- Vemurafenib plus cobimetinib.
- Encorafenib plus binimetinib.

- **Oncolytic virus therapy:** A type of targeted therapy that is used in the treatment of melanoma. Oncolytic virus therapy uses a virus that infects and breaks down cancer cells but not normal cells. Radiation therapy or chemotherapy may be given after oncolytic virus therapy to kill more cancer cells. Talimogene laherparepvec is a type of oncolytic virus therapy made with a form of the herpesvirus that has been changed in the laboratory. It is injected directly into tumors in the skin and lymph nodes.
- **Angiogenesis inhibitors:** A type of targeted therapy that is being studied in the treatment of melanoma. Angiogenesis inhibitors block the growth of new blood vessels. In cancer treatment, they may be given to prevent the growth of new blood vessels that tumors need to grow.

For patients with melanoma who are at high risk of the cancer coming back after it has been treated, there is a growing number of adjuvant therapy options which may be given to lower the risk. Adjuvant therapy may include immune checkpoint inhibitors and combinations of signal transduction inhibitors.

New targeted therapies and combinations of therapies are being studied in the treatment of melanoma.

New types of treatment are being tested in clinical trials.

This summary section describes treatments that are being studied in clinical trials. It may not mention every new treatment being studied. Information about clinical trials is available from the NCI website.

Vaccine therapy

Vaccine therapy is a cancer treatment that uses a substance or group of substances to stimulate the immune system to find the tumor and kill it. Vaccine therapy is being studied in the treatment of stage III melanoma that can be removed by surgery.

Treatment for melanoma may cause side effects.

Patients may want to think about taking part in a clinical trial.

For some patients, taking part in a clinical trial may be the best treatment choice. Clinical trials are part of the cancer research process. Clinical trials are done to find out if new cancer treatments are safe and effective or better than the standard treatment.

Many of today's standard treatments for cancer are based on earlier clinical trials. Patients who take part in a clinical trial may receive the standard treatment or be among the first to receive a new treatment.

Patients who take part in clinical trials also help improve the way cancer will be treated in the future. Even when clinical trials do not lead to effective new treatments, they often answer important questions and help move research forward.

Patients can enter clinical trials before, during, or after starting their cancer treatment.

Some clinical trials only include patients who have not yet received treatment. Other trials test treatments for patients whose cancer has not gotten better. There are also clinical trials that test new ways to stop cancer from recurring (coming back) or reduce the side effects of cancer treatment.

Clinical trials are taking place in many parts of the country. Information about clinical trials supported by NCI can be found on NCI's clinical trials search webpage. Clinical trials supported by other organizations can be found on the ClinicalTrials.gov website.

Follow-up tests may be needed.

As you go through treatment, you will have follow-up tests or check-ups. Some tests that were done to diagnose or stage the cancer may be repeated to see how well the treatment is working. Decisions about whether to continue, change, or stop treatment may be based on the results of these tests.

Some of the tests will continue to be done from time to time after treatment has ended. The results of these tests can show if your condition has changed or if the cancer has recurred (come back).

Reference

National Cancer Institute. (2023, June 30). *Melanoma treatment (PDQ®)–patient version*. https://www.cancer.gov/types/skin/patient/melanoma-treatment-pdq#_140