

Skin Cancer

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Every year, nearly 69,000 people in the United States are diagnosed with malignant melanoma, the most serious form of skin cancer. Like many cancers, melanoma is more difficult to treat once it has spread beyond the skin to other parts of the body. Cancer is considered locally advanced when it spreads from its original site to lymph nodes and nearby tissues. Metastatic cancer also spreads to lymph nodes and nearby tissues but may spread to distant organs as well. So researchers continue to search for effective ways to treat metastatic melanoma.

Melanoma

INTERFERON TREATMENT FOR MELANOMA

People with an ulcerated melanoma may benefit from interferon.

Melanomas are often described as being ulcerated or nonulcerated. For people with an ulcerated melanoma, the layer of skin over the tumor is broken. Those with ulcerated melanomas have a less favorable prognosis (expected outcome) than do people with non-ulcerated melanomas. Ulceration leads to a higher risk of the tumor spreading.

Researchers analyzed the results of two large clinical trials in which people with melanoma were treated with a medication called interferon (Intron A, PegIntron). They found that in patients who had ulcerated tumors, interferon significantly reduced the chances of the tumor spreading to other parts of the body. It also helped patients live longer with their cancer. However, interferon appeared to offer no such benefit to those who had non-ulcerated tumors.

Knowing whether a melanoma is ulcerated or not may help doctors select patients who might best respond to interferon, which can prevent the regrowth of tumors. People with non-ulcerated tumors, who are not likely to benefit from interferon, may be able to avoid unnecessary treatment and its side effects.

Further clinical trials on interferon treatment in select patients with ulcerated melanomas will be conducted.

SENTINEL LYMPH NODES AND MELANOMA

Some people with melanoma may be able to avoid extensive surgery and the side effects that can occur when doctors remove many lymph nodes.

When treating people with melanoma, doctors often look at sentinel lymph nodes to see whether the cancer is growing. Lymph nodes are a linked system of small bean-shaped

structures throughout the body that help filter out and destroy bacteria and other harmful substances. When cancer spreads to the lymph nodes, it can travel to other parts of the body. The sentinel lymph node is the first lymph node near the tumor to which cancer is likely to spread.

Sometimes, people who have melanoma and just a few cancer cells in the sentinel lymph node have



all the lymph nodes near their tumor surgically removed. However, according to a recent clinical trial, this surgery may be unnecessary.

Nearly 600 people who had a few cancer cells in their sentinel lymph nodes were treated for melanoma. All of the lymph nodes surrounding their tumors were removed.

But in the future, this extensive surgery may be avoided. Researchers found that these patients are not likely to have a return of their cancer. Ten years after treatment, tumors had returned in very few of the patients, 94 percent of whom were still alive. Their risk is the same as for patients who have no tumor cells in their lymph nodes.

Researchers plan to continue looking closely at more such patients. If the results remain positive, people who have melanoma and a few cancer cells in their sentinel lymph nodes may avoid removal of all their nearby lymph nodes in the future.

RADIATION THERAPY FOR ADVANCED MELANOMA

Radiation treatment after surgery may prevent a return of cancer cells to the lymph nodes.

People who have melanoma that has spread to the lymph nodes may be treated with surgery to remove some of these nodes. However, sometimes cancer returns to the area of the lymph nodes, which is called a regional recurrence. Researchers may have found a way to stop this from happening.

After surgery to remove some of the lymph nodes in people who have melanoma, radiation treatment appears to lower the chances that cancer will return to this part of the body.

Nearly 250 people with advanced melanoma who were at high risk for regional recurrence took part in a clinical trial. More than three years after treatment, of those people who had received radiation treatment, fewer had a regional recurrence than those who had not received radiation. However, there was no real difference in survival between those who received radiation and those who did not. Still, the results of this clinical trial provide strong evidence that radiation can help reduce the return of cancer to the same region of the body and prevent the complications associated with recurrence.

VACCINE FOR METASTATIC MELANOMA

A new vaccine-drug combination shows promise for people with skin cancer.

Researchers are very optimistic about a new treatment that combines a specialized vaccine and interleukin-2 (IL-2; Proleukin), a standard medication used for metastatic melanoma. According to the early results of a clinical trial, this vaccine is one of the first to show a benefit for people with cancer.



In a study of nearly 200 people with metastatic melanoma, those who received combination treatment with the vaccine survived almost five months longer than those who received only IL-2. The vaccine and IL-2 also caused the tumor to stop growing or to shrink

in more than twice as many patients who received the combination compared with those who received only IL-2.

This vaccine appears to have few side effects. Among them are an irregular heartbeat and swelling and redness at the injection site. Doctors are continuing to watch these people to find out how long the vaccine can help slow the growth of their tumors.

IPILIMUMAB FOR METASTATIC MELANOMA

The new targeted treatment ipilimumab appears to help people with skin cancer live longer.

Early results of three clinical trials of a new targeted treatment called ipilimumab are very encouraging. Researchers say that this medication is helping people with metastatic skin cancer live longer than ever before. Between 30 percent and 42 percent of nearly 500 patients treated with ipilimumab were alive two years after treatment. Based on past experience, doctors say this is far better than expected.

Ipilimumab belongs to a class of drugs called monoclonal antibodies. This type of targeted treatment is designed to zero in on specific molecules and cell mechanisms thought to be important for the survival and growth of cancer cells. This approach helps to spare healthy tissues and causes less severe side effects.

On the Horizon

PLX4032 AND IMATINIB FOR MELANOMA

Drugs that target changes in certain genes may be the wave of the future for skin cancer treatment.

Researchers believe that cancer stems largely from abnormal mutations (changes) in a person's genes. Genes are chemical instructions or recipes, found in every cell, that tell the cell how to make proteins that perform different tasks. When something goes wrong in one or more genes, the proteins they make can malfunction. Typically, cancer occurs when a number of genes are abnormal.

Recently, researchers have successfully treated some people with breast and colon cancers by targeting abnormal genes.

Early results of two small clinical trials have shown similar success in treating people with skin cancer.

A small group of people with metastatic melanoma have received a new medication called PLX4032. Sixteen of these patients had a mutated BRAF gene. BRAF is a gene that makes a protein called B-RAF, which is involved in cell growth. In many types of cancer, including melanoma, this gene may be mutated. This mutation causes a change in the B-RAF protein that can promote the growth of cancer and play a role in its spread.

The tumor shrank by at least 50 percent in more than half of these patients after they were treated with PLX4032.

Another small group of people with advanced melanoma received the drug imatinib (Gleevec). Introduced in 2001, this drug revolutionized the treatment of chronic myelogenous leukemia, a blood cancer. In this study, imatinib seemed to shrink tumors in about one-third of melanoma patients who had a mutated KIT gene. When the KIT gene is mutated, it signals cells to grow out of control, which can lead to cancer.

Although these are very early results found in small groups of people, researchers believe that such targeted treatments may be effective for people with melanoma. They are calling these encouraging results a major step forward in the treatment of people with melanoma.

Please note: Although the treatments discussed in this chapter are showing promise, most are still in clinical trials—some in earlier phases of research—and may not be available yet to the general public. Your doctor can help guide you as to which new medications could be right for you and whether you are eligible to take part in the clinical trials of these new treatments.