

HEALTH

What Is Immunotherapy? The Basics on These Cancer Treatments

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Some of the most promising advances in cancer research in recent years involve treatments known as immunotherapy. These advances are spurring billions of dollars in investment by drug companies, and are leading to hundreds of clinical trials. Here are answers to some basic questions about this complex and rapidly evolving field.

What is immunotherapy?

Immunotherapy refers to any treatment that uses the immune system to fight diseases, including cancer. Unlike chemotherapy, which kills cancer cells, immunotherapy acts on the cells of the immune system, to help them attack the cancer.

What are the types of immunotherapy?

Drugs called checkpoint inhibitors are the most widely used form of immunotherapy for cancer. They block a mechanism that cancer cells use to shut down the immune system. This frees killer T-cells — a critically important part of the immune system — to attack the tumor. Four checkpoint inhibitors have been

approved by the Food and Drug Administration and are on the market. They are given intravenously.

Another form of immunotherapy, called cell therapy, involves removing immune cells from the patient, altering them genetically to help them fight cancer, then multiplying them in the laboratory and dripping them, like a transfusion, back into the patient. This type of treatment is manufactured individually for each patient, and is still experimental.

Bispecific antibodies are an alternative to cell therapy, one that does not require individualizing treatment for each patient. These antibodies are proteins that can attach to both a cancer cell and a T-cell, that way bringing them close together so the T-cell can attack the cancer. One such drug, called Blnicyto, has been approved to treat a rare type of leukemia.

Vaccines, another form of immunotherapy, have had considerably less success than the others. Unlike childhood vaccines, which are aimed at preventing diseases like measles and mumps, cancer vaccines are aimed at treating the disease once the person has it. The idea is to prompt the immune system to attack the cancer by presenting it with some piece of the cancer.

The only vaccine approved specifically to treat cancer in the United States is Provenge, for prostate cancer. Another vaccine, BCG, which was developed to prevent tuberculosis, has long been used to treat bladder cancer. As a weakened TB bacterium, BCG appears to provoke a general immune system reaction that then works against the cancer. Researchers hope that other vaccines may yet be made to work by combining them with checkpoint inhibitors.

Which types of cancer are treated with immunotherapy?

Checkpoint inhibitors have been approved to treat advanced melanoma, Hodgkin's lymphoma and cancers of the lung, kidney, bladder and head and neck. The drugs are being tested in many other types of cancer.

So far, cell therapy has been used mostly for blood cancers like leukemia and lymphoma.

Which cancer drugs are checkpoint inhibitors?

The four on the market are: Yervoy (ipilimumab) and Opdivo (nivolumab), made by Bristol-Myers Squibb; Keytruda (pembrolizumab), by Merck; and Tecentriq (atezolizumab), by Genentech.

How well does immunotherapy work?

Though immunotherapy has been stunningly successful in some cases, it still works in only a minority of patients. Generally, 20 percent to 40 percent of patients are helped by checkpoint inhibitors — although the rate can be higher among those with melanoma. Some patients with advanced disease have had remissions that have lasted for years. In some cases, combining two checkpoint inhibitors increases the effectiveness. But for some people the drugs do not work at all, or they help just temporarily.

Cell therapy can produce complete remissions in 25 percent to 90 percent of patients with lymphoma or leukemia, depending on the type of cancer. In some cases the remissions can last for years, but in others relapses occur within a year.

What are the side effects?

Checkpoint inhibitors can cause severe problems that are, essentially, autoimmune illnesses, in which the immune system attacks healthy tissue as well as cancer. One result is inflammation. In the lungs it can cause breathing trouble; in the intestine it can cause diarrhea. Joint and muscle pain, and rheumatoid arthritis can also occur, and the immune system can also attack vital glands like the thyroid and pituitary. In rare cases, the immune system can attack the heart, especially when patients take two checkpoint inhibitors at the same time. These reactions are dangerous, but can often be controlled with steroid medicines like prednisone and

9 other immune-suppressing drugs.

Cell therapy can also lead to severe and potentially fatal reactions resulting from the overstimulation of the immune system. The reactions can usually be controlled, but patients may need to be treated in an intensive care unit.

What does immunotherapy cost? Does insurance cover it?

Checkpoint inhibitors can cost \$150,000 a year. Many insurers will pay if the drug has been approved for the type of cancer the patient has. But sometimes there are high co-payments. Patients in clinical trials may get the drugs free.

Manufacturers have not said yet how much they will charge for cell therapies, assuming they win approval and reach the market. But experts expect the price to be as high as a few hundred thousand dollars.

Where can I get immunotherapy?

Any oncologist can prescribe the checkpoint inhibitors that are on the market. Patients with cancers for which the drugs have not been approved may find insurers reluctant to pay, but may be able to get the drugs for free by volunteering for clinical trials.

Cell therapies are available only through clinical trials now. Most of the study sites are major medical centers.

How can I find out about clinical trials in immunotherapy?

Information is available on the Cancer Research Institute website, or by calling 1-855-216-0127 (Monday through Friday, 8:30 a.m. to 6 p.m. E.T.). Another source is ClinicalTrials.gov.

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