

Immunotherapy in Oncology – An Imminent Cancer Cure

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ABSTRACT

Immunotherapy is an emerging oncological treatment that helps the immune system to fight cancer. Immunotherapy works by helping the immune system recognise and attack cancer cells. It is also known as biological therapy. Although the immune system can prevent the cancer growth, cancer cells have various mechanisms to avoid their destruction by the immune system. Immunotherapy helps the immune system to function better against the cancer.

Various types of immunotherapies are used to treat cancers. These include immune checkpoint inhibitors, CAR T-cell therapy, therapeutic vaccines, oncolytic viral therapy, gene therapy, monoclonal antibodies and immunomodulatory agents.

Immunotherapy has been approved for treatment of many cancers. However, it is not used as widely as other conventional therapies like surgery, chemotherapy or radiation therapy. Much research and clinical trials are required before widely using immunotherapy in clinics.

Immunotherapy is an emerging oncological treatment that helps the immune system to fight cancer. The immune system is made up of white blood cells and organs of the lymphatic system. It helps the body fight infections and other diseases. Immunotherapy works by helping the immune system recognise and attack cancer cells. Immunotherapy is also known as biological therapy.¹

As part of its normal role, the immune system detects and destroys abnormal cells and restrains the growth of cancer. Immune cells may be found in and around tumors. These cells are called tumor-infiltrating lymphocytes or TILs.² The presence of tumor-infiltrating lymphocytes is a sign of the immune system responding to the tumor. Patients with presence of tumor-infiltrating lymphocytes in and around the tumor have a better prognosis compared to those whose tumors don't contain them.²

Although the immune system can prevent the cancer growth, cancer cells have various mechanisms to avoid their destruction by the immune system. The cancer cells may undergo genetic transformations that makes them less visible to the immune system, may have proteins on their surface that send turn off signals to immune cells, may change the normal cells surrounding the tumor such that they interfere with the immune system's response to cancer cells.³ Immunotherapy helps the immune system to function better against the cancer.

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Immune checkpoint inhibitors are agents that block the immune checkpoints. Immune checkpoints are a present on normal cells of the body and protect them from the immune responses. Cancer cells may also start expressing these immune checkpoints. By blocking these checkpoints, immune checkpoint inhibitory agents allow the immune cells to kill the cancer cells. Currently approved checkpoint inhibitors target the molecules CTLA4, PD-1, AND PD-L1. They comprise of drugs like pembrolizumab, nivolumab, ipilimumab, durvalumab, and atezolizumab.⁴

Chimeric antigen receptors (CAR) T-cell therapy is the use of genetically engineered T-cells for reducing the tumor bulk. Chimeric antigen receptors are the receptor proteins that have been genetically engineered to provides the new ability to T-cells to target specific cancer cell proteins. The receptors are chimeric as they combine both antigen-binding and T-cell activating functions into a single receptor.⁵ The first two FDA-approved CAR-T therapies are tisagenlecleucel and axicabtagene ciloleucel approved to treat relapsed/refractory diffuse large B-cell lymphoma (DLBCL).⁶

Therapeutic cancer vaccines work against cancer by boosting the body's immune system response to cancer cells. These vaccines are different from the ones that help preventing the disease. Sipuleucel-T: a dendritic cell based vaccine for prostate cancer and Bacillus Calmette-Guerin: a live attenuated vaccine used for bladder invasive cancer are being widely used as therapeutic cancer vaccines.⁷

Oncolytic virus therapy is the use of oncolytic viruses to kill cancer cells. Therapeutic efficacy of oncolytic virus therapy is achieved by a combination of selective tumor cell killing and establishment of anti-tumor immunity. Immune stimulation is caused by release of cell debris and viral antigens in the tumor microenvironment. In 2015, in a milestone for the field, talimogene laherparepvec became the first oncolytic virus to gain FDA approval.⁸

Gene therapy in oncology is the administration of normal functioning genes to replace the missing or non-functional genes, insert genes that inhibit the oncogenes (mutated genes that cause cancer), insert genes into cancer cells that trigger the immune system to kill the cancer cells as foreign bodies, insert genes into cancer cells to make them more susceptible to chemotherapy, radiation therapy or hormonal therapies, insert apoptotic genes that enter into the cancer cells kill them, and insert genes that protect normal cells in the body from side effects of cancer therapy so that high doses of chemotherapy or radiation therapy can be used.⁹

Monoclonal antibodies (therapeutic antibodies) are immune system proteins created in laboratories which are designed to bind to specific targets on cancer cells. Some monoclonal antibodies mark cancer cells such that they better recognised and killed by the immune system. Such monoclonal antibodies are a type of immunotherapy.¹⁰

Immune system modulators are the agents which enhance the body's immune response against cancer. These agents activate the T-cells and NK cells to kill cancer cells. Interferons, interleukins, thalidomide, lenalidomide, and pomalidomide are various immunomodulatory agents occasionally used in oncology.¹¹

Various adverse effects of immunotherapy are fever, chills, weakness, dizziness, nausea, vomiting, muscle or joint pains, fatigue, headache, difficulty in breathing, low blood pressure.

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