International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Immunotherapy for Cancer

Diksha Sharma

Maharishi Markendeshwar College of Nursing, Kumarhatti, Solan. H.P.
M.Sc. in Medical Surgical Nursing (Oncology).

Abstract:

Immunotherapy with another name called Biological therapy as a potential cancer treatment dates back to the 1800s. Generally defined, biotherapy is one that uses the immune system, including the cells and molecules that act as messengers between the various immune cells, works by stimulating the Immune system against the cancer. This therapy fuel the body's production of cancer-fighting cells or help healthy cells detect and attack cancer cells.

Knowledge regarding the immunology is essential when trying to understand biological therapy. Humoral (antibody-mediated or B cell) and cellular (T cell) immune system comprise the two major components of the immune system. It is believed that cell-mediated immunity provides the primary immune response in tumors responsible for tumor regression. There are two types of cellular responses: innate and adaptive immunity and both play a part in the immune response to tumors.

Keywords: Immunotherapy, Immune system, Immunity, Cancer

INTRODUCTION:

Scientific advancements for cancer treatment have grown by leaps and bounds in recent decades. Medical science has not been left out of this great leap forward and cancer research is one such field. Apart from a better understanding of the disease, we also have a host of novel cancer treatments.. Immunotherapy cancer treatment is a type of targeted therapy or biologic therapy that uses the body's natural immune system to kill cancer cells.[1]

Immunotherapy for cancer is known by other names such as immuno-oncology. Immune system involves many types of cells, organ, proteins and tissues, which further defends our body from invaders and the only Immune system keeps us healthy when we drift through the seas of pathogens. Biotherapy is a cancer treatment that engages your immune system to fight the disease. Immune cells produce cytokines, protein molecules that act on other cells. Immunotherapy introduces large amounts of these proteins into the body which stimulates the immune system to produce more disease-fighting immune cells and makes easier for the immune system to identify and target cancer cells.[2]

HOW IT WORKS:

The immune system helps the body to ward off diseases and illness, both caused by external as well as internal factors. However, the immune system cannot detect cancer cells since cancer cells lack the external markers that the immune system uses to identify hostile bodies, essentially 'hiding' from the immune system. The cancer cells can also signal the immune system to not destroy them or the immune system may be too weak to destroy cancer cells even if it can identify them. This is where immunotherapy cancer treatment steps in. The immune system should be able to destroy tumor cells and immunotherapy treatment is a way to help the body's immunity to do that.[3]

CANCER AND IMMUNOTHERAPY

Our body cells grow and divide naturally, action within the cells is further controlled by different factors along with genes. Further when no more growth is needed, cells are told to stop growing. Cancer is made up of damaged cells, they may have antigens that your immune cells recognize and attack but some cancer cells have ways to avoid destructions by the immune cells. Or unfortunately, sometimes faulty or missing gene in the cancer cells when interfere with the normal instruction in a cell might cause cells to grow out of control and divide abnormally and form a lump called tumour.[4]

Cancer cells grow and behave in abnormal ways, this can make them stand out to the immune system, which can recognize and eliminate cancer cells through a process called *immunosurveillance*.

Cancer cells avoid destruction through checkpoint proteins, both cancer and immune cells may have these protein, when they attach other wont attack on the cancer cells and another way for cancer cell avoid destruction happens when the cancer cells are under attack from the immune system, during the attack the cancer cells release certain substances that call them other type of immune cells which slows down and stop the immune response.

Immunotherapy have the several ways that work to help your immune system to fight cancer cells one way is by creating a special antibodies in lab , these antibodies attached to cancer cells and kills them directly and another group of antibody blocks the checkpoint proteins and keeps them from attaching each other as result the immune cells can attack and kill the cancer cells and still other antibodies prevent the growth of cancer cells ,some of them block the signals that cause new blood vessels to grow and feed the cancer. However, Therefore, immunotherapies are designed to boost or enhance the cancer-fighting capabilities of immune cells and tip the scales in the immune system's favour.[6]

TYPES OF IMMUNOTHERPY

Immunotherapy uses our immune system to fight cancer. It works by helping the immune system recognise and attack cancer cells. Different types of immuno therapy they include are:

- **Monoclonal antibodies and tumor-agnostic treatments, such as checkpoint inhibitors**
- **Oncolytic virus therapy**
- **T-cell therapy**
- **Cancer vaccines**

1. Monoclonal antibodies and tumor-agnostic treatments, such as checkpoint inhibitors

The goal of this therapy is to help prevent hospitalizations, reduce viral loads and lessen symptom severity. This type of therapy relies on monoclonal antibodies. These are antibodies that are similar to the ones your body would naturally make in response to infection. However, monoclonal antibodies are mass-produced in a laboratory and are designed to recognize a specific component of this virus — the spike protein on its outer shell. By targeting the spike protein, these specific antibodies interfere with the virus' ability to attach and gain entry into human cells. They give the immune system a leg up until it can mount its own response.

Checkpoint inhibitors don't kill cancer cells directly but they work by helping the immune system to better find and attack the cancer cells, wherever they found in the body.

PD-1 and PD-L1 inhibitors

PD-1 is a checkpoint protein on immune cells called *T cells.* It normally acts as a type of “off switch” that helps keep the T cells from attacking other cells in the body. It does this when it attaches to PD-L1, a protein on some normal (and cancer) cells. When PD-1 binds to PD-L1, it basically tells the T cell to leave the other cell alone. Some cancer cells have large amounts of PD-L1, which helps them hide from an immune attack. Both PD-1 and PD-L1 inhibitors have been shown to be helpful in treating many different types of cancer.[5]

PD-1 inhibitors

Examples of drugs that target PD-1 include:

- Pembrolizumab (Keytruda)
- Nivolumab (Opdivo)
- Cemiplimab (Libtayo)

PD-L1 inhibitors

Examples of drugs that target PD-L1 include:

- Atezolizumab (Tecentriq)
- Avelumab (Bavencio)
- Durvalumab (Imfinzi)

Both PD-1 and PD-L1 inhibitors have been shown to be helpful in treating many different types of cancer.

CTLA-4 inhibitors

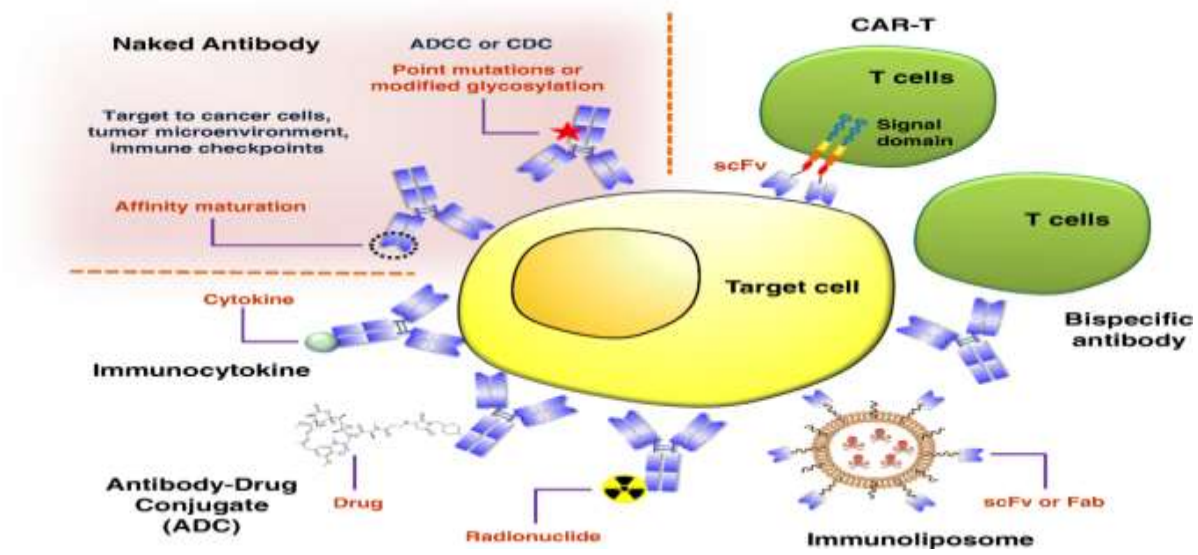
CTLA-4 is another checkpoint protein on some T cells that acts as a type of "off switch" to help keep the immune system in check.

Ipilimumab (Yervoy) is a monoclonal antibody that attaches to CTLA-4 and stops it from working. This can help boost the body's immune response against cancer cells.

LAG-3 inhibitors

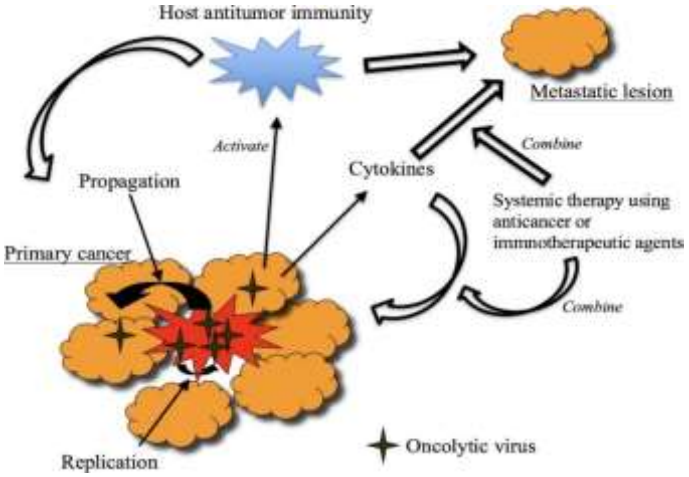
LAG-3 is a checkpoint protein on some types of immune cells that normally acts as a type of "off switch" to help keep the immune system in check.

Relatlimab is a monoclonal antibody that attaches to LAG-3 and stops it from working. This can help boost the body's immune response against cancer cells.This drug is given along with the PD-1 inhibitor nivolumab.



2. Oncolytic virus therapy:

An oncolytic virus can be described as a genetically engineered or naturally existing virus that can selectively replicate in cancer cells and then kill them without damaging the healthy cells. Oncolytic viruses have been taking the front stage in biological therapy for cancer recently. The first and most potent virus to be used in oncolytic virotherapy is human adenovirus.



In cancer treatment the patient's safety is of utmost importance and treatment, using oncolytic viruses seems to be the most promising in this aspect. Most of the oncolytic viruses chosen for cancer therapy are attenuated strains or strains that can infect and replicate in humans without causing any serious disease. It is also important that the viruses chosen must be capable of utilizing the host immune system to recognize and destroy the cancer cells.

Although oncolytic viruses are potentially powerful therapeutic agents for cancer treatment, a single type of oncolytic virus is not enough to destroy all the cancer cells due to the heterogeneity of cancer tissues and complexity of cancer cells.

Chimeric antigen receptor (CAR) T-cell therapy is a way to get immune cells called T cells (a type of white blood cell) to fight cancer by changing them in the lab so they can find and destroy cancer cells. CAR T-cell therapy is also involves altering the genes inside T cells to help them attack the cancer. This type of treatment can be very helpful in treating some types of cancer, even when other treatments are no longer working. The immune system recognizes foreign substances in the body by finding proteins called *antigens* on the surface of those cells. Immune cells called *T cells* have their own proteins called *receptors* that attach to foreign antigens and help trigger other parts of the immune system to destroy the foreign substance.

Cancer vaccines Vaccines are medicines that train the body's immune system to fight disease. There are two types of cancer vaccine. One targets the viruses that can cause cancer. This will only work if a person receives them before they have exposure to the virus. Receptors and antigens are unique to each immune cell and each virus. They fit together like a lock and key. When an immune cell finds the antigen that "fits" in its lock, it binds to it and destroys the virus.[6]

https://www.cancer.gov/about-cancer/treatment/types/immunotherapy

WHAT TYPES OF CANCER ARE TREATED

Immunotherapy has proven beneficial in the treatment of most cancer types. The various common types of cancer that can be treated with immunotherapy include lung cancer, some skin cancers, kidney cancer, bladder cancer, head and neck cancers, lymphoma. Not as widely used as radiation therapy, surgery or chemotherapy, some studies indicate that immunotherapy has shown 20-30% positive results on the patients.

ROUTE OF ADMINISTRATION:

Different forms of immunotherapy may be given in different ways. These include:

- **Intravenous (IV)**

  The immunotherapy goes directly into a vein.

- **Oral**
  The immunotherapy comes in pills or capsules that you swallow.

- **Topical**
  The immunotherapy comes in a cream that you rub onto your skin. This type of immunotherapy can be used for very early skin cancer.

- **Intravesical**
  The immunotherapy goes directly into the bladder.

https://www.cancer.gov/about-cancer/treatment/types/immunotherapy#how-does-immunotherapy-work-against-cancer

EFFICACY OF IMMUNOTHERAPEUTIC AGENTS

Cancer and the immune system has progressed rapidly now the days. The most attractive features of cancer immunotherapies is that they target malignant cells while sparing normal, healthy tissues from the damage often seen with radiation and chemotherapy that contributes to patient morbidity and mortality. Immunotherapy is effective across a wide variety of cancers. Immunotherapy along with chemotherapy or radiation produces durable responses in around 20-30% patients. In many cancer immunotherapies, such as monoclonal antibodies, cytokines, cancer vaccines, and cell-based therapies, has been demonstrated into clinical practice with higher efficacy and great responses and along with better survival rate.

HOW IT COSTS

Depending on the patient's conditions, there are numerous immunotherapy sessions taking place in a month's interval. The cost of each session is between ₹1-1.5 lakh and ranges as per clinical terms. Immunotherapy is an expensive treatment that does not agree with all the cancer patients. The drugs are patented and imported from foreign nations, and the cost itself is a huge concern for many. With its efficiency in targeted cancer cells and with few side effects, this therapy is gaining popularity among the masses.

POTENTIALITY OF IMMUNOTHERAPY:

Almost 40 percent of men and women will be diagnosed with cancer during their lifetime. Thankfully, in this day of medical advancements and innovation, cancer is no longer a certain death sentence. More than 15.5 million people lived beyond a cancer diagnosis as of Jan. 1, 2016, and that number is expected to surpass 20 million by 2026. The goal in cancer treatment now is to target care more precisely to patients through individualized health care. This is called precision medicine, and it is an especially welcome change for cancer patients who traditionally have been exposed to treatment such as chemotherapy and radiation that attacks their cancer but often damages healthy tissue in the process.[8]

Precision medicine is at the heart of immunotherapy, currently one of the hottest areas of cancer research. Immunotherapy is a new approach that harnesses the power of our immune systems to identify and control diseases such as cancer. Immunotherapy is being studied in just about every type of cancer. The number of cancers successfully treated by immunotherapy stands at 15 and growing and includes skin, lung, kidney and bladder cancers.

https://www.hopkinsmedicine.org/inhealth/about-us/immunotherapy-precision-medicine-action-policy-brief.html#:~

FUTURE PERSPECTIVE:

At present, neoadjuvant therapy is becoming an increasingly popular therapeutic strategy for resectable NSCLC. However, studies have reported that neoadjuvant chemotherapy only slightly improves recurrence rates, making it inadequate for extending patient survival. The significant survival benefits of immunotherapy in advanced NSCLC have greatly stimulated researchers' interests in applying immune checkpoint inhibitors (ICIs) for treating early-stage resectable NSCLC.

In recent years, immunotherapy has revolutionized the fixed therapy pattern for advanced NSCLC with the emergence of immune checkpoint inhibitors (ICIs). The significant increase in treatment efficacy achievable with immunotherapy based on ICIs has gradually made this approach becoming the first-line treatment choice in patients with advanced NSCLC. The higher response rates, improved survival benefits, fewer adverse events, and better tolerability offered by immunotherapy have been proven in multiple randomized clinical trials. [9]

The significant benefits of immunotherapy based on PD-1 and PD-L1 antibodies in regarding the improving long-term survival have increased scholars' interests in translating the benefits of ICIs for early-stage resectable NSCLC treatment. In trials exploring the effects of ICIs in the perioperative period, neoadjuvant immunotherapy was shown to improve the survival rates of patients with melanoma and glioma.[10]

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