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Review Article

Immunotherapy in cancer: A review

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ABSTRACT

Cancer is the most threatening disorder with increasing stuffers globally. Immune system of human body carries a set of defensive processes whenever cancer is detected by its specialized cells. While immunosurveillance, the host fight against foreign antigens. By targeting surface antigens expressed in tumor cells, monoclonal antibodies have demonstrated efficacy as cancer therapeutics. The checkpoint blockade therapy involves the use of antibodies to block pathways inhibiting the endogenous immune response to cancer. Adoptive cell transfer (ACT) is highly personalized cancer bearing host of immune cells with direct anticancer activity. We emphasize how the history of cancer immunotherapy paved the path for discoveries that are now standard of care in this review article.

1. Introduction

Cancer is the biggest cause of death and a worldwide problem. Our immune systems keep us safe from infections. Immunotherapy boosts the body's immune system's ability to recognize and destroy cancer cells that can be located in tumors. Tumor infiltrating lymphocytes, or TILS, are the name given to these cells. This is an indication that the immune system is attacking the tumor. Patients whose cancers contain TIL's fare better than those whose tumors do not contain them.[1] Despite the fact that the immune system can prevent cancer from spreading. Cancer cells have the ability to evade being destroyed by the immune system. For example, cancer cells' genetic alterations make them less apparent to the immune system.

Cancer cells may carry a protein on their surface that turns off immune cells; cancer immunotherapy has extended the lives of patients with quickly deadly cancer.[2] When the immune system detects a foreign cell in the body, it initiates a sequence of processes to identify, target, and remove the foreign cell. There are three kinds of lymphocytes (WBC) that fight infections and diseases: B-lymphocytes, T-lymphocytes, and NK-lymphocytes (B-cells). T-lymphocytes (T-cells) and natural killer (NK) cells.[3] B-lymphocytes produce antibodies that identify and target antigens. These B-cells are located in the bone marrow and other sections of the lymphatic system. T-cells aid B-cells in the production of antibodies that detect and combat invading bacteria. The main cancer fighter cells of immune system are T-lymphocytes, natural killer cells also destroy the cancer.[4–7]

1.1. Types of immunotherapies

Immunotherapies for blood cancer includes

1. Immune checkpoint inhibitors.

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2. Monoclonal antibodies
3. Adoptive cell transfer /chimeric antigen receptor (CAR) T cell therapy
4. Therapeutic vaccines.

1.2. Immune checkpoint inhibitors

Checkpoint proteins are discovered on T-cells. Checkpoints control how low T-cells respond to invading cells. These T-cells move throughout the body, detecting any signs of infection or sickness, including cancer. When T cells cancer get close to another cell, they use T-cell receptors to transfer particular proteins to the surface of that cell. If the protein of the investigated cell reveals that the cell is alien, the cell is foreign. It is being attacked by T-cells. Checkpoints allow T-cells to grow in order to attack the intruder. After the invader is eliminated, checkpoints instruct the T-cell to switch off and cease T-cell multiplication. After eliminating the invader, checkpoints tell the T-cell to turn off and shut off the T-cell proliferation activity. If T-cells remain active for an extended period of time, they will begin to kill healthy cells and tissues, perhaps leading to autoimmune illnesses such as Crohn's disease or rheumatoid arthritis. The immune system combats alien cells in order to keep the immune system from attacking healthy cells. The immune system generates enough WBCs to combat invading cells. Two checkpoint proteins, PD-1 and PD-L1, collaborate to block T cells, and PD-L1 is a protein found on both normal and malignant cells. When PD-1binds to PD-L2, it gives message to immune system to leave the other cell alone. It results in decreased production of T-cells. [8,9]

1.2.1. Examples of PD-1 inhibitors

Pembrolizumab, Nivolumab -These drugs are given by IV. Example of PD-L1 Inhibitors -Atezolizumab, Avelumab

1.2.1.1. Common side effect of check point inhibitors.

1. Inflammation in the lungs Rashes, Itching
2. Kidney Infection
3. Contusion Muscle pain
4. Abdominal pain
5. Nausea, Vomiting

1.3. Monoclonal antibodies

Antibodies are commonly found in blood and aid in the fight against infections. Monoclonal antibodies, which imitate natural antibodies, are created in labs. Antibodies circulate through the body until they bind to a specific antigen. When an antibody binds to it, it can call other sections of the immune system to eliminate the foreign cells containing the objectionable antigen. MAB specifically targets antigens on cancer cells while causing minimal harm to normal cells. MABs can trigger the immune system, causing it to hunt and kill cancer cells.

1.4. Example of MABs

1. Rituximab used to treat chronic lymphocytic leukemia (CLL and same types of non-Hodgkin lymphoma
2. Trastuzumab used in treatment of breast cancer of stomach cancer.

1.5. Adoptive cell transfer

Adoptive cell transfer immunotherapy uses the patient's own T-cells to combat cancer. T-cells from the tumor or the patient's blood are extracted and then treated in the laboratory with drugs that make them more capable of targeting and killing cancer cells. Chimeric antigen receptor (CAR)T-cell therapy is one of numerous forms of adoptive cell transfer treatments under advanced research. In this CAR T-cell treatment, the patient's own T-cells are harvested from the blood through wing apheresis. Blood is taken from the patient's large veins and then pumped through an apheresis machine, which separates the T-cells from the blood and then returns the remainder blood to the body of the patient. T-cells are then genetically modified in the lab to protect receptors on their surfaces, which are known as chimeric antigen receptors (CARs). T cells can recognize and adhere to particular antigens on tumor cells thanks to these chimeric antigen receptors.

Before receiving CAR T-cells, the patient is given chemotherapy to prepare the body for the incoming CAR T-cells. After being put into the patient's blood, the CAR T-cells begin to grow and then recognize and destroy the cancer cells. CAR T-cells may persist in the body after the injection and result in remission for certain blood cancer patients.

Examples- Tisagenlecleucel is approved to treat the patient of age 25 years or younger with acute lymphoblastic leukemia. Axicabtagene is approved to treat adult patients with B-cell lymphoma after two or more lines of systemic therapy.

1.6. Side effect

1.6.1. Cytokine release syndrome

Happens as a result of the fast and massive release of cytokines into the bloodstream by immune cells impacted by immunotherapy.

1.6.2. CAR-related encephalopathy syndrome

This syndrome's signs and symptoms include fever, headache, fast heartbeat, and trouble breathing.This occurs when CAR T-cell treatment creates neurologic disorders that impact the brain or peripheral nervous system. Symptoms include handwriting difficulties, trouble speaking, hallucinations, and changes in sleep.

1.7. Therapeutic cancer vaccines

Cancer vaccines enable the immune system to recognize cancer cells and protect itself against them. Some cancer therapy vaccines are made from cancer cells, portions of cells, or pure antigens. Sometimes a patient's own immune cells are harvested and then exposed to these compounds in a laboratory to create a vaccine. e.g., Sipuleucel-T

This vaccination, which is used to treat advanced prostate cancer, has adverse effects such as fever, chills, and headache. High blood pressure and respiratory difficulties may also be present.[10,11, 12]

1.8. Talimogene laherpareprec

This is approved to treat for treatment of advanced melanoma skin cancer. It is prepared from a herpes virus.

2. Conclusion

Cancer immunotherapy has significantly improved patients' safety and quality of life when compared to traditional standards of care (including chemotherapy, radiation, and surgery). Immunotherapy has established itself as a foundation of cancer treatment, enhancing the prognosis of several patients suffering from a wide range of hematological and solid malignancies. Checkpoint inhibitors (CPIs) and chimeric antigen receptor (CAR) T cells are the two key drivers of this achievement. Because the immune system has the ability to recall and recognize and eliminate tumor variations as they appear, immunotherapy will always have an inherent edge over alternative treatments that do not have these two critical characteristics. The hurdles ahead include figuring out why immunotherapy therapies work so effectively in certain malignancies and people but not in others, and how tumors that were formerly responsive to treatment might develop resistance. To be more specific, for cancer immunotherapy to be effective, it must find ways to manipulate the immune system in the (likely majority of) patients who show little or no immune response to their tumors, perhaps to the point where its tumor microenvironment is a "immune desert" without no tumor-infiltrating T-cells. The amazing variety and adaptability of immunotherapy is stressed, so positioning this strategy within the arsenal of curative therapies accessible throughout the disease's spectrum.

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4. Conflict of Interest

The author declares that there is no Conflict of interest

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