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IMMUNOTHERAPY IN CANCER TREATMENT - A REVIEW

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ABSTRACT

Cancer is a disease in which abnormal cells divide without control and can invade nearby tissues.[1] In recent times, there have been many advancements in the field of cancer treatment, some of which include advancements in immunological therapy. Immunotherapy is a type of cancer treatment that helps your immune system fight cancer. Immunotherapy uses our immune system to recognise and attack cancer cells. Recent innovations include cell transfer therapy and immune checkpoint inhibitors.[2]

KEYWORDS: Cancer, Immunotherapy, Cell Transfer Therapy, Immune Checkpoint Inhibitors.

INTRODUCTION

Cancer is a disease in which abnormal cells divide without control and can invade nearby tissues. Cancer cells can also spread to other parts of the body through the blood and lymph systems.[1] In 2024, investigators estimated that there will be 2,001,140 new cancer cases, with an estimated 611,720 deaths. The most common diagnosis would be genital system cancers with 427,800 new cases and 70,100 deaths followed by digestive system cancers with 353,820 new cases and 174,320 deaths, and breast cancers with 313,510 new cases and 42,780 deaths.[3]

Immunotherapy is a type of cancer treatment that helps your immune system fight cancer. Immunotherapy uses our immune system to recognise and attack cancer cells.[2],[4]As part of its normal function, the immune system detects and destroys abnormal cells and most likely prevents or curbs the growth of many cancers. For instance, immune cells are sometimes found in and around tumours. These cells, called tumour-infiltrating lymphocytes or TILs, are

a sign that the immune system is responding to the tumour. People whose tumours contain TILs often do better than people whose tumours do not contain them.[2]

Cancer immunotherapy is an innovative treatment for tumours today. In various experiments and clinical studies, it has been found that immunotherapy does have incomparable advantages over traditional anti-tumour therapy, which can prolong progression-free survival and overall survival.[5] Immunotherapy targets the cancer cells directly without affecting the healthy cells surrounding the tumour. Recent studies have shown that cancer stem cells have a much lower chance of surviving immunotherapy than chemotherapy and it has also been seen curing resistant mutations that were previously considered incurable.[6]

Although immunotherapy has advantages over other cancer treatment methods, immunotherapy can also cause side effects. The major reason for side effects is when the immune system starts attacking healthy cells and tissues in the body.[7]

There are several types of immunotherapies. They include immune checkpoint inhibitors, CAR-T cell therapy and many more.[8]

Immune checkpoint inhibitors

Checkpoint inhibitors are a type of immunotherapy. They block proteins that stop the immune system from attacking the cancer cells. Cancer drugs do not always fit easily into a certain type of treatment. This is because some drugs work in more than one way and belong to more than one group. Checkpoint inhibitors are also described as a type of monoclonal antibody or targeted treatment.[4] It is used for the treatment of advanced solid tumours as well as advanced endometrial cancer.[9]

Dostarlimab is a collection of laboratory-synthesized molecules which can act as substitute for human antibodies.[9] Dostarlimab attaches to PD-1, found on the surface of T cells. PD-1 in healthy T cells acts as a brake that prevents the cells from starting an uncontrollable immune response. However, PD-1 can inactivate T cells in tumours as well as prevent them from destroying the cancer cells. Cancer cells have an increased concentration of PD-L1 and PD-L2 molecules on their surfaces, which bind to PD-1. When these two molecules (PD-L1 and PD-L2) attach with the PD-1 receptor present on the T cell, the T cell is inactivated and cannot kill the cancer cells. Dostarlimab binds to the PD-1 in a way that prevents PD-L1 and

PD-L2 from attaching with the PD-1 receptor. This blockade on PD-1 allows the T cells to activate and to attack and kill cancer cells.[9]

Car-T Cell Therapy

T Cell Transfer Therapy is a developed way to potentially increase the effectiveness of T cell–based immunotherapy treatments, such as CAR T-cell therapy, against solid tumours. Chimeric Antigen Receptor [CAR] T-Cell Therapy is a form of cellular immunotherapy that involves engineering T cells in the laboratory so they can specifically target and kill tumours. CAR T Cell Therapy uses the patient's own genetically engineered immune cells to bind to specific target proteins on the surface of cancer cells to kill the cancer cells. In recent times, the focus was shifted on a protein called CD229, which is very prevalent on multiple myeloma cancer cells and less common on healthy cells. Later demonstration revealed that CD229 CAR T cells still attacked some healthy blood cells, a potentially serious toxic side effect. Using a sophisticated approach called Affinity Tuning; CD229 CAR T cells were engineered in such a way that they only attack the malignant cells but spare healthy cells. Optimized receptor that had been engineered apparently caused the CAR T cells to grow more slowly resulting in the therapy not being efficient. This difficulty was prevailed by providing additional copies of a protein naturally present in our CAR T cells, called c-Jun which allowed them to grow normally and attack cancer cells over a longer period. Clinical studies are being initiated to ensure the safety and efficacy of CD229-targeted CAR T cells for the treatment of multiple myeloma and possibly also other malignancies. In animal studies, the enhanced T-cell therapies were effective against cervical cancer and neuroblastoma [a common solid tumour in children]. So far CAR T-cell therapy has been successful in treating blood cancers, but it hasn't worked well for solid tumours. To improve the effectiveness of T-cell therapy against solid tumours they were engineered to carry cytokines, which are proteins that can boost T-cell function. In both laboratory studies and mouse models of cervical cancer, CAR T cells modified to express the cytokines IL-15 and IL-21 on their surface killed far more cancer cells than T cells carrying just one of these cytokines or neither of them. Mice treated with T cells carrying both cytokines also lived longer than mice treated with T cells carrying just one cytokine. The approach also showed potential in mouse models of paediatric neuroblastoma, a difficult-to-treat form of childhood cancer for which new therapies are needed. The co expression of membrane tethered IL15 and IL21 represents a technology to enhance the resilience and function of engineered T cells against solid tumours and could be applicable to multiple therapy platforms and diseases. The

research is being continued to test the IL-15- and IL-21-expressing T-cell therapies in lab and animal model studies of other solid tumours, with the goal of translating the approach into human clinical trials in the next few years.[10],[11]

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