Cancer Immunotherapy

The immune system targets cancer cells and prevents their invasion and migration, however, cancer cells can avoid the immune system recognition. To overcome this, different types of treatments used for cancer like Radiation therapy, Bone Marrow transplant, chemotherapy, and Immunotherapy. Cancer Immunotherapy considered as biological therapy as it treats the cancer patients by using components made by the patient's body. Different types of cancer immunotherapy available, examples include Immune checkpoint inhibitors, T-cell transfer therapy, vaccines, Monoclonal antibodies, Cytokines and Immune system modulators.

Immune Checkpoint inhibitors are drugs that facilitate the blockage of immune checkpoints. Cancer cells can utilize these checkpoints to escape the immune system recognition so targeting and blocking theses checkpoints, enhance the response of the immune cells to cancer cells. Examples of Checkpoint inhibitor drugs include Checkpoint inhibitor drugs that target PD-1/PD-L1 and Checkpoint inhibitor drugs that target CTLA-4.

Checkpoint inhibitor drugs that target PD-1 or PD-L1 provide a high impact in treating cancer patients. T-cells have a checkpoint protein called PD-1, which binds to PD-L1. This binding prevents the T-cells from destructing these normal cells that have PD-L1. However some cancer cells have a large quantity of PD-L1 which will help them to avoid the immune system recognition due to the inhibition of CTL activation. Drugs that target these proteins, will block the binding, activates CTL, and increase the immune system response against these cancer cells. Examples of PD-1 inhibitors drugs include Pembrolizumab and PD-L1 inhibitors drugs include Atezolizumab. Both show a high efficiency in treating different types of cancer.

Moreover other Checkpoint inhibitor drugs are those that target CTLA-4, which is a protein (inhibitory receptor) found on T-cells. The binding of the monoclonal antibody, Ipilimumab, to CTLA-4, prevent its action which as a result will boost the immune response against tumor cells. Another effect of such binding is the reduction of the regulatory T cell that express CTLA-4. Such drugs used to treat melanoma of the skin however, researchers still study the ability of these drugs to treat other types of cancer. New trials demonstrate the high efficiency of treatments based on targeting the inhibition of both PD-1 and CTLA-4. However, this type of treatment arise some limitations of its usage, as it may cause autoimmune and inflammatory reactions. This limitation can be overcome by anti-inflammatory medications.

Chimeric antigen receptor (CAR) T-cell therapy or what is known also as adoptive cell therapy, increases the ability of T cells to attack cancer cells. This is done by selecting the most active T-cells from the patients, followed by enhancing the ability of these cells to target specific cancer cells by the addition of a specific man-made receptor called a chimeric antigen receptor or CAR to these cells, this will generate CAR T-cell (each CAR is designed to target specific cancer cell antigens), then growing them in large quantities and re-injecting them back into the patient's body. Once CAR T-cells recognize cancer cells, they proliferate and destroy more and more cancer cells. This therapy is not yet approved for wide usage however, it has the approval to treat some types of lymphomas, and specific patients who failed to be treated for leukemia.

Current protocols, amply the stimulation of T cells with anti-CD3 and/or anti-CD28 antibodies,

then performing gene transduction of these T cells with CAR-encoding vectors. CAR-T cell-specific for CD19 shows a high efficiency in treating patients with B cell malignancies. One limitation of such therapy includes the killing of the good B cells that fight against germs by the CAR T cells which may result in a patient with a high risk of infection. Indeed, CAR T-cell therapy has shown severe side effects result in cytokine release syndrome (the release of massive quantities of the cytokines from the CAR T cells proliferation into the blood).

Therapeutic antibodies or what is known also as Monoclonal antibodies are immune system proteins designed in the lab, recognize specific targets on tumor cells. These proteins will label tumor cells which as a result will enhance the recognition and attacking of these tumor cells by the immune system. It is referred to as targeted therapy since antibodies are designed specifically to target specific antigens on cancer cells. One example is the one used to treat patients with chronic lymphocytic leukemia (CLL), that target and bind to CD52 antigen on lymphocytes. Another example is the one used to treat breast and stomach cancer by antibody specific against the HER2 protein which inactivate this protein and stop cancer cell proliferation. Also, Radiolabeled antibodies (anti-CD20) used to treat B cell lymphoma by targeting CD20 antigen on B cells. Besides it is efficiency, it has some limitations, one is concerning the loss of antigen variants on the tumor cells which yield a tumor cell unable to express antigens that are recognized by the antibodies. However, this is can be avoided by using different kinds of antibodies targeting different antigens on the tumor cell.

Another type of cancer immunotherapy is the cancer vaccines. There are two types of vaccines, one that treats cancer, and the other one that prevents cancer or the recurrence of the cancer. Vaccines that aid in the prevention of cancer are designed for cancers caused by viruses. Vaccines that protect against infection caused by viruses may be used to prevent cancer caused by the same virus. One example is the vaccine against the hepatitis B virus (HBV) which helps to prevent HBV infection and reduce the risk of liver cancer. Other examples include the vaccine against the human papillomavirus (HPV), which aid in the prevention of cervical cancer and other types of cancer caused by this virus. One limitation of these vaccines is that it is only efficient for cancers caused by infections. Another type of vaccine is the one that treats cancer, these vaccines boost the immune system response against cancer cells. They are made from cancer cells, parts of cells, or pure antigens (certain proteins on the cancer cells) and linked to adjuvants which increase the immune response more. An example of these vaccines is a tumor antigen vaccine. It is performed by collecting blood from the patient, followed by monocytes purification and culture, then the addition of granulocyte-macrophage colony-stimulating factor which will yield the differentiation of monocytes into dendritic cells. These Dendritic cells then cultured with either protein extracted from tumor lysate or synthesized peptides and then injected to the patient. This vaccine used to treat prostate cancer.

Cytokines are another kind of treatment which uses the different types of cytokines to boosts the immune cell response (NK cells and T lymphocytes) to fight cancer cells. The most common types are interleukins and interferon. Interleukin-2 (IL-2) enhances immune cell growth and proliferation, in which high-dose IL-2 used to treat Kidney cancer, renal cell carcinoma, and melanoma. Other interleukins like IL-7, IL-12, and IL-21 are still under study to be used for cancer treatment. Moreover, Interferon, increase the ability of the immune cell to recognize and attack cancer cells by increasing the cytotoxicity activity of NK cells and increasing the expression of MHC class I on cancer cells. Also, it reduces the rate of growth of cancer cells and blood vessels needed for tumor growth. IFN-alfa used to treat melanoma, certain types of leukemia (like CML), certain types of lymphoma (like CTCL), and kidney cancer. However

interferon may result in low white blood cell counts which boosts the risk of infection.

Bacillus Calmette-Guérin (BCG) is a type of cancer immunotherapy that has a key role in activating the immune system after infecting the human tissues. It is used to treat bladder cancer, by injecting killed BCG into the bladder through the catheter which will activate macrophages to mediate the destruction of bladder cancerous cells. Besides activating macrophages, it has a role in stimulating T cell response to target antigens on tumor cells. Moreover, it can also be used to treat melanoma skin cancers.

Immunotherapy drugs have FDA approval for their implementation into clinical practice for cancer treatment, yet it is not widely used as an option to treat cancer and many factors found to affect the efficiency and rise challenges for it is usage. It is found to have an unpredictable efficiency that's mean it is effective only in a selected group of patients who have the same cancer. Also it works better in certain types of cancer rather than others as well as some types of cancer have shown higher efficiency when treated with other types of cancer treatments. Also, another issue is related to the usage of chemotherapy as first-line cancer treatment rather than using cancer immunotherapy which may affect and reduce the ability of cancer immunotherapy due to the compromised immunity of these patients. Moreover, the efficiency is also affected by the difficulty of identifying significant biomarkers and the availability of targetable tumor-specific antigens expressed on tumor cells. Other limitations like tumor heterogeneity and resistance to cancer immunotherapy treatment.

Cancer immunotherapy, takes the focus and attention of cancer field researches to improve it. Examples of current studies include: finding solutions to avoid resistance to immunotherapy, finding answers to which patients will have a good respond to immunotherapy treatment, and which may not and ways to minimize the side effects of immunotherapy treatment.