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New Approach For Cancer Treatment: an Overlook

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Abstract

Cancer treatments a now days are very expensive and having much more side effects rather than effectiveness. So, Immune checkpoint therapy is the treatment of cancer which having less side effects as compare to chemotherapy. Cytotoxic T lymphocyte antigen is the target for immune checkpoint therapy. Immune system will play key role through the T cell immune response and restrict undesired growth of cells. This treatment is more effective with the combination of with other traditional cancer treatments. In current review emphasis was made on various modern treatments for cancer.

Key Words: Cancer, Therapy, Immune checkpoint, Antibody, Inhibitors.

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Introduction

The immune system plays a crucial role in controlling cancer. Nevertheless, in the case of malignancy, multiple mechanisms of immune suppression may exist that prevent effective antitumor immunity. Antibody therapy directed against several negative immunologic regulators (checkpoints) is showing prominent success and is likely to be a major component of treatment for patients with a variety of malignancies (Postow, M.A., *et al*., 2015).

Cytotoxic T lymphocyte antigen 4 (CTLA 4) is a member of the CD-28 immunoglobulin superfamily acts as a key mediator of immune response. CTLA 4 is a B7 family member that is upregulated on T cells after activation. CTLA 4 is predominantly found in intracellular vesicle in activated conventional T cell (Ribas A., *et al*., 2005). Inhibiting the activity of CTLA 4 with monoclonal antibodies blocks T-cell which results in immune cell activation. The concept of immunity gives idea about, if there are cancer cells grows on the body there will be resistance shown by the healthy individual on that cancerous cells. The tumor cells are capable of turning off immune responses against them by active suppression of immune response. There is lot of T cell costimulatory ways by which investigations has been done to treat cancer. From which Anti- CTLA 4 therapy is the most effective. Blocking CTLA 4 increases antitumor response by allowing the immune system to maintain immunity responsiveness against antigen (Hakansson A., *et al*., 2003).

Combination with other therapies CTLA 4 blocking gives effective way to treat cancer. CTLA 4 plays most important role in suppression of T regulatory cells. T regulatory cells, which mainly inhibit effector T cell responses, are typically concentrated in tumor tissues and are thought to locally inhibit anti-tumor immunity. Therefore, CTLA-4 blockade may affect intra tumoral immune responses by inactivating tumor-infiltrating T regulatory cells. CTLA 4 acts as negative immune regulator of autoimmune disease. T cell activation requires two signals. First one is antigen specific that provides by antigen – MHC (major histo-compatabilty complex) and second one is co-stimulatory signal by B7 family of molecule (Tarhini A., *et al*., 2010).

Cytotoxic T Lymphocyte Antigen

The CTLA 4 is immunologic checkpoint. T cell activation requires MHC (major histo-compatabilty complex) and co stimulatory signal achieved when B7 on an antigen-presenting cell (dendritic cell shown) interacts with CD28 on a T cell. Early after activation, to maintain immunologic homeostasis, CTLA-4 is translocated to the plasma membrane where it downregulates the function of T cells. CTLA-4 was the first immune checkpoint receptor to be clinically targeted (Peggs K.S., Etal., 2009). CTLA-4 as a negative regulator of immunity, investigators shows that antibody

blockade of CTLA-4 could result in antitumor immunity in preclinical models (Bachmann M. F., Etal.,2001).

Immune checkpoint therapy, which targets regulatory pathways in T cells to enhance antitumor immune responses, this provided a new weapon against cancer. This therapy has generated durable clinical responses and, in some of patients, long-term where patients exhibit no clinical signs of cancer for many years (Zitvogel L., *et al*., 2015). The field of immune checkpoint therapy has joined the ranks of surgery, radiation, chemotherapy, and targeted therapy as a pillar of cancer therapy. Three new immune checkpoint agents have now been approved by the U.S. Food and Drug Administration (FDA) for the treatment of melanoma, and there is a high expectation that these agents, and others in this class, will also be approved over the next several years for treatment of patients with lung cancer, kidney cancer, bladder cancer, prostate cancer, lymphoma (Sharma P., *et al*., 2015).

The antibody against CTLA-4 ipilimumab was approved in 2011, and two antibodies against PD-1 (pembrolizumab and nivolumab) were approved in 2014. These drugs represent causing change in cancer therapy in two ways. First, they do not target the tumor cell, but target molecules involved in regulation of T cells, the soldiers of the immune system. The goal of the therapy is not to activate the immune system to attack particular targets on tumor cells, but rather to remove inhibitory pathways that block effective antitumor T cell responses (Peggs K.S., *et al*., 2008).

CTLA 4 Inhibition in Cancer Treatment

CTLA 4 blockade therapy comes from the use of combination of agents that control pathways of immune system and rise immune response. Ipilimumab gives long term benefit to the cancer patients and there are very less chances of tumor cells growth in body.

The most of the adverse effects related to the mechanism of action of ipilimunab. The most common are colitis and diarrhea. Because of colitis there is rash, prutitis, deficiencies of endocrine organ (pituitary, adrenal, thyroid). Although the ipilimunab has the high efficacy but the patient with high risk of melanoma should use vaccine along with it. Administration of steroids with ipilimunab does not affect the immune of steroids with ipilimunab does not affect the immune response to anticancer activity (Van Elsas A., Etal., 1999).

Immune Checkpoint Inhibitors Advantages

Adverse effects associated with Chemotherapy, Radiotherapy are too Severe compared to the Immune checkpoint inhibitors and they require special treatments and shows Adverse effect like Bone marrow suppression, Alopecia, nausea, vomiting are highly distressing to the patient and these adverse effects are not associated with the Checkpoint inhibitors, hence they are quite good.

Action of Checkpoint inhibitors is highly target specific and this leads to decrease in the adverse effects which are not observed in the case of other therapies. Due to less adverse effects, small range of dose required, target specificity immune checkpoint blockers has higher efficacy. It initiates the innate immune response of the human body that is highly useful and this are the drugs which extend the survival of patients in the last stage of melanoma (Michot J.M., *et al*., 2016).

Conclusion

T cell is the soldiers of our body which protect body from any foreign material enter into body and cause infection. Cytotoxic T lymphocyte 4 is the antigen which plays very important role in the maintaining the all immune responses related to disease. Inhibition of CTLA 4 gives good result in cancer therapy as good as by chemotherapy. There are very less side effects or we can say immune related adverse effects are less as compared to other therapy. Because of it does not affect host cell directly there is very less chances of again growth of tumor cell in the body. In future there may be way to treat various diseases like diabetes and hepatitis.

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