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The impact of immunotherapy on cancer treatment outcomes: Mechanisms, efficacy, and future directions

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ABSTRACT

Immunotherapy, a transformative approach in oncology, enhances the body's immune system to target and eliminate cancer cells. Key components such as immune checkpoint inhibitors, 'CAR-T cell therapy', monoclonal antibodies, and cancer vaccines play a crucial role. The study explores personalized treatment strategies and future directions, including epigenetic modulation and local immunotherapy. This study includes the details of factors that invade tumour progression and associated immunotherapies to prevent those. The future direction offers the new pathways and approaches such as epigenetic modulation to improve the process of immunotherapy.

Keywords: immunotherapy, cancer treatment, tumour, immune cells, checkpoints, antitumor, inhibitory, monoclonal antibodies, CAR T-cell therapy, cytokines

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INTRODUCTION

In the era of advanced medical therapies, immunotherapy become a highly significant treatment along with traditional processes in the field of oncology. The commonly practiced treatments such as chemotherapy and radiotherapy work by targeting the cancer cells directly and often harm surrounding healthy tissues. Hence, the innovative approach of immunotherapy offers efficiency in curing different types of cancer by strengthening the immune system of the patients. This treatment regulates the microenvironment of the tumour and activates the immune cells by involving Immune Checkpoint Inhibitors (ICIs) to prevent the invasion of malignancy of tumours. ICIs, such as 'anti-PD and anti-PD-L1 drugs', have offered higher efficacy and broad applicability across different types of cancers [1]. A number of 'inhibitory immunoreceptors' have been identified and studied in cancer in previous research, including CTLA-4, LAG3, TIM3, TIGIT, and BTLA [2]. They are named "immune checkpoints" which refers to molecules that act as gatekeepers of immune responses. This research aims to explore the impact of the immunotherapy on cancer treatment by delving into the mechanism efficiency with the combination of other therapeutic agents. Several targeting pathways including surface expression level and interactions of checkpoints will be broadly discussed in regulating the immune responses.

LITERATURE REVIEW

Despite significant progress in cancer diagnosis and treatment, the global challenge of cancer persists. Traditional therapies such as chemotherapy, radiation, and surgery have been mainstays for years. However, immunotherapies offer innovative alternatives, extending patient survival times. Immunotherapy stands out for its tolerability, safety, prolonged response duration, and effectiveness in advanced cancer stages. Previously published scholarly articles by researchers focus on the evaluation of the efficacy of cancer immunotherapy treatment as a neoadjuvant in the early stages of the disease. Distinguished from conventional treatments, immunotherapy aims to enhance the immune system's recognition of cancer cells, amplify immune responses, and prevent the immune suppression that fuels tumour growth. It includes genome editing techniques such as CRISPR/Cas9 gene to mitigate the limitation of adaptive immunotherapy.

An article suggests that this process of cancer treatment involves 'Cytokine-Induced Killer (CIK) cells' which are an ideal

subgroup of 'immune effectors' used in immunotherapy [3]. They exhibit 'MHC-unrestricted cytotoxicity' to prevent both 'haematological and solid malignancies.' CIK cells consist of 'CD3+/CD56+ Natural Killer (NK) T cells', 'CD3−/CD56+ NK cells', and 'CD3+/CD56− cytotoxic T cells.' The authors added that in comparison with other 'antitumor immune cells', 'CIK cells' demonstrate improved 'in vitro proliferation,' 'enhanced migration' to tumour regions, and broader antitumor activity (Figure 1).

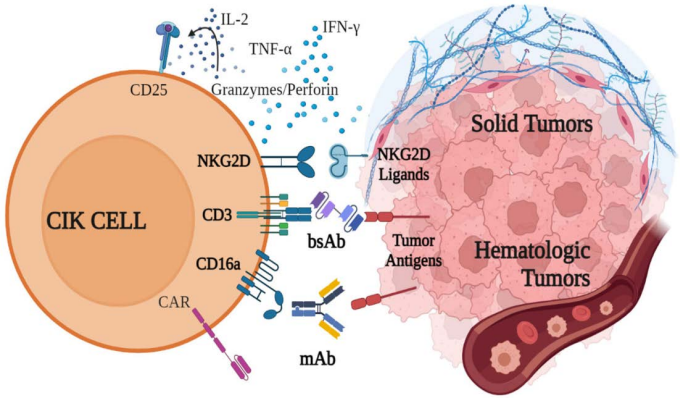

Fig. 1. An overview of the function of 'Cytokine induced killer cells' in expansion of malignant tumour [4]

Another paper mentions that Cytokine-Induced Killer (CIK) cells based therapy has shown efficacy in low Graft Versus Host Disease (GVHD) against hematologic malignancies [3]. Immunotherapy has significantly improved cancer treatment outcomes. It enhances overall survival rates and quality of life for cancer patients.

The comprehensive field of 'immunobiology of the TME' is regulated by a number of factors, including tumour cell-intrinsic determinants of 'immune cell infiltration' [5]. The tissue in which the tumour is located, and the stromal and vasculature content of the tumour also contribute to the tumour progression by exhausting the T-cells. 'Pro-tumorigenic Myeloid Derived Suppressor Cells (MDSCs)' mediate the suppression of T cells through different types of mechanisms including 'depletion of arginine', 'oxidative stress of target cells', and 'release of the Di carbonyl radical methylglyoxal' [6]. The biomarkers are used to predict the different responses as the result of immunotherapy including infiltration of 'cytotoxic T lymphocyte', microsatellite instability, and tumour mutational burden.

There are a few studies that support chemotherapy as a newly emerging path that shows the huge impact on cancer treatment in recent times. 'Cytotoxic drugs' directly kill 'tumour cells' and block their proliferation via multiple mechanisms including 'DNA damage', 'inhibiting DNA replication', and 'preventing mitosis'.

Immunotherapy works best when tumours express specific antigens that the immune system can recognize. Some cancers, such as lung, head and neck, and bladder cancer, respond well to immunotherapy. For example, brain tumours such as glioblastoma represents unique challenges due to the distant environment of brains. 'Programmed Death-Ligand 1 (PD-L1)' is a 'protein expressed by cancer cells' [7]. Tumours have been shown that exhibiting high levels of PD-L1 are highly sensitive to immune checkpoint inhibitors such as pembrolizumab, and nivolumab. Lung and bladder cancer has been seen to display high PD-L1 level which eases immunotherapy in handling the cancer. For example, Tumour-Infiltrating Lymphocytes (TILs) refers to immune cells, for instance, T cells, present in the tumour microenvironment [8]. Lysine bodies have been found to have a critical function in identifying and killing cancerous cells. Lung and head and neck cancers are known to have the higher TIL infiltration as far as the expression of specific antigens is concerned. Mutations of tumour that are more identified are referred as high mutational load tumours produce distinct antigens. Immunotherapy receives advantages from this diversity, as it can target a broader range of cancer-specific proteins. For instance, lung cancers, especially those associated with smoking, tend to have higher mutational loads. Some head and neck cancers result from Human Papillomavirus (HPV) infection. Viral antigens in these tumours attract immune responses, making them more amenable to immunotherapy.

METHODS

This project is based on the mechanism and effectiveness of immunotherapy in cancer treatment. It explores the opinions of the developers, users, and administrators about the significance and performance of the therapy procedures. The research provides the complete framework of cell mediated immunotherapy in a cancer environment. This research investigates the efficacy of the integration of immunotherapy in the deployment cancer cancer-causing tumour cells. Through qualitative data this project provides the opinion of previously working individuals through data collection and analysis. To collect and analyses the data about the performance of immunotherapy in the medical context of cancer treatment, the secondary qualitative method is used. It helps to provide an overview of the mechanism, efficacy, and future opportunities of the research.

The data collection is performed through peer review of previously published scholarly articles, and journals accessed through Science Direct, Google Scholar and PubMed. The obtained information is accumulated and analysed based on thematic analysis. In this process, keywords such as immunotherapy, immune checkpoint inhibitors and cancer treatment is used. The inclusion criteria are that the articles selected for peer review must be on immunotherapy in cancer treatment. Exclusion criteria include that the research articles published more than 5 years ago is not considered for review. The accumulated data from various academic journals are analysed through qualitative thematic analysis. This shares a cohesive understanding of the impact of immunotherapy on positive outcomes of cancer-curing methods. The findings show loopholes in the existing research for obtaining focus for future investigations.

In this study, the maintenance of the ethical perspectives is one of the most significant sections. Firstly, the privacy and permission laws must be followed when using the confidential information about the cancer patients and associated treatment processes. The performance of the immunotherapy needs to be managed by eliminating biases.

RESULTS

Immune checkpoint inhibitors

'Immune checkpoint inhibitors' acts as a crucial player in 'cancer immunotherapy'. These are a type of drugs that act to block the inhibitory pathways used by cancer-invading cells to prevent immune detection. Immune checkpoints are natural regulators that prevent excessive immune responses, safeguarding healthy cells. In normal circumstances, when T cells recognize and bind to partner proteins called checkpoint proteins on other cells including tumour cells, they receive an "off" signal [9]. This prevents the immune system from attacking cancer cells. At the time of requirement, 'Immune Checkpoint Inhibitors (ICIs)' block 'checkpoint proteins' from attaching with their associating proteins. By preventing the "off" signal, ICIs allow 'T cells' to recognize and kill 'cancer cells' effectively (Figure 2).

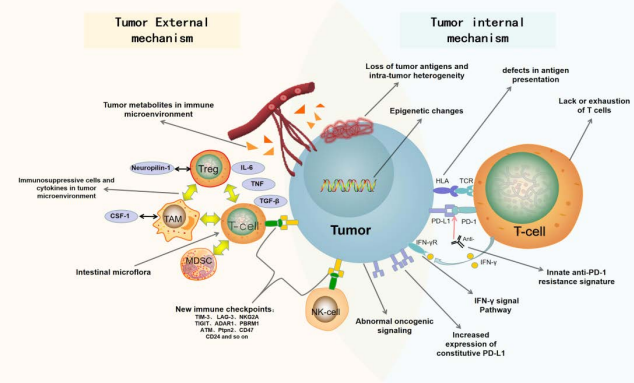

Fig. 2. Mechanism of Immune checkpoint inhibitors [10]

For example, targeting CTLA-4, PD-1, or PD-L1 prevent excessive immune responses to safeguard healthy tissues from the effect of autoimmunity. ICIs are approved for various cancers, including breast, bladder, lung, liver, and skin cancers. They benefit patients whose tumours cannot repair DNA errors during replication. 'Checkpoint inhibitors' for example, 'anti-CTLA-4' such as 'ipilimumab and anti-PD-1/PD-L1', for instance, nivolumab, and pembrolizumab act as a blockage of checkpoints to foster robust immune responses against tumours.

CAR-T cell therapy

CAR-T (Chimeric Antigen Receptor) Cell Therapy' involves the process of modification of a patient's own T cells a major type of white blood cell in the laboratory through medical technology [11]. These modified T cells are equipped with a Chimeric Antigen Receptor (CAR), which allows them to recognize and bind to specific cancer cell antigens. 'CAR T-cell therapy' represents a powerful weapon in our fight against cancer, harnessing the body's immune system to target and destroy 'malignant cells'. This process of immunotherapy, 'CAR T-cell' therapy has shown remarkable success, especially when other treatments fail. It is mostly effective against blood cancers such as leukaemia and lymphoma. CAR has a specific 'antigen binding domain' derived from 'heavy (VH) and light (VL) chains' of 'monoclonal antibodies', connected via a 'flexible linker' to form 'a single chain variable fragment (scFv)'. This targets 'extracellular surface' of cancer antigens through CARs leading to the T cell activation without depending on 'Major Histocompatibility Complex (MHC)'. The hinge regions of CARs are derived from 'amino acid sequences from CD8, CD28, IgG1, or IgG4. IgG-derived spacers.'

Monoclonal antibodies

In the case of immunotherapy against cancer, monoclonal antibodies work to block 'the PD-1/PD-L1 pathway.' These engineered proteins have been widely applied for clinical immunotherapy to fight against a fraction of advanced cancer. It includes Antibody-Dependent Cellular Cytotoxicity (ADCC) for direct apoptosis of cancer cells. Various pieces of evidence show that cases of breast cancer are treated most effectively by the activation of monoclonal antibodies for example, trastuzumab in HER2-positive breast cancer. However, this immunotherapy technique may act as a resistance mechanism by losing antigens and terminating the long-term efficacy of the process (Figure 3).

Interferon and interleukins

Another important component of oncology, is IFN, a cytokine that effectively works against cancer-bearing tumour cells. For example, the FDA approved IFN-α2b as the most effective remedy for patients with melanoma at stage IIB or IIC [13]. IFN-γ has been used as a monotherapy in certain cancers, such as melanoma and renal cell carcinoma by inducing regression tumour cells. Immunotherapy by interleukins for the treatment of metastatic tumours requires a high dose of 'recombinant IL-2 (rhIL-2)' which was suggested by the FDA. However, it requires precaution because of its potential for organ failure and stimulating proinflammatory cytokines.

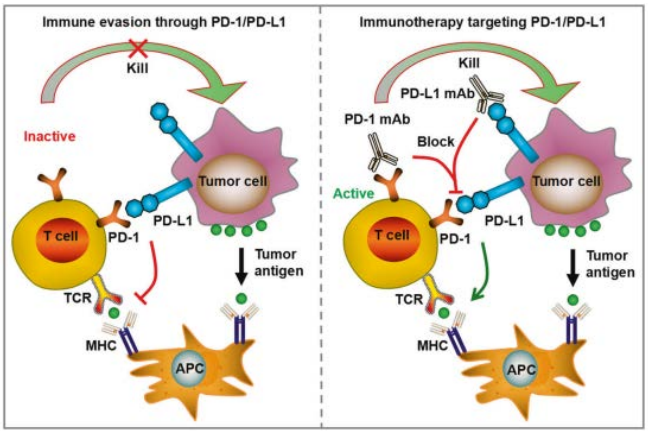

Fig. 3. Actions of immunotherapy targeting PD-1 or PD-L1 [12]

Cancer vaccines

It is widely observed that cancer vaccines are another mechanism of immunotherapy for cancer treatment. A vaccine named 'sipuleucel-T' with drugs 'Provenge and Dendreon', has been approved for the treatment of prostate cancer in men [14]. The 'polyvalent cell-based cancer vaccines' such as dendritic-cell or tumour-cell vaccines offer a promising way in oncology with a wide range of tumor-associated antigens. The basic components of vaccines are peptides, overall cells, and nucleic acids for encoding tumor antigens and deploying cancer cells by activating T cells.

From the above outcomes on the peer review of journals through secondary data collection about the components and mechanism of immunotherapy, the following are summarized (Table 1).

Tab. 1. Various kinds of immunotherapy

	Type of Immunotherapy	Type of Cancer
Cell-Based Therapy	Autologous T-cell transfer	Multiple Myeloma (MM)
	Genetically engineered T-cell therapy	Leukaemia, lymphomas
	Allogeneic stem cell transplant	Acute Myeloid Leukaemia (AML), blood cancers
Cytokine mediated Therapy	High-dose IL-2	Multiple Myeloma (MM), Renal Cell Carcinoma (RCC)
	IFN-α2b	Melanoma
Monoclonal Antibodies	Immune checkpoint inhibitors	Colorectal Cancer (CRC), Lymphomas, HER-2 positive breast cancer
	Therapeutic antibodies	Renal Cell Carcinoma (RCC), Non-Small Cell Lung Cancer (NSCLC), Multiple Myeloma (MM)
Cancer Vaccines	'Sipuleucel-T'	Prostate cancer

DISCUSSION

Efficacy of immunotherapy in cancer outcomes

The tumour microenvironment acts as a major player in the progression of cancers and evasion of immune response. Various immune cells, stromal cells and extracellular matters are the major components of TME which facilitate the immunosuppressive function of tumours proliferating cells. Along with this the TME mainly includes factors such as hypoxia contributing to the inhibition of effective immune responses. In this regard, immunotherapy offers a remarkable shift in cancer treatment. In detail explanation it can be discussed that TGF-β, a multifunctional cytokine associated with immune suppression regulates cell growth, differentiation, and immune responses [15]. It promotes the inhibition and 'proliferation of cytotoxic T cells' and 'the differentiation of naive T cells' into regulatory T cells (Tregs) to support the growth of tumours. It downregulates the expression of Natural Killer (NK) cells as well. In this regard, 'immune checkpoint inhibitor' targets 'Cytotoxic T-Lymphocyte-Associated protein 4 (CTLA-4)' to facilitate the 'T cell-mediated antitumor immune response'. Cancer immunotherapy by ICIs involves the expression of programmed cell death Protein 1 (PD-1) inhibitors.

Immune checkpoints composed a group of molecules that are expressed on immune cells and can tune up the degree of immune activation, act as gatekeepers during the immune response provided by the body against the overactivation of the immune system. The situation of bladder cancer responds well to immune checkpoint inhibitors such as atezolizumab, and durvalumab. These drugs block PD-L1 or PD-1, allowing T cells to attack cancer cells more effectively. In the case of melanoma, the immune checkpoint inhibitors target the PD-L1 or PD-1 and CTLA-4 pathways. These can be equally effective in treating cancers including 'Non-Small Cell Lung Cancer (NSCLC)' and Renal Cell Carcinoma (RCC) and Hodgkin lymphoma. The CAR T cells are designed to attach to a particular cancer cell antigen for instance CD19 in certain leukaemia or lymphomas. The cases of haematological malignancies include the CAR-T cell therapy which targets CD 19 antigen [16]. It represents the efficacy of curing cancer in paediatric and adult individuals. CAR T type of therapy including axicabtageneciloleucel and tisagenlecleucel offers higher efficacy in diffusing large B lymphocyte carcinoma. CAR T-cell therapy has shown remarkable success, especially when other treatments fail.

It is effective against blood cancers such as leukaemia and lymphoma. However, in case of complexity within the tumor micro environment, it causes side effects and may lead to cytokine release

syndrome with neurotoxicity. Immunotherapy including monoclonal antibodies such as trastuzumab reacts potentially by targeting the HER2 receptor in 'HER 2 positive breast cancer' [17]. It reduces the chances of recurrence by working together with chemotherapy. In the case of colorectal cancer, monoclonal antibody mediated immunotherapy targets the EGFR receptor. Mab such as cetuximab is effective in treating metastasis of wild-type KRAS tumours. The immunotherapy aims for enduring, specific anti-tumour responses. By harnessing the immune system's ability to identify and eradicate cancer cells, its tailors' treatment to each patient. Adoptive cell therapy and checkpoint inhibitors are key strategies in this case. These treatments target cancer cells specifically while not affecting the normal cells or healthy tissue.

Future aspects of immunotherapy in cancer treatment

Immunotherapy as the sub-section of oncology medicines is unlikely to be a promising future domain in cancer management. In doing so, it offers a changed process depending on patient characteristics meaning that it takes a patient-centered approach. With biomarkers, genetic tests and many other factors, treatment plans will be enhanced to provide better results. Scientists are studying the way immunotherapy can be used alongside other therapies such as chemotherapy, molecularly targeted therapy, and radiation therapy. Both of which increase immune activity and support higher survival rates, these synergistic approaches. Researchers are discovering new checkpoint inhibitors that can modulate other immune checkpoints. These agents will increase the total amount of cancers that can receive immunotherapy. Personalized cancer vaccines, designed to stimulate the immune system against specific tumour antigens, hold great promise. They may prevent cancer recurrence and improve long-term survival. It involves the research on the field of gut microbiome's impact on immune response will lead to innovative therapies. To enhance the effectiveness of the immunotherapy in cancer treatment requires manipulation of gut microbiota. While treating blood cancers, CAR-T cell therapy may extend to solid tumours with a focus for the improvement in safety and efficacy. The application of epigenetic modulation in cancer cells can enhance immune recognition by complementing immunotherapy with epigenetic drugs. Local Immunotherapy minimizes systemic side effects and maximizes local immune response by directly working on the tumours.

CONCLUSION

The field of oncology has undergone a significant transformation with the advent of immunotherapy, which has reshaped the landscape of cancer treatment. This way immunotherapy is more selective and with less side effects compared to classical techniques such as chemo therapy or radio therapy that work directly on cancer cells but often harm the rest of the tissues. This conclusion draws conclusions based on the analysis of immunotherapy meaning in cancer treatment, its dynamics, effectiveness, and prospects. Possibly the most attractive aspect of immunotherapy is that the response achieved are usually long-lasting and highly specific to tumour antigens. It can be done with the help of various methods such as immune checkpoint inhibitors, CAR-T cell therapies, monoclonal antibodies as well as cancer vaccines. Anti-CTLA-4, PD-1 and PD-L1 are some of the successful immune checkpoint inhibitors which have been used across different cancers include melanoma, NSCLC and RCC. These inhibitors disable the mechanisms that cancer cells implement in avoiding the tracking down by the immune system and in feeling immune responses; instead, they promote immune.

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