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Revolutionizing Healthcare: Exploring the Latest Breakthroughs in Immunotherapy Advancements

Rabia Erum[1], Veena G.[1], Praveena Devi CH.B.[2]*, Maheshwari K.[3] and Maheshwari B.[4]

[1]Department of Pharmacy Practice, Joginpally B.R. Pharmacy College, Yenkapally, Moinabad, Hyderabad, Telangana 500 075, India
[2]Department of Pharmaceutical Chemistry, Joginpally B.R. Pharmacy College, Yenkapally, Moinabad, Hyderabad, Telangana 500 075, India
[3]Department of Pharmaceutics, Joginpally B.R. Pharmacy College, Yenkapally, Moinabad, Hyderabad, Telangana 500 075, India
[4]Department of Pharmacology, Joginpally B.R. Pharmacy College, Yenkapally, Moinabad, Hyderabad, Telangana 500 075, India

**Corresponding Author*
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Abstract: Immunotherapy has emerged as a transformative approach in the field of cancer treatment, offering new hope to patients with previously untreatable malignancies. This review explores recent advancements in immunotherapy, focusing on various strategies that harness the power of the immune system to combat cancer. Immune checkpoint inhibitors, such as PD-1, PD-L1, and CTLA-4 inhibitors, have revolutionized cancer care by unleashing the body's immune response against tumours. Additionally, CAR-T cell therapy has shown remarkable efficacy in hematological malignancies, while cancer vaccines and oncolytic viruses offer promising avenues for both prevention and treatment. Despite these successes, challenges such as immune-related adverse events and resistance mechanisms remain significant hurdles. Looking ahead, the integration of precision medicine, combination therapies, and novel immune modulators holds the promise of further enhancing the effectiveness of immunotherapy across a broader spectrum of cancers and diseases. This review underscores the immense potential of immunotherapy and emphasizes the need for continued research and collaboration to realize its full therapeutic benefits.

Keywords: Immunotherapy, Combination therapy, Autoimmune disorders, Personalized medicine, Lymphokine-Activated Killer (LAK) cell therapy

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Introduction

Leveraging the patient's immune system to destroy cancer is known as immunotherapy. After erysipelas infection, two German doctors named Fehleisen and Busch saw a notable tumour

reduction, which led them to undertake immunotherapy for the first time in the late 19th century. William B. Coley, conducted experiments in which patients with incurable bone cancers were injected with live bacteria, *Staphylococcus pyogenes* and *Serratia marcescens* (also known as Coley's toxin), over the course of the next few years. The immune system has a critical role in determining how patients with breast cancer respond to standard and adjuvant therapy, according to mounting evidence in recent years.

"Immunosurveillance" is the term for the monitoring mechanisms that make up the immune system that identify and react to the presence of cancer cells. The three stages of immuno-surveillance, specifically elimination, balance, and escape the immune system cells, identify antigens unique to tumours during the elimination phase and react by eliminating the tumour cells. Tumour immunogenicity and the interaction of tumour-specific antigens with immune system cells are responsible for the latter outcome. The ability of a tumour to elicit immune responses that prevent its survival and growth is referred to as immunogenicity. After surviving the elimination phase, tumour cells move on to a state of equilibrium, which is a stage between the disease's beginning and the elimination phase. Finally, tumour cells can evade immune monitoring.(Vasileiou *et al.*, 2023)

Immunotherapy has emerged as a promising approach in cancer treatment, with recent advancements showing potential impact on modern medicine. The understanding of molecular mechanisms in cancer cells has led to the development of immunotherapeutic approaches such as immune checkpoint inhibitors and therapeutic cancer vaccines. Immunotherapy has emerged as a promising approach in cancer treatment, with recent advancements showing potential impact on modern medicine. Immunotherapy is a promising therapeutic strategy for cancer, autoimmune diseases, and infectious diseases, involving the induction, enhancement, or suppression of the immune system (Vritika and Sawarkar, 2021)

Significance of immunotherapy in modern medicine:

Immunotherapy has become increasingly important in modern medicine due to its potential to revolutionize the treatment of various diseases, particularly cancer and autoimmune disorders. Followings are some key reasons why immuno-therapy is considered crucial:

(1) *Cancer Treatment Advancement*: Immunotherapy has emerged as a promising approach for treating cancer. Traditional cancer treatments like chemotherapy and radiation therapy can be highly toxic and have significant side effects. Immunotherapy, on the other hand, harnesses the body's immune system to target and destroy cancer cells, leading to more targeted and potentially less toxic treatments.

(2) *Personalized Medicine*: Immunotherapy has the potential for personalized treatment approaches. By understanding the immune system's interactions with cancer cells, researchers can develop therapies tailored to an individual's specific immune profile and tumour characteristics. This personalized approach can lead to more effective treatments with fewer adverse effects.

(3) *Treatment of Previously Incurable Cancers*: Immunotherapy has shown remarkable success in treating certain types of cancer that were previously considered incurable. For example, immune checkpoint inhibitors have demonstrated efficacy in treating metastatic melanoma, lung cancer, and other advanced cancers, offering hope to patients with limited treatment options.

(4) *Long-term Responses*: Unlike traditional cancer treatments that often provide temporary relief, immunotherapy can lead to long-term remission and even cure in some cases. Immune memory can persist, allowing the immune system to continue to recognize and attack cancer cells, providing durable responses.

(5) *Combination Therapies*: Immunotherapy can be combined with other treatments such as chemotherapy, radiation therapy, and targeted therapy to enhance efficacy. These combination approaches can improve response rates and outcomes for patients with various types of cancer.

(6) *Treatment of Autoimmune Disorders*: In addition to cancer, immunotherapy holds promise for treating autoimmune disorders such as rheumatoid arthritis, multiple sclerosis, and inflammatory bowel disease. By modulating the immune system's response, immunotherapy can help alleviate symptoms and slow disease progression.

(7) *Reduced Reliance on Traditional Treatments*: Immunotherapy may reduce the need for extensive surgeries and aggressive treatments like chemotherapy in some cases, leading to improved quality of life for patients.

(8) *Research and Development*: The development of immunotherapy has spurred significant research into understanding the immune system and its role in disease. This ongoing research continues to uncover new targets and therapeutic approaches, driving innovation in the field of medicine.

Types of Immunotherapy:

- *Immune checkpoint inhibitors*:

The immune system plays a vital role for both defending the body against illness and getting rid of the body's own sick cells. Immune system T cells may identify and eliminate infections or unhealthy cells, such as cancer cells, by coordinating a coordinated immune response that includes both innate and adaptive immune responses. Numerous checkpoints make sure that during an immune response (also called an autoimmune reaction), immune system cells do not unintentionally damage healthy cells. These immunological checkpoints can be used by cancer cells to avoid immune recognition and destruction. The immune system can defeat cancer's resistance to immune responses by using monoclonal antibodies to disrupt immune checkpoint proteins, such as PD-1, PD-L1, and CTLA-4. This will activate the body's defence mechanisms to stay.

T cells that have been activated exhibit the PD-1 (programmed cell death-1) receptor on their surface. The surface of dendritic cells and macrophages expresses its ligands, PD-L1 and PD-L2. PD-1 and PD-L1/PD-L2 are members of the immune checkpoint protein family, which functions as a co-inhibitory factor to prevent or restrict the T cell response's progression. To reduce the risk of persistent autoimmune inflammation, the PD-1/PD-L1 interaction makes sure that the immune system is only engaged when necessary.

The role of PD-1/PD-L1 in cancer:

The immune system normally carries out a sequence of actions known as the "cancer immunity cycle" which results in the death of tumour cells and an anticancer immune response:

(i) Mutant antigens produced by tumour cells are taken up by dendritic cells.

(ii) The dendritic cells activate cytotoxic T cells by priming T cells with tumour antigen.

(iii) After that, activated T cells reach the tumour and penetrate its surroundings.

(iv) The cancer cells are recognized and bound to by the activated T cells.

(v) The attached effector T cells release cytotoxins that cause the cancer cells they target to undergo apoptosis.

Tumour cells use the PD-1/PD-L1 pathway as an adaptive immune resistance mechanism in response to endogenous immunological activity that targets the tumour (Fig. 1). In the tumour the microenvironment, PD-L1 is highly expressed on cancerous cells or non-transformed cells2. The cytotoxic T cells are inhibited when PD-L1 produced on the tumour cells interacts to PD-1 receptors on the activated T cells. The tumour microenvironment still inhibits these deactivated

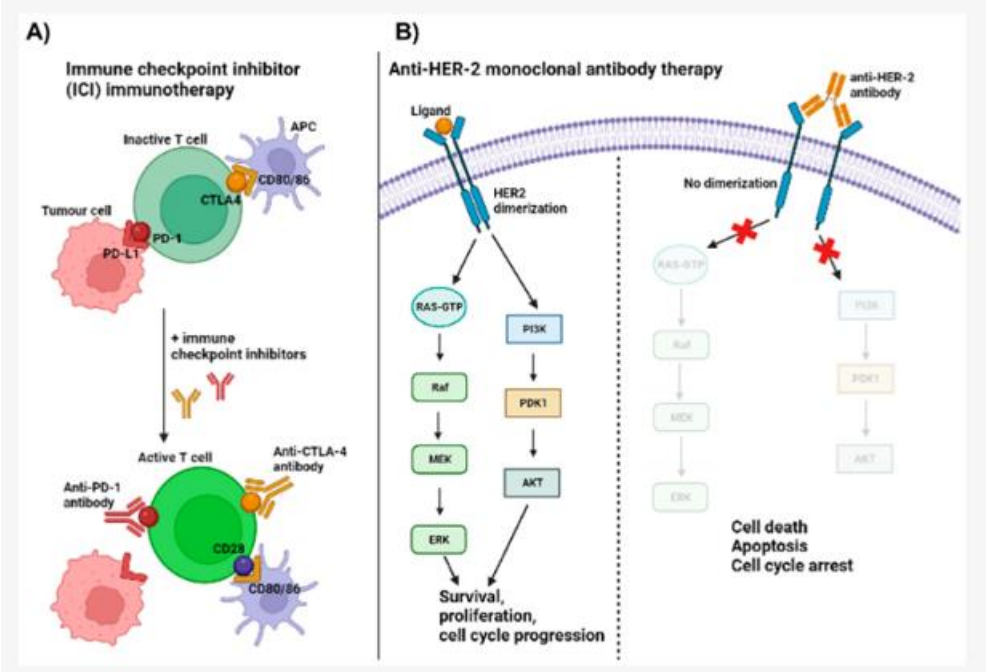

Fig. 1: Monoclonal antibody immunotherapies. (A) Demonstrates the mechanism of action of anti-PD-1 and anti-CTLA-4 immune checkpoint inhibitors. T cells require a total of 3 signals for proper activation. Antigen-specific recognition through T cell receptor (TCR): major histocompatibility complex (MHC) interaction between costimulatory molecules and cytokine signals . Cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4) and programmed cell death-1 (PD-1) are negative checkpoint molecules that drive the inactivation of T cells upon interaction with their corresponding ligands, CD80/86 on antigen-presenting cells (APCs) and PD-L1 on tumour cells. Immune checkpoint inhibitors block that interaction and allow positive checkpoint molecules (e.g., CD28) to interact with their corresponding ligands (i.e., CD80/86) and deliver the 2nd signal for T cell activation. (B) Illustrates the mechanism of action of an anti-HER-2 monoclonal antibody by preventing dimerization of HER subunits. This ultimately leads to the perturbation of downstream signalling events and consequently promotes cell death, apoptosis and cell cycle arrest. (Source: https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/monoclonal-antibodies).

T lymphocytes (Chen and Mellman, 2013).

Using PD-1/PD-L1 and immunotherapy:

The following monoclonal antibody treatments against PD-1 and PD-L1 are frequently employed:

Nivolumab, an anti-PD-1 medication created by Bristol-Myers Squibb, is authorized for the treatment of squamous non-small cell lung cancer and metastatic melanoma that has already been treated. Merck's pembrolizumab is approved for the treatment of metastatic melanoma that has already been treated. Other immunotherapy methods are being developed or are in use (Hwang *et al.*, 2020).

Combination immunotherapy:

Although monoclonal antibodies that inhibit immunological checkpoints are incredibly effective in treating cancer, not every patient responds to this kind of treatment. The next step is to combine medicines with synergistic modes of action to increase and widen immune checkpoint inhibition's anti-tumour efficacy. The effectiveness of combining complimentary checkpoint inhibitor CTLA-4 with PD-1/PD-L1 inhibitory blocking in melanoma and non-small cell lung cancer is one example of this (Ott *et al.*, 2017).

Traditionally, cancer treatment has been based on three main components: radiotherapy, chemotherapy, and surgery. Immunotherapy has surfaced as a potential fourth pillar in recent years. It targets cancer via its intrinsic immune system mechanisms that discriminate between pathologic and healthy tissue, rather than by the anatomic location or tendency to divide of the malignancy. One cornerstone of this new pillar is

adoptive T cell therapy (ACT), a potentially potent cancer treatment strategy based on the injection of T cells specific to tumours.

Adoptive T cell therapy:

The process of adoptive T cell treatment starts with the *ex vivo* expansion of tumour-specific T cells isolated from patients. Patients can then get infusions of the tumour-specific T cells, which will enable their immune systems to destroy any leftover tumour cells (Perica *et al.*, 2015).

It seems that traditional cancer therapies including radiation, chemotherapy, and surgery are not working well enough. Immunotherapy appears to be a more promising approach for treating cancer, according to recent studies. Adoptive cell therapy, a cancer passive immunotherapy, has also been shown through clinical trials to be highly effective against cancer

Lymphokine-Activated Killer (LAK) Cell Therapy:

The creation of lymphokine-activated killer (LAK) cells for the treatment of cancer marked the beginning of the development of adoptive cell therapy Peripheral blood mononuclear cells (PBMC) from both healthy donors and cancer patients can be used to manufacture leukemia-associated killer cells (LAK cells), which are produced by *in vitro* cultivation in the presence of IL-2 (Dudley *et al.*, 2008; Rosenberg and Dudley, 2009).

Dendritic cell (*DC*) *CIK Cell Therapy*:

Lack of tumour antigen specificities may lead to the clinical ineffectiveness of CIK cell therapy for cancer. DC-CIK cells were thus investigated. Following CIK cell culture in the presence of antigen-specific pulsed DC, DC-CIK cells demonstrated increased lytic activity *in vitro* against cancerous cells, including osteosarcoma cells (Zhu *et al.*, 2003), multiple myeloma cells and chronic myelogenousleukemia cells (Marten *et al.*, 2001). DC-CIK cells exhibited markedly enhanced anticancer activity *in vitro* and *in vivo* in comparison to CIK cells (Shetty and Ott, 2021). In BALB/c nude mice, DC-CIK cells also significantly inhibited the development of A549 lung cancer cells. These findings imply that DC-CIK cells may be applied to cancer patients (Zhang *et al.*, 2021).

T cells can be isolated from peripheral blood (peripheral blood lymphocytes, PBLs) or from the patient's tumour (tumour-infiltrating lymphocytes, TILs). PBLs require the induction of tumour specificity via genetic engineering or antigen-specific expansion4. Tumour-specific T lymphocytes can be reinfused into the cancer patient after they have grown *in vitro.*

- *CAR-T Cell Therapy*:

CAR T cell treatment is an additional form of adoptive cell therapy in which T cells are modified to express chimeric antigen receptors (CARs), which are antigens specific to malignancy. In other words, scientists can stimulate the cells to identify and eliminate tumour cells that might otherwise evade immune recognition. Certain solid tumours and hematological malignancies have anti-tumour activity when treated by CAR-T cells and T cells bearing modified tumour-specific TCRs (Ge and Li, 2004; Wongkajornsilp *et al.*, 2005; Grupp *et al.*, 2013).

- *Cancer Vaccines*:

By supplying tumour-specific or tumour-associated antigens (TAA) for the immune system to eliminate, cancer vaccines seek to stimulate and magnify pre-existing T-cell and immunological responses (Table 1). The goal of cancer vaccines is to produce targeted, long-lasting antitumour immunity. It is difficult to develop tumour-specific antigens for cancer vaccinations. TAAs are antigens that are over-expressed or preferentially expressed in cancers, but they are also expressed in healthy tissues.

Neoantigens are not present in normal tissues and can be recognized by T lymphocytes, presented on target cell surfaces, and unaffected by tolerance. Lately, the accessibility and cost-effectiveness of next-generation sequencing have resulted in the extensive detection and identification of several neoantigens as possible targets for the immune system (Shetty and Ott

Table 1: FDA approved vaccines for cancer therapy (Spira *et al.*, 2021)

FDA approved and examples of ongoing clinical trials for cancer vaccines.

3.1 FDA Approved				
Approved Diseases	**Agent**	**Target/Function**	**Type of Vaccine**	**First Approved**
Prostate cancer	Sipuleucel-T (Provenge)	Prostatic acid phosphate (PAP)	Cell: DC	2010 NCT00065442
Melanoma	Talimogene laherparepvec (T-VEC or Imlygic)	Replicate within tumors and produce GM-CSF	Oncolytic virus; Herpes	2015 NCT00769704
3.2 Ongoing Trials				
Trial Identifier	**Disease**	**Candidate(s)**	**Type of Vaccine**	**Phase**
NCT02301611	Melanoma	TLPLDC	DC	II
NCT00045968	Glioblastoma	DCVax-L	DC	III
NCT03632941	Breast cancer	VRP-HER2 ± Pembrolizumab	Adenovirus	II
NCT02773849	NMIBC	Nadofaragene firadenovec (Instiladrin)	Adenovirus	III
NCT04747002	AML	DSP-7888	Peptide	II
NCT03721978	Cervical cancer (cervical HSIL)	VGX-3100	DNA	III
NCT03444376	Cervical cancer	GX-188E	DNA	II
NCT03739931	TNBC, HNSCC, NHL, urothelial cancer, melanoma, NSCLC	mRNA-2752	mRNA	I
NCT01970358	Melanoma	NeoVax (Poly-ICLC (Hiltonol) + Neoantigen peptides)	Peptide	I
NCT02149225	Glioblastoma	GAPVAC	Peptide	I
NCT02287428	Glioblastoma	PNACV ± RT ± Pembrolizumab	Peptide	I

2021; Zhang *et al.*, 2021). Immunotherapy with oncolytic viruses targets tumour cells and triggers anticancer responses. Adenoviruses and herpes simplex viruses are employed as vectors to express particular genes and tumour antigens. Clinical research has benefited from their wide host cell tropism and rapid bulk manufacturing. T-VEC (Imlygic), a first-generation recombinant herpes simplex virus vector that is FDA-approved for the treatment of recurrent, incurable melanoma, represents the greatest clinical advancement (Liu *et al.*, 2022).

Advances in cancer immunotherapy (Fig. 2) have had a significant impact on the diagnosis and treatment of various types of cancer. Immunotherapy has revolutionized cancer treatment and improved patient outcomes for several tumour types. It has become a preferable option compared to conventional therapies like chemotherapy, surgery, and radiotherapy. The understanding of immune checkpoints, therapeutic cancer vaccines, genetic modification of immune cells, and activation of antitumour immune response has led to the development of novel cancer treatments. Combination strategies that target independent cellular pathways are predicted to enhance the efficacy of immuno-therapy. Additionally, the use of immunotherapy in combination with other treatments, such as radiotherapy, has shown promise in managing

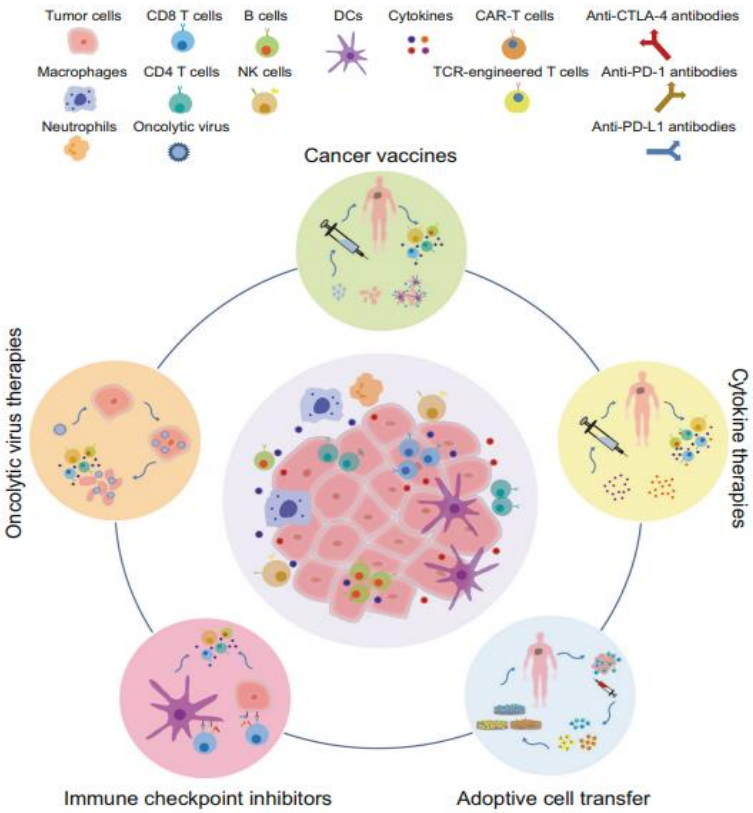

Fig. 2: Advances in cancer immunotherapy (Zhang and Zhang 2020).

certain types of cancer. However, challenges remain to be addressed. These include the need for specific biomarkers to predict treatment efficacy, the development of immunity against immunotherapies, the lack of updated clinical evaluation plans, and high therapy costs. Further research is needed to address these challenges and unlock the full potential of immunotherapy in revolutionizing cancer treatment.

Immunotherapy has emerged as a promising approach in cancer treatment, with significant advancements in recent years.

- The use of immune checkpoint inhibitors, such as PD-1 and CTLA-4 inhibitors, have shown remarkable success in improving patient outcomes in various cancer types.
- Combination therapies, including the use of immunotherapy in combination with chemo-therapy or targeted therapy, have demonstrated enhanced efficacy in certain cancers.
- Despite these advancements, challenges remain in the form of resistance to immunotherapy, limited response rates, and immune-related adverse events.
- Ongoing research efforts are focused on identifying predictive biomarkers, developing novel immunotherapeutic agents, and improving treatment strategies to overcome these challenges and further optimize the use of immunotherapy in cancer treatment (Zhang and Zhang, 2020).
- Advances in immunology have been increasingly visible in the past year, with new vaccines for Sars-cov-2 developed and deployed at an unprecedented speed, and the FDA granting over 30 new approvals for anti-PD-1/PD-L1 immune checkpoint inhibitors for the treatment of various cancer types. Immunotherapeutic drugs traditionally used for autoinflammatory diseases have also been

repurposed for COVID-related pathologies. Immunotherapy has positively impacted various areas of medicine.

- A new trial is discussed that targets an early inducer of inflammation, the production of reactive oxygen species (ROS) by mitochondria, in ulcerative colitis (UC). Excessive mitochondrial ROS induces inflammatory signaling through the cGAS-STING pathway, leading to dysregulated immunity and death of epithelial cells. Current therapies for UC are improving but expensive and immunosuppressive, with a risk of infection.
- Cross-fertilization between disease areas is seen in research on chimeric antigen receptor T-cell therapy and induced immune non-responsiveness. Overcoming challenges in applying CAR-T therapy to solid cancers generates insight into shared immunological mechanisms. Common ground between allergy and autoimmunity is explored, suggesting routes to developing new immunological treatments for autoimmunity.
- Immunotherapy has emerged as a groundbreaking approach in cancer treatment, leveraging the body's own immune system to target and destroy cancer cells. Several significant advancements have been made in the field of immunotherapy for cancer treatment:
- Checkpoint inhibitors, such as drugs targeting programmed cell death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), have revolutionized cancer treatment. These drugs work by blocking the inhibitory signals that cancer cells exploit to evade immune detection and destruction. Pembrolizumab, nivolumab, and ipilimumab are some examples of checkpoint inhibitors approved for various cancer types.
- Chimeric antigen receptor T-cell (CAR-T) therapy involves genetically modifying a patient's T cells to express a synthetic receptor that targets cancer cells. This therapy has shown remarkable success, particularly in certain blood cancers like leukemia and lymphoma. Approved CAR-T therapies include tisagenlecleucel (Kymriah) and axicabtageneciloleucel (Yescarta).
- Tumour-Infiltrating Lymphocytes (TILs) therapy involves isolating immune cells from a patient's tumour, expanding them in the laboratory, and then infusing them back into the patient. These activated immune cells can then mount a targeted attack against the cancer. TIL therapy has shown promise in melanoma and certain other solid tumours.
- Cancer vaccines aim to stimulate the immune system to recognize and attack cancer cells. Some vaccines target specific cancer antigens, while others are designed to stimulate a broader immune response. Sipuleucel-T (Provenge) is a vaccine approved for prostate cancer that works by stimulating the patient's immune cells to target prostate cancer cells.
- Bispecific antibodies are engineered to simultaneously bind to both cancer cells and immune cells, bringing them into close proximity and enhancing the immune system's ability to destroy cancer cells. Blinatumomab, a bispecific antibody approved for acute lymphoblastic leukemia, redirects T cells to target cancer cells expressing CD19.
- Combining different types of immune checkpoint inhibitors or combining checkpoint inhibitors with other cancer treatments, such as chemotherapy or targeted therapy, has shown synergistic effects and improved treatment outcomes in some cases.
- Advances in understanding predictive biomarkers, such as PD-L1 expression levels and tumour mutational burden, help identify patients who are more likely to benefit from immunotherapy, enabling personalized treatment approaches.

Certainly, here are a few additional points to further elaborate on the advancements in cancer immunotherapy:

(i) *Combination Therapies*: Researchers are exploring the synergistic effects of combining different types of immunotherapy agents, as well as combining immunotherapy with traditional treatments like chemotherapy, radiation therapy, and targeted therapy. These combination approaches aim to enhance the immune response, overcome resistance mechanisms, and improve treatment outcomes.

(ii) *Localized Immunotherapy*: Localized immunotherapy involves delivering immunotherapy agents directly to the tumour site, thereby minimizing systemic side effects and maximizing treatment efficacy. Approaches such as intra-tumoural injections of immune-stimulating agents or oncolytic viruses are being investigated as potential strategies to activate the immune system within the tumour microenvironment.

(iii) *Microbiome Modulation*: Emerging evidence suggests that the gut microbiome plays a crucial role in shaping the body's immune response, including its response to cancer. Researchers are exploring the potential of modulating the gut microbiome through probiotics, prebiotics, or fecalmicrobiota transplantation to enhance the effectiveness of immunotherapy and improve patient outcomes.

(iv) *Neoantigen Vaccines*: Neoantigens are unique proteins expressed by cancer cells as a result of mutations in their DNA. Neoantigen vaccines are personalized vaccines designed to target these specific mutations, stimulating a targeted immune response against cancer cells while sparing normal cells. Clinical trials investigating neoantigen vaccines have shown promising results in various cancer types, offering a highly personalized approach to cancer immunotherapy.

(v) *Immune-Modulating Agents*: Beyond checkpoint inhibitors, researchers are exploring novel immune-modulating agents that target different components of the immune system. These agents include agonists of co-stimulatory molecules, such as OX40 and 4-1BB, as well as cytokines that enhance immune cell function, such as interleukin-2 (IL-2) and interleukin-12 (IL-12). These agents aim to amplify the immune response and overcome immune suppression within the tumour microenvironment.

(vi) *Liquid Biopsies for Monitoring Response*: Liquid biopsies, which involve analysing circulating tumour DNA, RNA, or proteins in the blood, are emerging as valuable tools for monitoring response to immunotherapy. These non-invasive tests can provide real-time information about tumour burden, genetic alterations, and immune response dynamics, enabling clinicians to tailor treatment strategies and identify early signs of treatment resistance.

(vii) *Predictive Biomarkers beyond PD-L1*: While PD-L1 expression has been widely studied as a predictive biomarker for response to checkpoint inhibitors; researchers are identifying additional biomarkers that may better stratify patients for immunotherapy. These biomarkers include tumour mutational burden, immune cell infiltration, and gene expression profiles within the tumour microenvironment, providing insights into the complex interplay between tumours and the immune system.

Certainly, here are some additional points highlighting advancements in cancer immunotherapy:

- *Adoptive Cell Therapy* (*ACT*): Apart from CAR-T cell therapy, other forms of adoptive cell therapy involve isolating immune cells, such as tumour-infiltrating lymphocytes (TILs) or natural killer (NK) cells, from patients, expanding them ex vivo, and then reintroducing them into the patient to target and kill cancer cells. ACT has shown promising results in various cancers, including melanoma, ovarian cancer, and sarcoma, and ongoing research aims to optimize this approach further.

- *Cytokine Therapy*: Cytokines are signalling molecules that regulate the immune response. Interleukin-2 (IL-2) and interferon-alpha (IFN-α) were among the first cytokines used in cancer immunotherapy. While IL-2 has been approved for metastatic melanoma and renal cell carcinoma, newer cytokines and cytokine-based therapies are being developed to enhance immune activation and improve treatment outcomes.
- *Immune Cell Engineering*: In addition to CAR-T cells, researchers are exploring other strategies for engineering immune cells to enhance their anti-cancer activity. This includes modifying dendritic cells, macrophages, and other immune cells to better recognize and eliminate cancer cells. These engineered immune cells hold the potential to overcome immune evasion mechanisms and improve the durability of response to immunotherapy.
- *Immune Checkpoint Targets Beyond PD-1/PD-L1 and CTLA-4*: While PD-1/PD-L1 and CTLA-4 are well-known immune checkpoints, researchers are investigating other inhibitory and stimulatory checkpoints as potential targets for immunotherapy. These include checkpoints such as LAG-3, TIM-3, TIGIT, and VISTA. Targeting multiple checkpoints simultaneously or sequentially may offer enhanced therapeutic efficacy and overcome resistance to current immunotherapies.
- *Nanoparticle-Based Immunotherapy*: Nanoparticles can be engineered to deliver immunotherapeutic agents selectively to tumour sites, improving drug delivery and minimizing off-target effects. Nanoparticle-based immunotherapy approaches include nanoparticles loaded with immune-stimulating agents, such as toll-like receptor agonists or cytokines, as well as nanoparticles conjugated with antibodies for targeted drug delivery.
- *Artificial Intelligence and Machine Learning*: The integration of artificial intelligence (AI) and machine learning algorithms into cancer immunotherapy research holds promise for accelerating drug discovery, identifying predictive biomarkers, and optimizing treatment strategies. AI-based platforms can analyse vast amounts of biological data, identify patterns, and predict patient responses to immunotherapy, facilitating personalized treatment approaches.
- *Combining Immunotherapy with Radiotherapy and Hyperthermia*: Preclinical and clinical studies have demonstrated the synergistic effects of combining immunotherapy with radiotherapy or hyperthermia (heat therapy). These treatments can induce immunogenic cell death, release tumour antigens, and modulate the tumour microenvironment to enhance the immune response and improve treatment outcomes.
- *Immunotherapy for Rare Cancers and Paediatric Cancers*: While immunotherapy has shown remarkable success in certain common cancers, efforts are underway to extend its benefits to rare cancers and paediatric cancers. Clinical trials are evaluating the safety and efficacy of immunotherapy in these patient populations, with the aim of providing effective treatment options for patients with historically limited therapeutic options (Dhar *et al.*, 2021; Braidotti *et al.*, 2024).

Conclusion

This review provided a detailed study about the aetiology of cancer as this disease is one of the fast growing diseases in the world. Also we gave in detail about the various treatment strategies and recent advances for treating various cancers,

Ethical Statement

This is a review article hence no Ethical Approval needed.

Author Contributions

Each author has contributed equally to the study's

planning, analysis, writing, and editing. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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