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Schedule Immunotherapy of Cancer; Current Status and Prospectus

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Abstract

In the past decades, our knowledge about the relationship between cancer and the immune system has increased considerably. Immunotherapy has been a promising and rapidly evolving field in cancer treatment. However, keep in mind that the information might have advanced since then. Drugs like pembrolizumab and nivolumab, which target PD-1/PD-L1 pathways, have shown success in treating various cancers. These drugs release the brakes on the immune system, allowing it to better recognize and attack cancer cells. This involves harvesting and modifying a patient's immune cells outside the body before infusing them back to target cancer cells. Researchers are exploring combinations of different immunotherapies and traditional treatments to enhance effectiveness and overcome resistance. Efforts to identify predictive biomarkers aim to personalize immunotherapy, ensuring it benefits patients who are most likely to respond. In summary, immunotherapy has made significant strides in cancer treatment, with ongoing research focusing on refining existing therapies, discovering new targets, and expanding the range of treatable cancers. The prospectus is promising, but addressing challenges remains critical for realizing the full potential of immunotherapy in the fight against cancer.

Keywords: Immune System; Target Inhibitor; Checkpoint; Antibody; Immunotherapy; Types Of Cancer

Abbreviations: GLOBOCAN: Global Cancer Observatory; CARs: Chimeric Antigen Receptors; NK: Natural Killer; NSCLC: Non-Small Cell Lung Cancer; RCC: Renal Cell Carcinoma; ALL: Acute Lymphoblastic Leukemia; IRAEs: Immune-Related Adverse Events; TMB: Tumor Mutational Burden; MSI: Microsatellite Instability; CRS: Cytokine Release Syndrome.

Introduction

Global Cancer Observatory (GLOBOCAN) estimated36 types cancer in 185 countries. 19.65 million Incident cancer cases worldwide for the year 2023. According to GLOBOCAN, India ranked third in terms of incident cancer cases, following China and the United States of America. GLOBOCAN predicted a significant increase in cancer cases in India to 2.08 million by 2040. This projection suggests a rise of 57.5% in cancer cases in India from 2020 to 2040. Understanding the trends and projections in cancer incidence is crucial for healthcare planning, resource allocation, and the development of effective prevention and treatment strategies. The increasing burden of cancer underscores the importance of public health measures, early detection, and access to quality healthcare services [1]. The estimated number of incident cases of cancer in India for 2022 was 14, 61,427. The crude rate was reported as 100.4 per 100,000 population. One in nine people in India is estimated to develop cancer during their lifetime. Lung cancer was reported as the leading cancer site among males. Breast cancer was reported as the leading cancer

site among females. Among childhood cancers (0-14 years), lymphoid leukemia was identified as the leading site. Boys had a slightly higher incidence of lymphoid leukemia (29.2%) compared to girls (24.2%). The incidence of cancer cases is estimated to increase by 12.8% in 2025 compared to 2020. It's crucial to recognize the impact of cancer on public health and the need for comprehensive strategies for prevention, early detection, and treatment. Additionally, ongoing surveillance and research are essential to understand the evolving patterns of cancer incidence and to develop targeted interventions [2]. Therapeutics have continued to advance rapidly, with ongoing developments in various approaches. Please note that the field is dynamic, and new treatments may have emerged since then [3]. Several common practices in cancer therapeutics have been widely used [4]. There are some of the common therapeutic approaches for cancer like Surgery, Chemotherapy, Radiation Therapy, Immunotherapy, Targeted Therapy, Hormone Therapy, Precision Medicine, Bone Marrow/Stem Cell Transplantation, Palliative Care, and Combination Therapies [5]. In all these systematic therapeutics, immunotherapy has emerged at a crucial time by providing very effective treatments which is providing a breakthrough in cancer treatment and we are more optimistic about curing cancer [6]. Immunotherapy has emerged as a promising and revolutionary approach to cancer treatment.

Harnessing the Immune System

Immunotherapy works by leveraging the body's own immune system to recognize and attack cancer cells. This is a fundamental shift from traditional treatments that directly target cancer cells [7]. The immune system plays a crucial role in defending the body against foreign invaders, including abnormal cells like cancer cells. Immunotherapy seeks to enhance the body's natural ability to recognize cancer cells as foreign or abnormal. Cancer cells often develop mechanisms to evade detection by the immune system, allowing them to proliferate unchecked [8]. Cancer cells can exploit immune checkpoints, which are regulatory proteins that prevent the immune system from attacking normal cells [9]. Tumors often overexpress these checkpoints, inhibiting immune responses. Immunotherapy includes the use of immune checkpoint inhibitors, such as anti-PD-1 (programmed cell death protein 1) and anti-PD-L1 (programmed death-ligand 1) antibodies [10]. These inhibitors block the interaction between immune checkpoint proteins, allowing immune cells to recognize and attack cancer cells. By blocking immune checkpoints, immunotherapy enhances the activity of T cells, a type of immune cell responsible for recognizing and destroying abnormal cells, including cancer cells [11]. Another approach involves CAR-T cell therapy, where a patient's T cells are genetically engineered to express chimeric antigen receptors (CARs). These receptors enable T cells to recognize specific proteins on the surface of cancer cells, leading to their destruction. Immunotherapy aims to activate the immune system's cytotoxic (cell-killing) response against cancer cells [12]. This can involve stimulating the production of immune cells, such as cytotoxic T cells and natural killer (NK) cells. Successful immunotherapy can also create a memory immune response [13]. This means that even after the initial treatment, the immune system retains the ability to recognize and respond to cancer cells, providing a potential long-term defense against recurrence. Immunotherapy is adaptable and can be tailored to the individual patient's immune profile. Personalized medicine approaches involve identifying specific biomarkers that indicate the likelihood of a positive response to immunotherapy [14]. Immunotherapy is often used in combination with other treatments, such as chemotherapy, radiation therapy, or other immunotherapeutic agents. Combinations aim to enhance overall treatment efficacy by targeting cancer cells through multiple mechanisms [15]. The idea behind harnessing the immune system is to empower the body's natural defenses to recognize and eliminate cancer cells, providing a more targeted and potentially less toxic approach compared to traditional treatments like chemotherapy. While immunotherapy has shown remarkable success in certain cancers, ongoing research is focused on expanding its applications and addressing challenges, including resistance and optimizing combinations for broader effectiveness [16].

Durable Responses

In some patients, immunotherapy has demonstrated more prolonged and durable responses compared to conventional treatments. Some individuals experience long-term remission even after stopping immunotherapy. The concept of durable responses in the context of cancer treatment, specifically immunotherapy, refers to the ability of the treatment to induce long-lasting remissions or control over the disease [17]. This is a notable characteristic that sets immunotherapy apart from some traditional cancer treatments. Immunotherapy has shown the ability to induce responses that are not only effective but also durable [18]. In some cases, patients experience extended periods of remission, where the cancer remains under control for a significant amount of time. The durability of responses in immunotherapy has been observed in certain cancers, leading to improved long-term survival rates for some patients [19]. This is particularly significant in advanced or metastatic cancers where long-term survival was historically challenging. Immunotherapy often stimulates the immune system to create a memory response. Even after the completion of treatment, the immune system retains the ability to recognize and respond to cancer cells. This immune memory contributes to durable responses and can provide

ongoing protection against cancer recurrence. In some cases, patients may continue to experience benefits from immunotherapy even after the treatment course is completed [20]. This contrasts with certain traditional treatments where the effects may diminish after treatment cessation. Clinical trials evaluating immunotherapies, especially immune checkpoint inhibitors and CAR-T cell therapies, have reported instances of durable responses. Patients who achieve durable responses contribute to the growing body of evidence supporting the effectiveness of these therapies. It's important to note that responses to immunotherapy can vary among individuals and cancer types [21]. While some patients experience durable responses, others may have different outcomes. Factors influencing the likelihood of durable responses include the type of cancer, the stage at which treatment is initiated, the presence of specific biomarkers, and the overall health of the patient [22]. The ability of immunotherapy to induce durable responses has been a transformative aspect of cancer treatment, offering hope to patients with historically challenging prognoses. Ongoing research is focused on understanding the mechanisms underlying durable responses and optimizing treatment strategies to enhance the likelihood of sustained benefits for a broader range of cancer patients [23].

Broad Applicability

Immunotherapy has shown effectiveness across a variety of cancer types. It has been approved for use in melanoma, lung cancer, bladder cancer, kidney cancer, lymphoma, and more. Ongoing research explores its potential in additional cancers. His concept of durable responses in the context of cancer treatment, specifically immunotherapy, refers to the ability of the treatment to induce long-lasting remissions or control over the disease [24]. This is a notable characteristic that sets immunotherapy apart from some traditional cancer treatments. The broad applicability of immunotherapy is a key strength in its role as a cancer treatment [25]. Unlike some traditional treatments that are specific to certain cancer types, immunotherapy has demonstrated effectiveness across a variety of cancers.

Approval for Multiple Cancer Types

Immunotherapy has received regulatory approval for use in various cancer types, reflecting its effectiveness and potential to benefit patients across different malignancies. Immunotherapy, particularly immune checkpoint inhibitors like pembrolizumab and nivolumab, has shown significant success in the treatment of advanced melanoma, leading to durable responses and improved survival rates. Immune checkpoint inhibitors have been approved for the treatment of non-small cell lung cancer (NSCLC), demonstrating efficacy in both first-line and advanced settings [26]. Atezolizumab, Nivalumab and pembrolizumab are immune checkpoint inhibitors approved for advanced bladder cancer, offering new treatment options for patients. Immunotherapy, including immune checkpoint inhibitors and cytokine therapies, has been integrated into the standard of care for advanced renal cell carcinoma (RCC) [27]. Certain immunotherapies, such as monoclonal antibodies like rituximab, have been successful in the treatment of lymphomas, including non-Hodgkin lymphoma. Pembrolizumab has received approval for the treatment of recurrent or metastatic head and neck squamous cell carcinoma. Immunotherapy has demonstrated efficacy in gastrointestinal cancers, including colorectal cancer and liver cancer. Immune checkpoint inhibitors are being explored in clinical trials for these indications [28]. Ongoing research is investigating the role of immunotherapy in breast cancer, with some success seen in specific subtypes, such as triple-negative breast cancer. CAR-T cell therapy has shown remarkable success in certain hematological malignancies, including acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma [29]. Ongoing research is exploring the potential of immunotherapy in additional cancer types, including brain tumors, pancreatic cancer, ovarian cancer, and more. Immunotherapy is often used in combination with other treatment modalities, such as chemotherapy or targeted therapy, further expanding its applicability [30]. The ability of immunotherapy to elicit responses in a diverse range of cancers highlights its potential as a versatile and transformative approach to cancer treatment. Ongoing research aims to uncover new applications and optimize immunotherapy regimens to improve outcomes for a broader spectrum of patients.

Immune Memory

Immunotherapy often stimulates the immune system to create a memory response. Even after the completion of treatment, the immune system retains the ability to recognize and respond to cancer cells. This immune memory contributes to durable responses and can provide ongoing protection against cancer recurrence [31]. The concept of immune memory is a critical aspect of immunotherapy and contributes to the durability of responses observed in some patients. Immunotherapy, particularly immune checkpoint inhibitors and CAR-T cell therapy, aims to activate and proliferate T cells [32]. These are a type of immune cell with a critical role in recognizing and destroying abnormal cells, including cancer cells. During immunotherapy, the stimulation of T cells can lead to the formation of memory T cells. These cells are specifically programmed to "remember" the characteristics of cancer cells, including their unique antigens. Memory T cells have the ability to recognize specific antigens associated with cancer cells [33]. Antigens

are proteins or other molecules on the surface of cells that the immune system identifies as foreign or abnormal. Unlike effector T cells, which are involved in the immediate immune response, memory T cells have the capacity for long-term persistence. They can remain in the body for extended periods, providing ongoing surveillance. If cancer cells reappear or residual cancer cells remain after treatment, memory T cells can quickly recognize and mount a targeted immune response [34]. This rapid response contributes to the prevention of cancer recurrence. Immune memory enhances the immune system's ability to surveil the body for any signs of cancer resurgence. This ongoing surveillance is crucial for maintaining long-term control over the disease. The presence of memory T cells and their ability to respond to cancer cells contribute to the durability of responses seen in some patients undergoing immunotherapy. This can result in prolonged periods of remission. Immunotherapy activates the adaptive immune system, which includes T cells and B cells [35]. The adaptive immune system is characterized by its ability to "remember" previous encounters with specific antigens. In some immunotherapeutic strategies, such as cancer vaccines, the goal is to induce immunologic memory by exposing the immune system to cancer-specific antigens. This primes the immune system to respond more effectively if cancer cells are encountered [36]. The existence of immune memory opens avenues for potential future treatments, including booster immunotherapies or strategies to reactivate memory T cells if necessary. Understanding and harnessing immune memory is a fundamental principle in the development of effective immunotherapeutic strategies. Ongoing research aims to optimize these processes and further improve the durability and long-term efficacy of immunotherapy in cancer treatment.

Reduced Side Effects

Immunotherapy often has different side effect profiles compared to traditional treatments like chemotherapy. While it can cause immune-related adverse events, these are generally different from the toxicities associated with chemotherapy. Immunotherapy and chemotherapy are two distinct approaches to treating cancer, and they have different mechanisms of action and side effect profiles. Chemotherapy works by targeting rapidly dividing cells, which includes both cancerous and healthy cells. As a result, chemotherapy often leads to side effects such as nausea, hair loss, fatigue, and suppression of the immune system [37]. On the other hand, immunotherapy aims to enhance the body's natural immune response against cancer cells. While it can also have side effects, they are generally related to the immune system itself and are often referred to as immune-related adverse events (irAEs). These may include inflammation of organs, skin rashes, diarrhea, and thyroid dysfunction, among others. However, the immune system-related side effects can still pose challenges and require careful management by healthcare professionals. Despite this, the unique mechanism of immunotherapy has shown promising results in treating various types of cancers and has become an important part of cancer treatment strategies [38].

Biomarker Identification

Advances in understanding biomarkers associated with immunotherapy response help identify patients more likely to benefit. For example, the expression of PD-L1 (programmed death-ligand 1) is often used as a predictive biomarker. Absolutely, biomarker identification has become crucial in the field of immunotherapy to predict and understand the response of patients to these treatments [39]. PD-L1 is one of the well-studied biomarkers in the context of immunotherapy, particularly in treatments involving immune checkpoint inhibitors.PD-L1 is a protein that can be expressed on the surface of cancer cells. It interacts with PD-1 (programmed cell death protein 1) on immune cells, leading to the suppression of the immune response against cancer. Immune checkpoint inhibitors, such as anti-PD-1 or anti-PD-L1 antibodies, work by blocking this interaction, thereby unleashing the immune system to target and destroy cancer cells [40,41]. The expression of PD-L1 in tumor cells has been used as a biomarker to predict the likelihood of response to immune checkpoint inhibitors. Higher levels of PD-L1 expression in tumors have been associated with better response rates to anti-PD-1 or anti-PD-L1 therapies in certain cancers [42]. However, it's important to note that PD-L1 expression is just one of many factors influencing the response to immunotherapy. The field is actively researching and identifying additional biomarkers, including tumor mutational burden (TMB), microsatellite instability (MSI), and the overall immune microenvironment of the tumor. As our understanding of the complex interactions between the immune system and cancer grows, the identification of reliable biomarkers will play a crucial role in tailoring immunotherapy treatments to individual patients, improving response rates, and minimizing potential side effects [43].

Checkpoint Inhibitors

Immune checkpoint inhibitors, such as anti-PD-1, anti-PD-L1, and anti-CTLA-4 drugs, have shown remarkable success. These inhibitors block the proteins that suppress the immune system, allowing it to recognize and attack cancer cells [44]. Yes, that's an accurate description. Immune checkpoint inhibitors, such as anti-PD-1 (programmed cell death protein 1) and anti-PD-L1 (programmed death-ligand 1) drugs, have indeed demonstrated remarkable success in the treatment of various cancers. The immune system has

built-in checkpoints, including the PD-1/PD-L1 pathway, to regulate immune responses and prevent excessive activation that could harm normal cells. However, cancer cells can exploit these checkpoints to evade detection and attack by the immune system [45]. PD-1 is a receptor on the surface of immune cells, and PD-L1 is a protein expressed on some cancer cells [46]. When PD-1 on immune cells binds to PD-L1 on cancer cells, it sends inhibitory signals that suppress the immune response, allowing the cancer cells to evade destruction.Anti-PD-1 and anti-PD-L1 drugs work by blocking this interaction. By inhibiting the PD-1/PD-L1 pathway, these drugs release the "brakes" on the immune system, allowing it to recognize and attack cancer cells more effectively [47]. This has resulted in significant clinical benefits for some patients with various types of cancer. It's important to note that while these immune checkpoint inhibitors have shown great promise, they are not effective for all patients or all types of cancer [48]. Ongoing research is focused on identifying biomarkers and understanding the factors that influence response to these therapies, as well as developing combination treatments to enhance their effectiveness [49].

CAR-T Cell Therapy

CAR-T cell therapy involves engineering a patient's T cells to express chimeric antigen receptors (CARs), which target specific proteins on cancer cells. This approach has shown significant success, particularly in certain blood cancers. Absolutely, your description is accurate [50]. CAR-T cell therapy (Chimeric Antigen Receptor T-cell therapy) is an innovative and promising form of immunotherapy that involves modifying a patient's own T cells to enhance their ability to target and destroy cancer cells. Collection of T Cells: T cells, a type of immune cell, are extracted from the patient's blood [51]. The T cells are then genetically modified in the laboratory to express chimeric antigen receptors (CARs). These CARs are designed to recognize specific proteins on the surface of cancer cells. The engineered CAR-T cells are cultured and allowed to multiply in the laboratory. The expanded and modified CAR-T cells are infused back into the patient's bloodstream. The CARs on the surface of these engineered T cells enable them to recognize and bind to the specific proteins on cancer cells [52]. Once bound, the CAR-T cells activate and initiate a targeted immune response against the cancer cells. CAR-T cell therapy has shown remarkable success, particularly in certain types of blood cancers, such as B-cell lymphomas and acute lymphoblastic leukemia (ALL). The therapy has achieved notable responses even in patients who have not responded to traditional treatments like chemotherapy. While CAR-T cell therapy represents a groundbreaking advance in cancer treatment, it is essential to note that there can be significant side effects, including cytokine release syndrome (CRS) and neurotoxicity. The field is actively researching ways to manage these side effects and expand the application of CAR-T cell therapy to other types of cancers [53].

Treatment of Late-Stage Cancers

Immunotherapy has demonstrated efficacy in treating advanced or metastatic cancers, where traditional treatments may have limited success. Immunotherapy has shown notable efficacy in the treatment of late-stage or metastatic cancers, offering new hope for patients who may not respond well to traditional treatments in these advanced stages [54]. The ability of immunotherapy to harness the body's own immune system to target and attack cancer cells has led to significant advancements in cancer care. Late-stage cancers often pose challenges for treatment because they may have spread to various parts of the body, making surgical removal difficult, and they may have developed resistance to conventional therapies like chemotherapy [55]. Immunotherapy provides a different approach by enhancing the body's immune response against cancer cells, and it has demonstrated success in various types of advanced cancers [56]. Certain immunotherapy strategies, such as immune checkpoint inhibitors (like anti-PD-1, anti-PD-L1 drugs anti-CTLA-4), CAR-T cell therapy, and other immune-modulating agents, have shown efficacy in extending survival and improving the quality of life for patients with late-stage cancers. It's important to note that the effectiveness of immunotherapy can vary among different types of cancers and even among individual patients [57]. Ongoing research is focused on identifying biomarkers and refining treatment strategies to maximize the benefits of immunotherapy in late-stage cancer cases. The success stories in treating advanced cancers with immunotherapy highlight the transformative potential of this approach in offering more personalized and effective treatment options for patients facing challenging diagnoses [58].

Patient-Centric Approach

Immunotherapy's potential for fewer side effects and improved quality of life aligns with a patient-centric approach to cancer care. While immunotherapy has shown remarkable progress, challenges still exist, including resistance, identifying optimal combinations, and expanding its effectiveness to a broader range of cancers. Research is ongoing to address these challenges and further refine the use of immunotherapy in cancer treatment [59]. Your statements accurately capture the patient-centric approach in the context of immunotherapy and acknowledge both its significant progress and the existing challenges. Compared to traditional treatments like chemotherapy, immunotherapy

often has a more favorable side effect profile. This is a crucial aspect of a patient-centric approach as it contributes to improved quality of life during and after treatment. Personalized Treatment: Immunotherapy's ability to target specific biomarkers or utilize a patient's own immune cells in therapies like CAR-T cell therapy aligns with the trend toward more personalized and targeted cancer treatments [60]. Increasing emphasis on identifying biomarkers to predict patient response. Personalized treatment plans based on individual tumor profiles. Combining different immunotherapies or combining immunotherapy with traditional treatments. Enhanced efficacy and reduced resistance. Side effects like immune-related adverse events are monitored and managed. Improved strategies to minimize side effects and enhance patient quality of life. Programs to provide access to immunotherapies outside of clinical trials. Increasing accessibility for patients, especially in regions with limited resources. Efforts to educate patients about immunotherapy and provide emotional support. Understanding and overcoming resistance to immunotherapy. Extending immunotherapy to more cancer types. Monitoring long-term effects and potential late toxicities. Immunotherapy is transforming cancer treatment, with ongoing efforts to refine approaches and make them more patient-centric [61].

Challenges in Immunotherapy

Some patients may not respond to immunotherapy or may develop resistance over time. Understanding the mechanisms of resistance and developing strategies to overcome it are active areas of research. Identifying the most effective combinations of immunotherapies and their integration with other treatment modalities remains a challenge. Combinatorial approaches aim to enhance efficacy and address resistance [62]. Expanding Effectiveness: While immunotherapy has shown success in certain cancers, extending its benefits to a broader range of cancer types remains a goal. Researchers are actively investigating how to make immunotherapy more effective across various tumor types. While immunotherapy has shown remarkable success in treating certain cancers, it is not without limitations [63]. Responses to immunotherapy can vary widely among patients and cancer types. While some individuals experience durable responses, others may not respond or may develop resistance over time. Immunotherapy has been more successful in certain types of cancers, such as melanoma, lung cancer, and certain hematological malignancies. Its efficacy in other cancers, including some solid tumors, may be more limited. Some tumors create a microenvironment that actively suppresses immune responses. This can hinder the effectiveness of immunotherapy by preventing immune cells from recognizing and attacking cancer cells. Identifying patients who are likely to respond to immunotherapy remains a challenge. While certain biomarkers, like PD-L1 expression, are used, they are not universally predictive, and new biomarkers are needed for accurate patient selection. Patients may exhibit primary resistance to immunotherapy, meaning they do not respond from the outset [64]. Additionally, acquired resistance can develop over time, limiting the duration of responses. Immunotherapy has shown more success in treating hematological cancers and some metastatic solid tumors. Immune checkpoint inhibitors and other immunotherapies can lead to immune-related adverse events, where the immune system attacks healthy tissues [65]. These side effects can range from mild to severe and may require additional management. The cost of some immunotherapies, particularly newer treatments and personalized approaches like CAR-T cell therapy, can be high. This cost can pose challenges in terms of accessibility and affordability for some patients and healthcare systems [66]. Tumors with a low mutational burden may be less responsive to immunotherapy. High mutational burden tumors tend to have more neo-antigens, making them more recognizable to the immune system. Immunotherapy's success in pediatric cancers, particularly solid tumors, has been more limited compared to adult cancers. The unique characteristics of pediatric tumors pose additional challenges. To overcome resistance and enhance efficacy, combination therapies are often explored [67]. However, finding optimal combinations without increasing toxicity can be challenging. Despite these limitations, ongoing research and clinical trials are focused on addressing these challenges and expanding the applicability of immunotherapy. Combining immunotherapy with other treatment modalities, identifying new biomarkers, and developing strategies to overcome resistance are areas of active investigation to enhance the effectiveness of immunotherapy in a broader range of cancers.

Ongoing Research

Continued research is essential for identifying reliable biomarkers that can predict patient responses to immunotherapy. Scientists are exploring innovative strategies, including novel immunotherapy agents, gene therapies, and approaches to modulate the tumor microenvironment, to address current challenges and enhance the effectiveness of immunotherapy [68]. While immunotherapy has marked a transformative shift in cancer treatment, acknowledging and addressing the challenges is crucial for its continued success. A patient-centric approach involves not only providing effective treatments with fewer side effects but also adapting and improving therapies based on ongoing research and understanding of the complexities of cancer biology and the immune system. However, please note that advancements may have occurred since then, and it's important to consult the latest medical literature or healthcare professionals for the most up-to-date information.

Currently Used Monoclonal Antibody

(Table 1) Approved/non-Approved Monoclonal Antibodies for Cancer provide a list of some monoclonal antibodies that were approved for cancer therapeutics up to that point. Please note that the information may have changed, and new drugs may have been approved since then. Additionally, the approval status can vary by country. Always consult the latest medical literature, clinical guidelines, or healthcare professionals for the most up-to-date information. The Antibody Society maintains a comprehensive list of approved/ non-approved antibody therapeutics in cancer [69-71].

NN	Brand name	Target; Format	1st indication approved / reviewed	1st EU approval year	1st US approval year
Linvoseltamab	(Pending)	BCMA, CD3; Human IgG4	Multiple myeloma	Review	NA
Axatilimab	(Pending)	CSF-1R; Humanized IgG4	Graft-versus-host disease	NA	Review
Patritumab deruxtecan	(Pending)	HER3; Human IgG1 ADC	Non-small cell lung cancer	NA	Review
Tarlatamab	(Pending)	DLL, CD3; scFv-scFv-scFc bispecific	Small cell lung cancer	NA	Review
Marstacimab	(Pending)	Tissue factor pathway inhibitor; Human IgG1	Hemophilia	Review	Review
Garadacimab	(Pending)	Factor XIIa; Human IgG1	Hereditary angioedema	Review	NA
Zolbetuximab	(Pending)	Claudin 18.2; Chimeric IgG1	Gastric or gastroesophageal junction adenocarcinoma	Review	Review
Odronextamab	(Pending)	CD20, CD3; Human IgG4, bispecific	Diffuse large B cell lymphoma, follicular lymphoma	Review	Review
Crovalimab	(Pending)	Complement C5; Humanized IgG1	Paroxysmal nocturnal hemoglobinuria	Review	Review
Camrelizumab	(Pending)	PD-1; Human IgG4	Hepatocellular carcinoma	NA	Review
Serplulimab	(Pending)	PD-1; Human IgG4	Small cell lung cancer	Review	NA
Sugemalimab	(Pending)	PD-L1; Human IgG4	Non-small cell lung cancer	Review	NA
Concizumab	Alhemo™	Tissue factor pathway inhibitor; Humanized IgG4	Hemophilia	Review	2nd cycle review
Cosibelimab	(Pending)	PD-L1; Human IgG1	Squamous cell carcinoma	NA	2nd cycle review
Trastuzumab duocarmazine	(Pending)	HER2; Humanized IgG1 ADC	Breast cancer	MAA withdrawn	2nd cycle review
Donanemab	(Pending)	Amyloid beta Humanized IgG1	Alzheimer's disease	NA	2nd cycle review
Sintilimab	(Pending)	PD-1; Human IgG4	Non-small cell lung cancer	NA	2nd cycle review
Narsoplimab	(Pending)	MASP-2; Human IgG4	Hematopoietic stem cell transplant-associated thrombotic microangiopathies	NA	2nd cycle review
Pozelimab	VEOPOZ	Complement 5; Human IgG4	CHAPLE disease	NA	2023

Elranatamab	Elrexfio	BCMA, CD3; Humanized IgG2	Multiple myeloma	2023	2023
Rozanolixizumab	RYSTIGGO®	FcRn; Humanized IgG4	Generalized myasthenia gravis	**2024**	2023
Talquetamab	TALVEY	G protein-coupled receptor 5D, CD3; Humanized IgG4 bispecific	Multiple myeloma	2023	2023
Epcoritamab	EPKINLY™	CD20, CD3; Bispecific humanized IgG1	Diffuse large B cell lymphoma	2023	2023
Lebrikizumab	Ebglys	IL-13; humanized IgG4	Atopic dermatitis	2023	NA
Glofitamab	Columvi®	CD20, CD3e; Bispecific 2+1 IgG1 CrossMab	Diffuse large B-cell lymphoma	2023	2023
Mirikizumab	Omvoh	IL-23p19;Humanized IgG4	Ulcerative colitis	2023	2023
Tislelizumab	TEVIMBRA	PD-1; Humanized IgG4	Esophageal squamous cell carcinoma	2023	2nd cycle review
Toripalimab	LOQTORZI, Tuoyi	PD-1; Humanized IgG4	Nasopharyneal carcinoma, esophageal squamous cell carcinoma	Review	2023
Retifanlimab	Zynyz	PD-1; Humanized IgG4	Merkel cell carcinoma	Review	2023
Lecanemab	Leqembi	Amyloid beta protofibrils; Humanized IgG1	Alzheimer's disease	Review	2023
Teplizumab	TZIELD	CD3; Humanized IgG1	Delay onset of type 1 diabetes	NA	2022
Ublituximab	BRIUMVI	CD20; Chimeric IgG1	Multiple sclerosis	2023	2022
Mirvetuximab soravtansine	ELAHERE	Folate receptor alpha; Humanized IgG1 ADC	Ovarian cancer	Review	2022
Nirsevimab	Beyfortus	RSV; Human IgG1	RSV infection	2022	2023
Tremelimumab	Imjudo	CTLA-4; Human IgG2A	Antineoplastic; liver cancer	2023	2022
Spesolimab	SPEVIGO®	IL-36 receptor; Humanized IgG1	Generalized pustular psoriasis	2022	2022
Teclistamab	TECVAYLI	BCMA, CD3; Humanized bispecific IgG4	Multiple myeloma	2022	2022
Mosunetuzumab	Lunsumio	CD20, CD3; Humanized bispecific IgG1	Follicular lymphoma	2022	2022
Tixagevimab, cilgavimab	Evusheld	SARS-CoV-2; Human IgG1	COVID-19	2022	EUA
Relatlimab	Opdualag (relatlimab + nivolumab combo)	LAG-3; Human IgG4	Melanoma	2022	2022
Tebentafusp	KIMMTRAK	gp100, CD3; Bispecific immunoconjugate (TCR-scFv)	Metastatic uveal melanoma	2022	2022

Faricimab	Vabysmo	VEGF-A, Ang-2; Human/ humanized IgG1 kappa/ lambda, with domain crossover	wAMD, DME	2022	2022
Sutimlimab	Enjaymo	C1s; Humanized IgG4	Cold agglutinin disease	2022	2022
Sotrovimab	Xevudy	SARS-CoV-2; Human IgG1	COVID-19	2021	NA
Regdanvimab	Regkirona	SARS-CoV-2; Human IgG1	COVID-19	2021	NA
Casirivimab + imdevimab	REGEN-COV, Ronapreve	SARS-CoV-2; Human IgG1	COVID-19	2021	EUA
Tezepelumab	Tezspire	Thymic stromal lymphopoietin; Human IgG2	Severe asthma	2022	2021
Tisotumab vedotin	TIVDAK	Tissue factor; Human IgG1 ADC	Cervical cancer	Review	2021
Amivantamab	Rybrevant	EGFR, cMET; Human bispecific IgG1	NSCLC w/ EGFR exon 20 insertion mutations	2021	2021
Anifrolumab	Saphnelo	IFNAR1; Human IgG1	Systemic lupus erythematosus	2022	2021
Loncastuximab tesirine	Zynlonta	CD19; Humanized IgG1 ADC	Diffuse large B-cell lymphoma	2022	2021
Bimekizumab	Bimzelx	IL-17A,F; Humanized IgG1	Psoriasis	2021	2023
Tralokinumab	Adtralza	IL-13; Human IgG4	Atopic dermatitis	2021	2021
Evinacumab	Evkeeza	Angiopoietin-like 3; Human IgG4	Homozygous familial hypercholesterolemia	2021	2021
Aducanumab	Aduhelm	Amyloid beta; Human IgG1	Alzheimer's disease	MAA withdrawn	2021
Dostarlimab	Jemperli	PD-1; Humanized IgG4	Endometrial cancer	2021	2021
Ansuvimab	Ebanga	Ebola virus; Human IgG1	Ebola infection	NA	2020
Margetuximab	MARGENZA	HER2; Chimeric IgG1	HER2+ breast cancer	NA	2020
Naxitamab	DANYELZA	GD2; Humanized IgG1	High-risk neuroblastoma and refractory osteomedullary disease	NA	2020
Atoltivimab, Maftivimab, and Odesivimab-ebgn	Inmazeb	Ebola virus; mixture of 3 human IgG1	Ebola virus infection	NA	2020
Belantamab mafodotin	BLENREP	BCMA; Humanized IgG1 ADC	Multiple myeloma	2020	2020
Tafasitamab	Monjuvi, Minjuvi	CD19; Humanized IgG1	Diffuse large B-cell lymphoma	2021	2020
Satralizumab	Enspryng	IL-6R; Humanized IgG2	Neuromyelitis optica and neuromyelitis optica spectrum disorders	2021	2020
Inebilizumab	Uplizna	CD19; Humanized IgG1	Neuromyelitis optica and neuromyelitis optica spectrum disorders	2022	2020

Sacituzumab govitecan	Trodelvy	TROP-2; Humanized IgG1 ADC	Triple-neg. breast cancer	2021	2020
Teprotumumab	Tepezza	IGF-1R; Human IgG1	Thyroid eye disease	NA	2020
Isatuximab	Sarclisa	CD38; Chimeric IgG1	Multiple myeloma	2020	2020
Eptinezumab	Vyepti	CGRP; Humanized IgG1	Migraine prevention	2022	2020
[fam]-trastuzumab deruxtecan	Enhertu	HER2; Humanized IgG1 ADC	HER2+ breast cancer	2021	2019
Enfortumab vedotin	Padcev	Nectin-4; Human IgG1 ADC	Urothelial cancer	2022	2019
Crizanlizumab	Adakveo	P-selectin; Humanized IgG2	Sickle cell disease	2020	2019
Brolucizumab	BEOVU	VEGF-A; Humanized scFv	Macular degeneration	2020	2019
Polatuzumab vedotin	Polivy	CD79b; Humanized IgG1 ADC	Diffuse large B-cell lymphoma	2020	2019
Risankizumab	Skyrizi	IL-23p19; Humanized IgG1	Plaque psoriasis	2019	2019
Romosozumab	Evenity	Sclerostin; Humanized IgG2	Osteoporosis in postmenopausal women at risk of fracture	2019	2019
Caplacizumab	Cablivi	von Willebrand factor; Humanized Nanobody	Acquired thrombotic thrombo- cytopenic purpura	2018	2019
Ravulizumab	Ultomiris	C5; Humanized IgG2/4	Paroxysmal nocturnal hemoglobinuria	2019	2018
Emapalumab	Gamifant	IFNgamma; Human IgG1	Primary hemophagocytic lymphohistiocytosis	NA	2018
Cemiplimab	Libtayo	PD-1; Human IgG4	Cutaneous squamous cell carcinoma	2019	2018
Fremanezumab	Ajovy	CGRP; Human IgG2	Migraine prevention	2019	2018
Moxetumomab pasudotox	Lumoxiti	CD22; Murine IgG1 dsFv immunotoxin	Hairy cell leukemia	2021	2018
Galcanezumab	Emgality	CGRP; Human IgG4	Migraine prevention	2018	2018
Lanadelumab	Takhzyro	Plasma kallikrein; Human IgG1	Hereditary angioedema attacks	2018	2018
Mogamulizumab	Poteligeo	CCR4; Humanized IgG1	Cutaneous T cell lymphoma	2018	2018
Erenumab	Aimovig	CGRP receptor; Human IgG2	Migraine prevention	2018	2018
Tildrakizumab	Ilumya	IL-23p19; Humanized IgG1	Plaque psoriasis	2018	2018
Ibalizumab	Trogarzo	CD4; Humanized IgG4	HIV infection	2019	2018
Burosumab	Crysvita	FGF23; Human IgG1	X-linked hypophosphatemia	2018	2018
Durvalumab	IMFINZI	PD-L1; Human IgG1	Bladder cancer	2018	2017
Emicizumab	Hemlibra	Factor IXa, X; Humanized IgG4, bispecific	Hemophilia A	2018	2017
Benralizumab	Fasenra	IL-5Rα; Humanized IgG1	Asthma	2018	2017
Ocrelizumab	OCREVUS	CD20; Humanized IgG1	Multiple sclerosis	2018	2017

Guselkumab	TREMFYA	IL-23 P19; Human IgG1	Plaque psoriasis	2017	2017
Inotuzumab ozogamicin	BESPONSA	CD22; Humanized IgG4, ADC	Hematological malignancy	2017	2017
Sarilumab	Kevzara	IL-6R; Human IgG1	Rheumatoid arthritis	2017	2017
Dupilumab	Dupixent	IL-4Rα; Human IgG4	Atopic dermatitis	2017	2017
Avelumab	Bavencio	PD-L1; Human IgG1	Merkel cell carcinoma	2017	2017
Brodalumab	Siliq, LUMICEF	IL-17R; Human IgG2	Plaque psoriasis	2017	2017
Atezolizumab	Tecentriq	PD-L1; Humanized IgG1	Bladder cancer	2017	2016
Bezlotoxumab	Zinplava	*Clostridium difficile enterotoxin* B; Human IgG1	Prevention of Clostridium *difficile infection* recurrence	2017	2016
Olaratumab	Lartruvo	PDGRFα; Human IgG1	Soft tissue sarcoma	2016#	2016#
Reslizumab	Cinqaero, Cinqair	IL-5; Humanized IgG4	Asthma	2016	2016
Obiltoxaximab	Anthim	Protective antigen of B. anthracis exotoxin; Chimeric IgG1	Prevention of inhalational anthrax	2020	2016
Ixekizumab	Taltz	IL-17a; Humanized IgG4	Psoriasis	2016	2016
Daratumumab	Darzalex	CD38; Human IgG1	Multiple myeloma	2016	2015
Elotuzumab	Empliciti	SLAMF7; Humanized IgG1	Multiple myeloma	2016	2015
Necitumumab	Portrazza	EGFR; Human IgG1	Non-small cell lung cancer	2015	2015
Idarucizumab	Praxbind	Dabigatran; Humanized Fab	Reversal of dabigatran-induced anticoagulation	2015	2015
Alirocumab	Praluent	PCSK9; Human IgG1	High cholesterol	2015	2015
Mepolizumab	Nucala	IL-5; Humanized IgG1	Severe eosinophilic asthma	2015	2015
Evolocumab	Repatha	PCSK9; Human IgG2	High cholesterol	2015	2015
Dinutuximab	Qarziba; Unituxin	GD2; Chimeric IgG1	Neuroblastoma	2017; 2015#	2015
Secukinumab	Cosentyx	IL-17a; Human IgG1	Psoriasis	2015	2015
Nivolumab	Opdivo	PD1; Human IgG4	Melanoma, non-small cell lung cancer	2015	2014
Blinatumomab	Blincyto	CD19, CD3; Murine bispecific tandem scFv	Acute lymphoblastic leukemia	2015	2014
Pembrolizumab	Keytruda	PD1; Humanized IgG4	Melanoma	2015	2014
Ramucirumab	Cyramza	VEGFR2; Human IgG1	Gastric cancer	2014	2014
Vedolizumab	Entyvio	α4β7 integrin; Humanized IgG1	Ulcerative colitis, Crohn disease	2014	2014
Siltuximab	Sylvant	IL-6; Chimeric IgG1	Castleman disease	2014	2014
Obinutuzumab	Gazyva	CD20; Humanized IgG1; Glycoengineered	Chronic lymphocytic leukemia	2014	2013
Ado-trastuzumab emtansine	Kadcyla	HER2; Humanized IgG1, ADC	Breast cancer	2013	2013

Raxibacumab	(Pending)	B. anthrasis PA; Human IgG1	Anthrax infection	NA	2012
Pertuzumab	Perjeta	HER2; Humanized IgG1	Breast Cancer	2013	2012
Brentuximab vedotin	Adcetris	CD30; Chimeric IgG1, ADC	Hodgkin lymphoma, systemic anaplastic large cell lymphoma	2012	2011
Belimumab	Benlysta	BLyS; Human IgG1	Systemic lupus erythematosus	2011	2011
Ipilimumab	Yervoy	CTLA-4; Human IgG1	Metastatic melanoma	2011	2011
Denosumab	Prolia	RANK-L; Human IgG2	Bone Loss	2010	2010
Tocilizumab	RoActemra, Actemra	IL-6R; Humanized IgG1	Rheumatoid arthritis	2009	2010
Ofatumumab	Arzerra	CD20; Human IgG1	Chronic lymphocytic leukemia	2010#	2009
Canakinumab	Ilaris	IL-1β; Human IgG1	Muckle-Wells syndrome	2009	2009
Golimumab	Simponi	TNF; Human IgG1	Rheumatoid and psoriatic arthritis, ankylosing spondylitis	2009	2009
Ustekinumab	Stelara	IL-12/23; Human IgG1	Psoriasis	2009	2009
Certolizumab pegol	Cimzia	TNF; Humanized Fab, pegylated	Crohn disease	2009	2008
Catumaxomab	Removab	EPCAM/CD3;Rat/mouse bispecific mAb	Malignant ascites	Review; 2009#	NA
Eculizumab	Soliris	C5; Humanized IgG2/4	Paroxysmal nocturnal hemoglobinuria	2007	2007
Ranibizumab	Lucentis	VEGF; Humanized IgG1 Fab	Macular degeneration	2007	2006
Panitumumab	Vectibix	EGFR; Human IgG2	Colorectal cancer	2007	2006
Natalizumab	Tysabri	a4 integrin; Humanized IgG4	Multiple sclerosis	2006	2004
Bevacizumab	Avastin	VEGF; Humanized IgG1	Colorectal cancer	2005	2004
Cetuximab	Erbitux	EGFR; Chimeric IgG1	Colorectal cancer	2004	2004
Efalizumab	Raptiva	CD11a; Humanized IgG1	Psoriasis	2004#	2003#
Omalizumab	Xolair	IgE; Humanized IgG1	Asthma	2005	2003
Tositumomab-I131	Bexxar	CD20; Murine IgG2a	Non-Hodgkin lymphoma	NA	2003#
Ibritumomab tiuxetan	Zevalin	CD20; Murine IgG1	Non-Hodgkin lymphoma	2004	2002
Adalimumab	Humira	TNF; Human IgG1	Rheumatoid arthritis	2003	2002
Alemtuzumab	MabCampath, Campath-1H; Lemtrada	CD52; Humanized IgG1	Chronic myeloid leukemia#; multiple sclerosis	2013; 2001#	2014; 2001#
Gemtuzumab ozogamicin	Mylotarg	CD33; Humanized IgG4, ADC	Acute myeloid leukemia	2018	2017; 2000#
Trastuzumab	Herceptin	HER2; Humanized IgG1	Breast cancer	2000	1998
Infliximab	Remicade	TNF; Chimeric IgG1	Crohn disease	1999	1998

Palivizumab	Synagis	RSV; Humanized IgG1	Prevention of respiratory syncytial virus infection	1999	1998
Basiliximab	Simulect	IL-2R; Chimeric IgG1	Prevention of kidney transplant rejection	1998	1998
Daclizumab	Zenapax; Zinbryta	IL-2R; Humanized IgG1	Prevention of kidney transplant rejection; multiple sclerosis	2016; 1999#	2016; 1997#
Rituximab	MabThera, Rituxan	CD20; Chimeric IgG1	Non-Hodgkin lymphoma	1998	1997
Abciximab	Reopro	GPIIb/IIIa; Chimeric IgG1 Fab	Prevention of blood clots in angioplasty	1995*	1994
Edrecolomab	Panorex	EpCAM; Murine IgG2a	Colorectal cancer	1995*#	NA
Nebacumab	Centoxin	Endotoxin; Human IgM	Gram-negative sepsis	1991*#	NA
Muromonab-CD3	Orthoclone Okt3	CD3; Murine IgG2a	Reversal of kidney transplant rejection	1986*	1986#

Table 1: Approved/non-Approved Monoclonal Antibodies for Various Cancer types.

Conclusion

Immunotherapy has emerged as a transformative approach in cancer treatment, with notable successes in unleashing the body's immune system against cancer cells. The prospects are exciting, with ongoing efforts in combining therapies, identifying biomarkers, and expanding indications. However, challenges such as response variability, autoimmune side effects, cost, and understanding complex mechanisms persist. Overcoming these challenges is crucial for realizing the full potential of immunotherapy and ensuring its broader accessibility. The journey of immunotherapy in cancer treatment is dynamic and promising. Collaborative efforts from researchers, clinicians, and the pharmaceutical industry will play a pivotal role in shaping the future of cancer immunotherapy, offering new hope and possibilities for patients worldwide. As research continues, it is essential to stay informed about the latest developments and consult with healthcare professionals for personalized treatment options.

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