Review Article

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Emerging technology trends in regulatory approvals of cancer immunotherapy drugs by the FDA and EMA

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Abstract

Immunotherapy is an emerging field in medicine using the body's immune to combat various diseases, particularly cancer. In recent years, several immunotherapy agents have obtained regulatory approval from the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) for the management of different types of neoplasms. Notable developments include approvals for bispecific antibodies, antibody-drug conjugates, checkpoint inhibitors, and CAR T-cell therapies. They work by stimulating the immune system, suppressing the pathways that support cancer cells in evading immune system detection, or introducing genetically engineered immune cells to target specific antigens on cancer cells. These agents have demonstrated remarkable safety and efficacy in various clinical trials, targeting different mechanisms of action, indications, and patient populations. This article presents a thorough overview of the recent immunotherapy approvals granted by the FDA and the EMA, highlighting their mechanisms of action, indications, and clinical evidence. Overall, the recent approvals constitute a remarkable achievement in the advancement of novel and efficacious cancer therapies that can enhance patient outcomes and quality of life.

Keywords: Immunotherapy, CAR T-cell, bispecific antibodies, checkpoint inhibitors, antibody-drug conjugate

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1. Introduction

Cancer treatment comprises a range of strategies designed to target and eradicate tumor cells. These strategies encompass conventional interventions such as chemotherapy, radiation therapy, and surgical procedures, alongside more recent advancements such as immunotherapy and targeted therapy. Nonetheless, the efficacy of these therapies is remarkably shaped by the tumor microenvironment (TME), which is pivotal in controlling growth, metastasis, and response to cancer treatment (1). The TME in blood cancers and solid tumors display distinctive features. In blood cancers, the TME is predominantly associated with the bone marrow and the lymphatic system, where cancerous cells, such as leukemia, lymphoma, and multiple myeloma (MM), frequently infiltrate and disrupt normal hematopoietic and immune functions (2). In solid tumors developed in specific tissues or organs, the TME is characterized by a multifaceted and dynamic network of components. These components include cancer cells, blood vessels, immune cells, fibroblasts, and the extracellular matrix. The existence of immunosuppressive

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elements, such as regulatory T cells and myeloid-derived suppressor cells presents distinct challenges that researchers are widely addressing (3).

Recently, substantial progress have been achieved in the advancement of new and improved immunotherapy technologies for both blood and solid tumors (4). One such technology is chimeric antigen receptor T-cell (CAR T-cell) therapy, wherein altering the T cells of a patient through genetic engineering enables the specific targeting and elimination of malignant cells. Another promising technology is checkpoint inhibitors, which effectively hinder the proteins employed by cancer cells to avoid the immune system. Bispecific antibodies (BsAbs), which are designed to identify two different targets at the same time, are also an emerging area of immunotherapy. These antibodies can target cancer cells more specifically while reducing side effects. Furthermore, novel approaches such as oncolytic viruses, cancer vaccines, and gene editing tools are being investigated for their potential in cancer immunotherapy. The ongoing research and development of these technologies hold great promise in improving the outcomes of cancer patients (5).

In recent years, a series of immunotherapies have been authorized via both the EMA and FDA for various types of malignancies. Several checkpoint inhibitors were approved, including the PD-1 inhibitors Jemperli (dostarlimab) and Imjudo (tremelimumab), for the management of hepatocellular carcinoma or endometrial cancer. Other checkpoint inhibitors, Opdualag (nivolumab and relatlimab), were also authorized for the management of specific forms of metastatic melanoma. Additionally, three CAR T-cell therapies designed for controlling MM and Large B-cell lymphoma (LBCL) have received approval. Another milestone in immunotherapy was the approval of four new antibody-drug conjugates (ADC) including Elahere, Padcev, Zynlonta, and Tivdak. Furthermore, BsAbs emerged as a promising immunotherapeutic approach. Among the notable approvals was the bispecific antibody Rybrevant, which has shown remarkable potential in non-small cell lung cancer (6, 7). These approvals represent important advances in the field of immunotherapy and grant additional treatment options for patients with cancer. In subsequent sections, we will conduct a comprehensive investigation of the mechanisms, indications, and implications of these groundbreaking immunotherapies.

2. Therapeutic monoclonal antibodies (mAbs)

Monoclonal antibodies (mAbs) are composed of immunoglobulins (Igs) featuring two Fab terminals responsible for target binding and an Fc end that attaches to immune cells' surface receptors. Although Fab terminals are primarily responsible for direct targeting, interactions between Fc and its receptor can also influence their mechanisms of action (MOA). Effector functions facilitated by Fc comprise antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and complement-dependent cytotoxicity (CDC) (8). ADCC and ADCP involve the interaction of FcγR and Fc with NK cells and macrophages, respectively. CDC involves Fc interacting with C1q, activating the complement system (9). In addition, mAbs can bind and block soluble antigens and disease mediators. Various mAbs targeting CD20, CD19, HER-2, VEGFA, EGFR, and CD52 have been approved by the FDA since rituximab was approved in 1997 (10). Besides unconjugated or naked mAbs, conjugated mAbs and BsAbs are employed in treating cancer. Unlike naked mAbs, conjugated mAbs are linked with radioisotopes or chemotherapy drugs, while BsAbs fuse two distinct binding fragments to unite two cells (11).

2.1. Checkpoint inhibitors mAbs

T-cells have important immune checkpoints on their surface to regulate the immune system and prevent hyperactivation and autoimmune disease. Nevertheless, cancerous cells utilize these checkpoints to avoid immune detection, leading to immune evasion. mAbs targeting immune checkpoints help restore T cell function by blocking them, permitting the immune system to work effectively. Among the numerous immune checkpoints identified, cytotoxic T lymphocyte-associated antigen-4 (CTLA-4) and programmed cell death ligand 1 (PD-1) have been extensively studied (12). Inhibitors targeting CTLA-4 and PD-1 proteins have demonstrated potential in enhancing the immune response against malignant cells and have been authorized for the management of various malignancies such as bladder cancer, melanoma, kidney cancer, and lung cancer (13). In recent

Table 1. Immunotherapeutics granted first approvals in 2021 by the EMA or the US-FDA.

International nonproprietary name	Trade name	Class	Target	First approved Indication	Date of first US approval	Date of first EU approval
Ropeginterferon alfa-2b	Besremi	Pegylated Protein	IFN a, b receptor	Polycythemia vera	11-12-2021	2-15-2019
Dostarlimab	Jemperli	Humanized IgG4	PD-1	Deficient mismatch repair endometrial cancer	4-22-2021	4-21-2021
Amivantamab	Rybrevant	Human IgG1 bispecific	EGFR, cMet	Non-small cell lung cancer	5-21-2021	positive opinion
Tisotumab vedotin	TIVDAK	Human IgG1 ADC	Tissue factor	Cervical cancer	9-20-2021	NA
Loncastuximab tesirine	Zynlonta	Humanized IgG1 ADC	CD19	Diffuse large B-cell lymphoma	4-23-2021	under review
Lisocabtagene maraleucel	Breyanzi	CAR T-cell	CD19	Large B-cell lymphoma	1-5-2021	4-4-2022
Idecabtagene vicleucel	Abecma	CAR T-cell	B-cell maturation antigen-expressing cells	Multiple myeloma	3-26-2021	8-18-2021

Abbreviations: INF; interferon; IgG, immunoglobulin; PD-1, programmed cell death protein 1; EGFR, epidermal growth factor receptor; ADC, antibody-drug conjugate; NA, not applicable; CAR, chimeric antigen receptor.

times, several checkpoint inhibitors have received authorization for treating various forms of cancer (refer to Tables 1 and 2).

Belonging to the CD28-B7 Ig superfamily, CTLA-4 is located on activated T cells. It plays a key role in regulating immune responses by inhibiting T-cell activation and proliferation (14). Tremelimumab (CP-675206), known as Imjudo, is a human IgG2κ antibody designed to target CTLA-4 in a variety of malignant tumors. In October 2022, the FDA approved its use with durvalumab for unresectable hepatocellular carcinoma (uHCC) in adult patients. Furthermore, in November 2022, it gained the FDA's approval for management of metastatic non-small cell lung cancer (mNSCLC) lacking specific genetic mutations or tumor aberrations (15).

PD-1 is also present in T cells functioning as an immune checkpoint. Different types of cancer cells produce programmed cell death ligand 1 (PD-L1) that binds to PD-1. mAbs targeting the PD-1/PD-L1 signaling pathway can improve T cell function and eliminate cancerous cells by decreasing immunosuppression (16). Dostarlimab (Jemperli) is a humanized mAB functioning as a PD-1 receptor antagonist, with its primary focus on the treatment of various cancer types. In April 2021, the FDA authorized Jemperli based on evidence derived from the GARNET trial (NCT02715284), which involved patients suffered from advanced or recurrent endometrial cancer that exhibited a deficiency in mismatch repair (dMMR) (17). Specifically, it is indicated for cases where certain forms of chemotherapy have failed to be effective or where there are no longer viable treatment options. Dostarlimab also received approval for endometrial cancer treatment in the European Union in April 2021, marking a significant milestone in the realm of oncology (18).

Additional immune checkpoints, like LAG-3, TIGIT, and TIM-3 are continuously being identified. LAG-3 interacts with its main ligand (MHC-II) to decrease T cell function (19). Nivolumab with relatlimab-rmbw (Opdualag) is a combination immunotherapy drug for melanoma treatment. Nivolumab and relatlimab-rmbw target different immune checkpoints, with nivolumab acting on the PD-1 receptor and relatlimab on the LAG-3 protein. Opdualag gained approval in the US and EU in March and September of 2022 respectively (20). The combo was first approved for unresectable or metastatic melanoma based on a trial showing better efficacy than nivolumab alone, with longer survival and slower disease progression (21).

Table 2. Immunotherapeutics granted first approvals in 2022 by the EMA or the US-FDA.

International nonproprietary name	Trade name	Class	Target	First approved indication	Date of first US approval	Date of first EU approval
Tremelimumab	Imjudo	Human IgG2κ	CTLA-4	Hepatocellular carcinoma	10-21-2022	under review
Nivolumab and relatlimab	Opdualag	Combination of Human mAbs	LAG-3 and PD-1	Unresectable or Metastatic Melanoma	3-18-2022	9-15-2022
Mosunetuzumab	Lunsumio	Humanized IgG1κ bispecific	CD20, CD3	Follicular lymphoma	under review	6-3-2022
Tebentafusp	Kimmtrak	Bispecific immunoconjugate	gp100, CD3	Metastatic uveal melanoma	1-25-2022	4-1-2022
Teclistamab	TECVAYLI	Humanized/human IgG4λ bispecific	BCMA, CD3	Multiple myeloma	10-25-2022	8-23-2022
Mirvetuximab soravtansine	ELAHERE	Humanized IgG1κ ADC	FRα	Ovarian cancer	11-14-2022	NA
enfortumab vedotin	Padcev	Human IgG1 ADC	Nectin-4	Urothelial cancer	12-18-2019	2-24-2022
Ciltacabtagene autoleucel	Carvykti	CAR T-cell	B-cell maturation antigen	Multiple myeloma	2-28-2022	5-22-2022

Abbreviations: IgG, immunoglobulin; CTLA-4, Cytotoxic T-lymphocyte associated protein 4; LAG-3, Lymphocyte-activation gene 3; PD-1, programmed cell death protein 1; NA, not applicable; BCMA, B cell maturation antigen; ADC, antibody-drug conjugate; FR, folate receptor.

2.2. Bispecific antibodies (BsAbs)

BsAbs are a class of immunotherapies that have shown significant promise in improving the therapeutic safety and efficacy for various indications, such as cancer and autoimmune diseases. The structure of BsAbs can vary, but most are designed to have a common IgG backbone with two Fab regions, each with the ability to attach to specific antigens. BsAbs can be classified into IgG-like and non-IgG-like classes (Figure 1). The IgG-like BsAbs are larger and offer benefits like enhanced stability, solubility, increased biological activity, and serum half-life. Non-IgG-like BsAbs lack Fc fragments, making them simpler to produce with low immunogenicity (22). Alterations in IgG-like BsAbs involve modifications of the heavy chain to achieve compatibility with different Fc regions. For example, methods such as "knobs-into-holes" change the Fc domain's nearby spatial arrangement, while the strand-exchange engineered domain (SEED) technique promotes heterodimer assembly using complementary sequences. The DuoBody platform involves the exchange of Fab regions through dynamic recombination, facilitated by a linker. The platforms of Dual variable domain immunoglobulin (DVD-IGg) and Fabs-in-tandem immunoglobulin (FIT-Ig) exhibit symmetrical structures. Molecular platforms like "Two-in-one" utilize phage display and employ Wuxibody and Crossmab platforms for light chains to ensure proper pairing (23). Non-IgG-like BsAbs, being Fc-free, have simpler designs. The bispecific T-cell engager (BiTE) connects two single-chain variable fragments using a linker. Dual affinity retargeting (DART) involves combining a variable light chain with a variable heavy chain from two different chains to create the Fv. Other non-IgG-like platforms use VH-only constructs (Bi-Nanobody) and adopt tetravalent antiparallel structures (TandAbs) (24). In cancer immunotherapy, BsAbs can activate T cells targeting and attacking the cancer cells. They can induce various stimulatory or inhibitory effects, as well as recruit and activate additional immune cells for tumor cell eradication (10).

Recent advancements in BsAb technology have led to the development of novel therapeutics. Amivantamab (Amivantamab-vmjw or Rybrevant) is a human BsAb that received FDA authorization in May 2021 for use in adults with

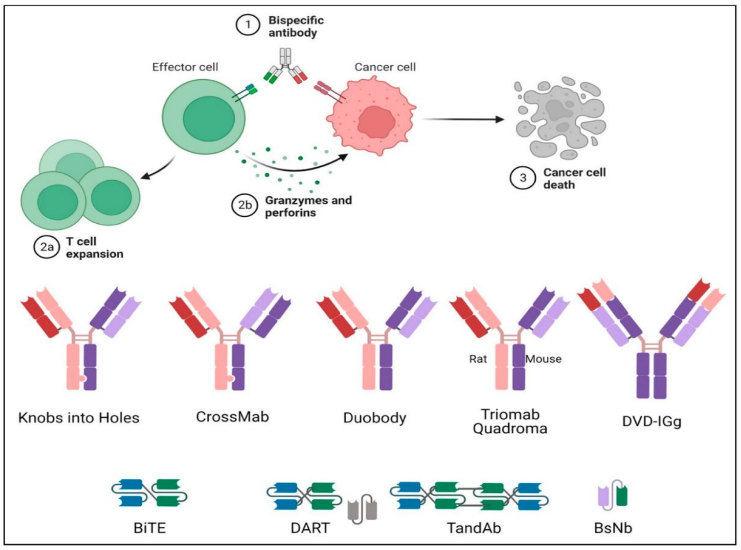

Figure 1. Elucidating the mechanism (upper panel) and structural diversity (lower panel) of bispecific antibodies (BsAbs). The fundamental operational mechanism of BsAbs entails the steps that culminate in T-cell expansion and activation (25).

advanced or metastatic NSCLC with EGFR Exon 20 insertion mutations after undergoing platinum-based chemotherapy. This innovative therapeutic agent is fabricated through cutting-edge DuoBody technology, which allows for precise Fab-arm exchange. The EGFR arm derives from zalutumumab, and the MET-binding arm effectively blocks the hepatocyte growth factor ligand. Amivantamab exhibits a high binding affinity, with dissociation constants of 1.43 and 0.04 nM for the EGFR and MET receptor extracellular domains, respectively (26). Remarkably, it demonstrates antitumor effects through both Fc receptor-independent and dependent pathways, acting to obstruct EGFR and MET signaling through binding to ligands and inactivating the receptor. These multifaceted attributes position amivantamab as a promising candidate in a continual search for improved treatments for NSCLC (26).

In January 2022, tebentafusp was granted approval in the USA following successful outcomes from the phase III IMCgp100-202 clinical trial. Also known as Kimmtrak, tebentafusp is a pioneering BsAb developed for uveal and malignant melanoma treatment. It functions by activating T cells through bridging gp100 peptide-HLA and CD3 T cell receptor (TCR), initiating a response that results in tumor cell destruction (27). Moreover, in February 2022, it received a favorable assessment for uveal melanoma treatment from the EU Committee for Medicinal Products for Human Use (28). Additionally, Teclistamab (JNJ-64007957), approved in October 2022, represents the first IgG4λ T-cell redirecting antibody, developed through Genmab's DuoBody and Ligand's transgenic mouse (OmniAb) technology (29). This BsAb targets CD3 and BCMA was approved by the FDA in adults with relapsed or refractory MM as part of the MajesTEC-1 clinical trials (NCT03145181 and NCT04557098) (30). Furthermore, in December 2022, Mosunetuzumab-axgb (Lunsumio) received FDA accelerated approval for the management of relapsed or refractory follicular lymphoma in adults, who have undergone a minimum of two previous systemic therapies (31). Lunsumio is a glycosylated IgG1κ BsAb, engineered using the innovative Knobs-into-Holes technology. In a comprehensive evaluation within the GO29781 study, this humanized mAb achieved an impressive 80% overall response rate (ORR), including 60% complete responses (32). Overall, numerous clinical trials are assessing the effectiveness and toxicity of BsAbs in diverse hematologic malignancies.

2.3. Antibody-drug conjugates (ADCs)

ADCs represent a targeted cancer therapy that merges the high selectivity of mAbs with the cytotoxic strength of chemotherapeutic drugs (Figure 2). An ADC typically includes three components: a cytotoxic drug, a linker, and a targeting antibody (33). The targeting antibody is chosen

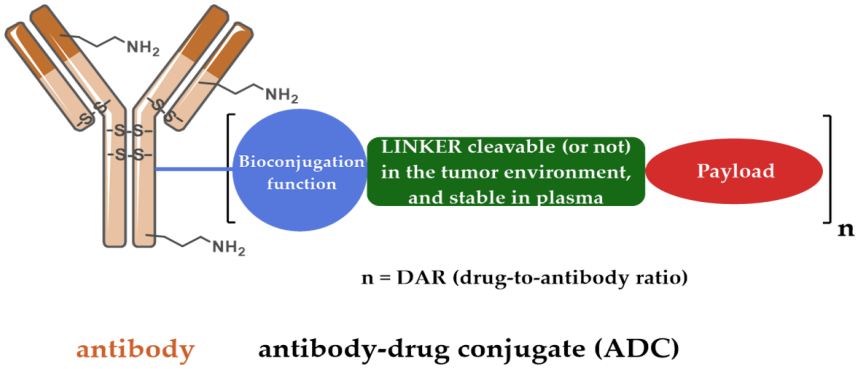

Figure 2. Scheme representing the structure of antibody-drug conjugate (ADC) (35).

based on its specific binding ability to an overexpressed cell-surface antigen found on cancer cells. The linker serves as a bridge between the cytotoxic drug and the antibody needing to remain stable in circulation but readily cleavable once it enters the specific cancerous cell. The cytotoxic drug is usually a highly potent small molecule that can induce cell death by disrupting key cellular processes such as DNA replication, protein synthesis, or microtubule assembly. The MOA of ADCs involves binding the targeting antibody to the cancer cell surface antigen, mostly followed by ADC internalization via receptor-mediated endocytosis. Once inside the cell, the linker can be cleaved, releasing the cytotoxic drug into the cytoplasm or lysosome (34). The drug then causes cell death by binding to its target and exerting cytotoxic effects. By selectively targeting cancer cells, ADCs can potentially reduce off-target toxicity and increase therapeutic efficacy. Despite their potential benefits, ADCs have several limitations and challenges. One major challenge is the design and optimization of the linker, which must balance stability in circulation with efficient drug release inside the target cell. Moreover, the selection of a suitable antibody target is crucial for achieving high specificity and minimizing off-target toxicity. Overall, the rising interest and progress in ADC research and development signify a growing acknowledgment of their capacity to meet the unmet requirements in cancer treatment, thereby providing novel therapeutic alternatives for individuals with challenging malignancies; however, they can cause side effects such as bone marrow suppression, liver toxicity, and infusion-related reactions, which should be carefully monitored and managed in patient care (33).

In recent years, several ADCs have attained regulatory approval, marking significant advancements in cancer therapy. Loncastuximab tesirine-lpyl (Zynlonta) is an ADC designed to bind CD19, a surface marker highly expressed in B-cell malignancies. Comprising a mAb targeting CD19, it delivers a pyrrolobenzodiazepine (PBD) dimer cytotoxin to cells (36). In April 2021, FDA approval for relapsed or refractory LBCL followed the LOTIS-2 trial, which demonstrated a 48.3% ORR and a complete response rate of 24.1%, with a median duration of response (DoR) of 10.3 months (37). Tisotumab vedotin-tftv (Tivdak) is another ADC targeting tissue factor, overexpressed in cancers like cervical cancer. Tivdak consists of a human IgG1κ antibody (TF-011), which is attached to monomethyl auristatin E cytotoxin via a protease-cleavable linker (38). In September 2021, it was granted accelerated approval by the FDA for metastatic or recurrent cervical cancer based on the innovative 204 trial (NCT03438396), showing a 24% ORR and an 8.3-month median DoR (39). In November 2022, Mirvetuximab soravtansine-gynx (IMGN853) was approved by the FDA for treating adults with platinum-resistant, folate receptor alpha-positive (FRα +) fallopian tube, primary epithelial or peritoneal ovarian cancer those who have experienced between one and three previous systemic treatments. IMGN853 consists of a potent maytansinoid drug DM4, a cleavable disulfide linker, and an IgG1κ antibody specifically binding to FRα (40). FDA approval relied on findings from Study 0417, or SORAYA (NCT04296890), revealing a notable ORR of 31.7% and a median DoR of 6.9 months (41). Furthermore, based on results from Cohort 1 of the EV-201 trial, the EMA authorized Enfortumab vedotin (Padcev) in 2022

to manage patients with locally metastatic or advanced urothelial cancer received chemotherapy and a PD-L1 or PD-1 inhibitor. Enfortumab vedotin-ejfv, an ADC, comprises a Nectin-4 targeted antibody linked to a microtubule-disrupting agent MMAE (42). Finally, the triumph of numerous ADCs in clinical trials emphasizes their ability to meet unmet medical demands and offer efficient treatment choices for individuals with different types of cancer. With continuous research and development endeavors dedicated to ADC technologies, the prospect of enhancing cancer therapy outcomes and enriching patient care appears highly promising.

3. Cytokines

Cytokines are pivotal in cancer immunotherapy, orchestrating the immune response against tumors by facilitating communication among immune cells, thereby impacting their activation, proliferation, differentiation, and function. Various cytokines, including tumor necrosis factors, interleukins, colony-stimulating factors, and interferons, have been explored for their therapeutic potential in cancer immunotherapy. These cytokines can be administered alone or in conjunction alongside other forms of treatment including cell therapies, immune checkpoint inhibitors, or cancer vaccines. Nonetheless, the clinical application of cytokine-based therapies is often hindered by their diverse effects and potential for systemic toxicity. Ongoing research endeavors strive to unveil novel cytokine-based strategies characterized by enhanced efficacy and safety profiles for combating cancer. In recent years, Besremi was authorized by the EMA in February 2019 and the FDA in November 2021 as the first and only interferon therapy for polycythemia vera, a rare blood cancer characterized by excessive production of red blood cells. It is a mono-PEGylated interferon alfa-2b that reduces the mutation burden of JAK2V617F, a gene implicated in the pathogenesis of polycythemia vera. The approval was based on the clinical development program by AOP Orphan, a European leader in rare and special diseases. It acts by binding to the interferon alfa receptor in the bone marrow and inhibiting the proliferation of abnormal hematopoietic stem cells (43). Besremi is given by subcutaneous injection every 2 to 4 weeks and has been shown to improve safety, tolerability, and adherence compared to conventional PEGylated interferon products (44).

4. Chimeric antigen receptor T-cell (CAR T-cell) therapy

Cancer cell therapies employ cells, sourced either from the patient (autologous) or a donor (allogeneic), to combat and eradicate cancer cells. These treatments leverage the inherent capabilities of immune cells to identify and eradicate malignant cells or genetically modify them to bolster their anti-tumor functions. Common forms of cancer cell therapies encompass CAR T-cell, natural killer cell, dendritic cell, tumor-infiltrating lymphocyte, and T-cell receptor therapies. CAR T-cell therapy is among commercialized immunotherapy methods where patient T cells are genetically engineered to attack and eliminate cancer cells. This personalized treatment involves extracting patient T cells and genetically modifying them in a lab to create CARs on their outer surface. CARs are designed for identifying and attaching to particular proteins found on the cancer cell surface, stimulating T cells to target and eliminate the malignant cells (45). CAR T-cell therapy involves several steps: initially, the patient's T cells are extracted from the blood via leukapheresis. Then the collected T cells are taken to a laboratory, where they undergo genetic modification to express chimeric antigen receptors (CARs). Subsequently, the modified T cells are cultured in large quantities before being reintroduced into the individual's blood, where they can target and destroy cancerous cells. Clinical trials of CAR T-cell therapy, including Yescarta (axicabtagene ciloleucel) and Kymriah (tisagenlecleucel), have demonstrated encouraging results in the treatment of blood malignancies. Nevertheless, CAR T-cell therapy is costly and associated with potentially severe adverse reactions, icluding cytokine release syndrome (CRS) and neurotoxicity (46).

CAR T-cell therapy has achieved significant advancements in lymphomas, with a primary focus on CD19. Lisocabtagene maraleucel (Breyanzi), represents a CD-19-directed CAR T-cell developed for treating LBCL in adult patients. Notably, it is a fusion of two distinct kinds of patient white blood cells, namely CD4+ T cells and CD8+ T cells (47). This cell therapy product utilizes genetically modified autologous T cells expressing

a CAR composed of a scFv, IgG4 hinge region, 4-1BB costimulatory domain, CD28 transmembrane domain, and a signaling domain CD3 zeta. When attaching to cells expressing CD-19, the CD3 zeta domain activates and proliferates CAR T cells, resulting in antitumor activity through cytokine secretion and cytotoxic killing of targeted cells (48). In February 2021, Breyanzi received FDA approval based on compelling evidence derived from the TRANSFORM clinical trial (49).

CAR T-cell directed BCMA represents an innovative approach for treating MM by altered T-cells to target BCMA specifically expressed on B-cell lineage cells and interacts with B-cell activating factor (BAFF), which are essential for plasma cell growth and signaling pathways (50). In March 2021, Abecma also known as idecabtagene vicleucel became the first FDA-approved CAR T-cell targeting BCMA for relapsed or refractory MM (51). It comprises a CD3ζ signaling domain, the 4-1BB costimulatory motif, a CD8 hinge and transmembrane domain, and a single-chain variable fragment targeting BCMA (52). In 2022, ciltacabtagene autoleucel (Carvykti) received approvals from the EMA and FDA for the treatment of relapsed or refractory MM patients (53). The approval, based on the CARTITUDE-1 trial, demonstrated a high ORR of 97.9% and a median DoR of 21.8 months (54).

5. Conclusion

Immunotherapy has emerged as a revolutionary method for treating a broad range of cancers, encompassing blood cancers such as leukemia, lymphoma, and MM, and solid tumors including lung, breast, and melanoma. In blood cancers, techniques such as mAbs, immune checkpoint inhibitors, and CAR T-cells have become indispensable in leveraging the immune system against these diseases. In solid tumors, immunotherapy shows potential by overcoming the immune system inhibition and enhancing its capacity to detect and eradicate cancer cells. Recent years have seen the approval of various immunotherapy drugs by both the FDA and EMA, primarily including bispecific antibodies, ADCs, checkpoint inhibitors, and CAR T-cell therapy. These strategies have demonstrated encouraging results in clinical trials, including improved survival rates, extended treatment options, long-lasting responses, and personalized medicine. However, challenges such as the diversity of solid tumors, resistance mechanisms, autoimmune toxicities, limited efficacy in certain cancers, and high cost and accessibility persist. Despite the existence of these obstacles, continuous research has the opportunity to transform cancer therapy. Therefore, it is more likely that further approvals of immunotherapy drugs by regulatory agencies like the FDA and EMA will occur for a broad range of cancer indications.

Conflict of Interest

The authors declare no conflict of interest.

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