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Antibody-drug conjugates in the treatment of breast cancer: advances, limitations, and future perspectives – a literature review

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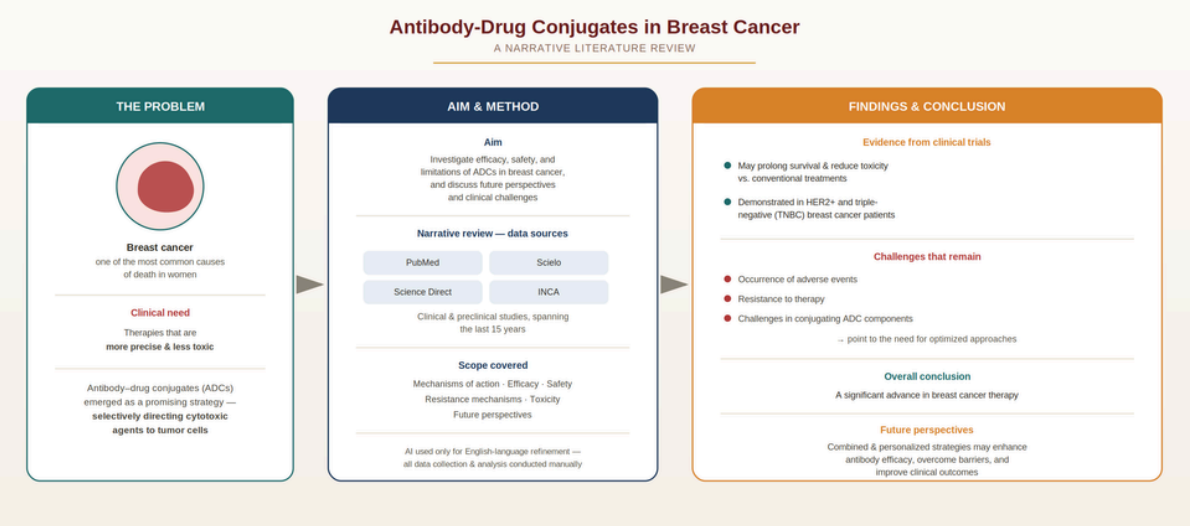

Abstract: Breast cancer is one of the most common causes of death in women and requires therapies that are both more precise and less toxic. Recently, antibody–drug conjugates (ADCs) have emerged as a promising strategy by selectively direct cytotoxic agents to tumor cells. The aim of this review was to investigate the efficacy, safety, and limitations of these antibodies in breast cancer treatment, and discuss their future perspectives and clinical challenges such as resistance and toxicity. This narrative review is based on a search of Pubmed, Scielo, Science Direct and INCA databases, including clinical and preclinical studies and reviews that have investigated the mechanisms of action, efficacy, and safety of ADCs over the last 15 years. Evidence from clinical trials suggests that therapy may prolong survival and reduce toxicity compared to conventional treatments, as demonstrated in clinical trials in HER2+ and TNBC patients. However, the occurrence of adverse events, resistance to therapy, and challenges in conjugating the components point to the need for optimized approaches. Overall, the results suggest that despite the challenges, this technology represents a significant advance in breast cancer therapy and that the integration of combined and personalized strategies may enhance antibody efficacy, overcome current barriers and contribute to better clinical outcomes.

Keywords: Breast Cancer; Antibody–Drug Conjugates; Clinical Trials; Treatment Resistance; Toxicity.

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Introduction

Breast cancer is the most common type among women, less frequent under age 40, more prevalent after the age of 50, and is one of the leading causes of cancer-related death. In 2020, approximately 2.3 million cases were diagnosed, and 685,000 deaths were recorded worldwide. Due to the aging population, it is estimated that by 2040 there will be 3 million new cases and 1 million deaths from this neoplasm [1-3]. Interestingly, about 30% of early-stage breast cancer cases progress to metastatic disease, with an average survival of 8 to 36 months [4]. In Brazil, breast cancer is the most common among women; in 2022, 19,000 deaths were recorded, and by 2025 an estimated 73,610 new cases per year are expected [5].

Although surgery is the treatment of choice for breast cancer, additional therapies such as chemotherapy, hormonal therapy, radiotherapy, or targeted therapy are used according to the disease subtype. While local procedures are becoming less invasive and more precise, targeted therapies are being studied for their lower systemic cytotoxic effects on healthy cells [2].

The therapy with antibody–drug conjugates (ADCs) has emerged as a promising strategy for treating cancer by targeting cancer cells with specific therapeutic molecules [6].

Currently, 14 ADCs are approved for the treatment of solid tumors and hematologic malignancies, three of which are indicated for the treatment of breast cancer in early or metastatic stages. Due to their reduced toxicity and high efficacy, these ADCs improve outcomes compared to conventional chemotherapy and may even be used as first-line treatment [6, 7]. However, some studies have observed resistance to these drugs, and new strategies, such as combination therapies and the use of predictive biomarkers, are being developed to overcome this resistance [8]. In addition to resistance, side effects such as toxicity to adjacent healthy tissues and the potential impact of the payload on immune mediators in the tumor microenvironment may affect treatment outcomes [9].

Methodology

This is a narrative literature review that explores the use of antibody–drug conjugates (ADCs) in breast cancer therapy conducted through a search in PubMed, Scielo, Science Direct and National Cancer Institute (INCA) databases. It included clinical and preclinical studies, as well as review articles published in Portuguese or English over the last 15 years that addressed efficacy, safety, resistance mechanisms and future perspectives of ADCs in breast cancer. This review provides a global overview, with specific data also presented for the Brazilian context to highlight regional challenges in access and production.

Artificial Intelligence tools were not used for data search or analysis. AI assistance (ChatGPT, OpenAI, San Francisco, CA, USA) was used exclusively for English language refinement. The authors conducted all data collection, article selection, and content analysis manually.

Results

Breast cancer

Breast cancer typically manifests as a painless breast nodule with irregular borders, firm consistency, and asymmetrical shape; however, other changes such as alterations in breast size and shape, skin changes (e.g., erythema, ulceration, “orange peel” appearance), or nipple inversion, texture changes, and secretions, can also serve as important warning signs [12].

The main risk factors for breast cancer include age over 50 years, female sex, hormonal or reproductive conditions, positive family history, and history of radiotherapy [13]. It is estimated that about 15% of breast cancers are hereditary, with 10% associated with germline mutations in the BRCA1 and BRCA2 genes, which are often linked to early onset and disease severity [1].

Classification of the different types of breast cancer is crucial to ensure precise diagnosis, predict tumor progression, and define the best therapeutic approach for each patient [14]. Most of these tumors are adenocarcinomas, 85% originate in the breast ducts (which may appear as ductal carcinoma in situ [DCIS] or invasive car-

cinoma) and 15% are lobular in origin, illustrating the clinical diversity of the disease [12].

DCIS is noninvasive and classified as stage 0. Stages I, IIa, and IIb represent early invasive cancer, whereas stages IIIa, IIIb, and IIIc indicate locally advanced disease. These stages are considered non-metastatic, in contrast to stage IV, which is metastatic and characterized by spread to other body regions [13].

From a molecular and histological standpoint, breast cancer is classified into three specific subtypes: tumors expressing estrogen or progesterone receptors (ER+ or PR+), tumors positive for human epidermal growth factor receptor 2 (HER2+), and triple-negative breast cancer (TNBC), which lack both hormonal receptors and HER2 expression [15].

ER+ or PR+ tumors represent 60 to 70% of cases and are usually treated with endocrine therapy using estrogen and progesterone blockers, sometimes complemented by chemotherapy based on the patient's profile [12]. HER2+ tumors are treated with immunotherapy using small-molecule inhibitors and monoclonal antibodies, such as trastuzumab [16]. TNBC, often associated with BRCA1 mutations, is more aggressive with a poorer prognosis. As TNBCs do not express HER2, endocrine therapy is ineffective, limiting patients to chemotherapy and radiotherapy [12].

Approximately 90% of diagnosed breast cancers are non-metastatic, with the primary goal being tumor eradication and recurrence prevention. In metastatic cases, treatment aims to prolong and improve quality of life by alleviating symptoms based on the disease subtype. TNBC, however, shows high recurrence rates and lower survival compared to other subtypes [4]. Neoadjuvant chemotherapy is widely used in TNBC and HER2+ subtypes to reduce tumor size prior to surgery, demonstrating good response rates. Surgical approaches include lumpectomy combined with adjuvant radiotherapy, removing the tumor with a margin of healthy tissue (which is analyzed for residual cancer cells to reduce recurrence risk), and mastectomy, which is indicated when lumpectomy is not feasible. Both methods show similar survival rates' [12].

Antibody-Drug Conjugates (ADCs)

Antibodies are glycoproteins composed of two heavy and two light chains, organized into Fc and Fab fragments. They bind to specific antigens and play immune roles. Their structure, particularly in the IgG2 and IgG4 subclasses, minimizes side effects in nontarget tissues through complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC), making them ideal for ADC production [17-21].

The development of ADCs dates back over a century, when in the early 20th century Paul Ehrlich introduced the concept of "magic bullets", substances capable of targeting specific cells to treat diseases by killing cancer cells while sparing normal ones [22]. Advances such as the ability to link antibodies to cytotoxic agents and the discovery of the hybridoma technique for monoclonal antibody (mAb) production in 1975 culminated in the FDA's approval of the first ADC, Mylotarg®, in 2000 [19, 22-23].

ADCs consist of three fundamental components: recombinant monoclonal antibodies (mAbs), highly potent cytotoxic payloads, and stable linkers [20]. The mAb recognizes antigens on the tumor cell surface and delivers the cytotoxic payload, triggering apoptosis while minimizing damage to healthy cells [9]. These antibodies exhibit high affinity for the antigen target, long plasma half-life, low immunogenicity, and minimal cross-reactivity, facilitating internalization and triggering both direct and indirect immune responses [11].

Payloads, also known as "cytotoxic molecules," play a crucial role in the efficacy and properties of ADCs [24]. They act on various cellular targets such as tubulin (via compounds like auristatins and maytansinoids, which inhibit microtubule polymerization) or DNA (using agents such as

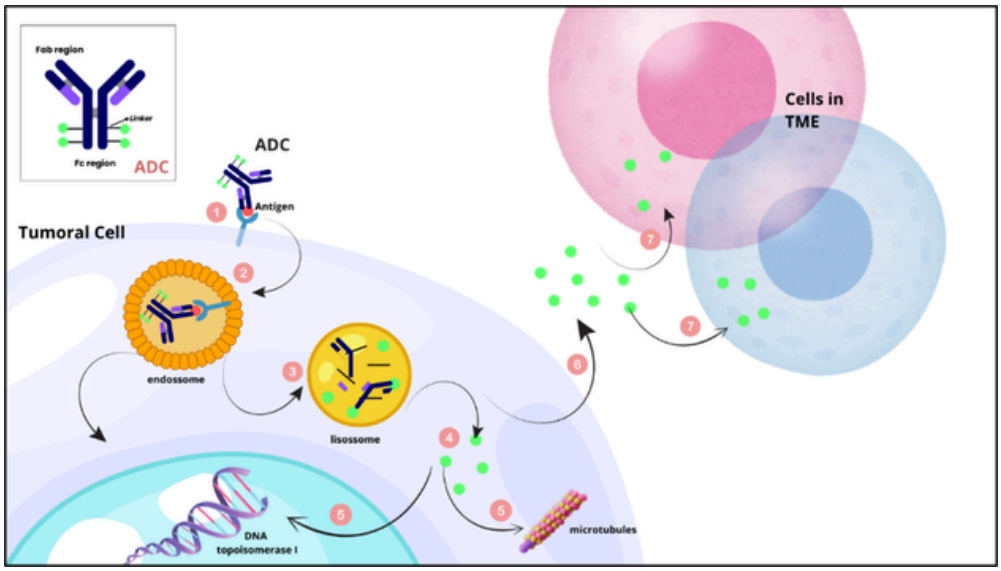
duocarmycins, calicheamicins, anthracyclines, pyrrolobenzodiazepines [PBDs], and SN-38, the active metabolite of irinotecan), causing DNA damage through double-strand breaks or alkylation [17-25].

Ideally, payloads should have high potency, metabolic stability in the bloodstream, good solubility, and functional groups that enhance membrane permeability and conjugation to antibodies [21]. Moreover, they must be selectively delivered to target cells, thus reducing toxicity to healthy cells and increasing the therapeutic index [21, 26-27]. Due to their inherent high potency, payloads are not used as standalone treatments; ADCs are designed to transport only small amounts of these molecules to the tumor [28]. Other factors, such as the number of molecules per ADC, the presence of efflux pumps, and the bystander effect (the ability to kill adjacent cells not expressing the target antigen), also affect their effectiveness [27,29].

Linkers, the stable bonds which connect payloads to antibodies, have specific cleavage mechanisms at the target site that influence the therapeutic window as well as pharmacokinetic and pharmacodynamic factors [20]. They must remain stable in circulation to keep the payload attached to the antibody yet cleavable once the ADC enters the cancer cell, thereby releasing the cytotoxic agent[17]. Additionally, the carrier connection to the antibody should be hydrophilic to facilitate conjugation without affecting the antibody's affinity for its receptor or causing inactive aggregate formation [30]. Linkers are classified as cleavable, allowing payload release without destroying the antibody, typically through acidic conditions, reducing agents, or enzymes, or non-cleavable, which require proteolysis of the antibody for payload release [31].

The classical mechanism of action of ADCs is as follows: the mAb of the ADC recognizes antigens on the target cell membrane and is internalized via antigen-dependent endocytosis (the more common route) or antigen-independent pinocytosis (Figure 1). Generally, the ADC is trafficked to early endosomes and then to lysosomes, where the acidic environment and enzymes degrade the ADC, releasing the cytotoxic drug into the cytoplasm. The released drug then binds to DNA or microtubule proteins, interrupting the cell cycle and inducing apoptosis. Other mechanisms include: (1) retention of the mAb's antitumor activity through ADCC, CDC, and Fc-mediated phagocytosis; (2) a bystander effect, in which payloads diffuse or are released after apoptosis to kill adjacent cells lacking the target antigen and affect the tumor microenvironment; and (3) non-internalizing mechanisms, where extracellular cleavage of linkers releases the payload directly into the tumor microenvironment [32].

Figure 1 - Structure and mechanism of action of conventional ADCs.



1 – Antibody binding to the antigen; 2 – Internalization of the ADC–antigen complex; 3 – ADC degradation in lysosomes; 4 – Payload release in the cytoplasm; 5 – Cellular damage; 6 – Possible extracellular release of a fraction of the payload; 7 – Bystander effect on tumor microenvironment cells. Source – Adapted from WEI (2024) [33] using an illustration created by the author using elements licensed from the Canva Pro platform.

Currently, all marketed ADCs use random conjugation with cysteine and lysine side chains, resulting in heterogeneous products. In these cases, the drug–antibody ratio (DAR) is not controlled, leading to mixtures of unconjugated, partially conjugated, and hyper conjugated mAb in unknown amounts, which compromises efficacy, the therapeutic window, and tumor penetration [10,29]. In contrast, site-specific conjugation, progressively adopted in new-generation ADCs, allows for controlled antibody and molecule binding at a predetermined site, ensuring greater homogeneity, stability, and improved activity [34].

Regarding the therapeutic target, the ideal antigen should be a structure expressed on the cell surface (e.g., proteins, glycoproteins, or aberrant gangliosides) that is abundant in tumor cells but minimal or absent in normal cells[10]. Initially, targeting cancer cells with antibodies was challenging due to the similarity between normal and tumor cells, a challenge that was mitigated with the discovery of the first tumor-specific antigen by Lloyd J. Old and colleagues in the late 1970s [35-36].

Factors such as low ADC penetration due to high antigen affinity, determination of the ADC's therapeutic window by antigen distribution, and high antigen expression on the cell surface do not necessarily guarantee therapeutic efficiency, which also depends on the tumor type [28].

ADCs' efficacy depends on the expression level of target antigens, with approximately 50 potential antigens identified as targets [31]. Additionally, components of the tumor microenvironment are being explored as novel potential ADC targets due to their close connection and constant communication with the tumor mass[37].

Based on drug composition and technological characteristics, ADC development can be divided into three generations [23]. First-generation ADCs are characterized by murine antibodies and nondegradable linkers, resulting in low precision and high toxicity [38]. Second-generation ADCs feature humanized mAb and more stable linkers yet still rely on random coupling and exhibit off-target toxicity [32]. Third-generation ADCs improve efficacy through site-specific conjugation techniques, reducing the DAR[2-4] and minimizing the proportion of unbound antibodies [38].

Since the approval of the first ADC, Mylotarg®, up to January 2024, a total of 15 ADCs has been approved. Of these, 13 remain on the market, while over 189 are currently under clinical evaluation. For breast cancer specifically, ADCs are in development targeting key antigens, including HER2, Trophoblast cell surface antigen (TROP-2), HER3 and the zinc transporter protein LIV-1. However, only four ADCs have received FDA approval for breast cancer treatment as shown on Table 1.

Table 1 – Antibody–Drug Conjugates in Breast Cancer: Targets, Payloads, and Clinical Status

ADC	Target	Antibody	Payload	Linker	Characteristics/Observations	Clinical Data/Status
Trastuzumab Emtansine (T-DM1) *	HER2	Trastuzumab	DM1 (maytansinoids derivative – microtubule inhibitor)	Non-cleavable (MCC: lysine-maleimidomethyl cyclohexane-1-carboxylate)	Retains trastuzumab's mechanisms of action (e.g., PI3K/AKT pathway inhibition); internalization and intracellular degradation enable controlled payload release.	Demonstrated significant improvement in overall survival in HER2+ metastatic disease (EMILIA, KATHERINE); FDA-approved for metastatic and, more recently, early breast cancer with residual disease.
Trastuzumab Deruxtecan (T-DXd) *	HER2	Trastuzumab	Exatecan derivative (topoisomerase I inhibitor)	Cleavable tetrapeptide	High drug-to-antibody ratio (DAR ~8), higher than T-DM1 (DAR ~3.5); selective release minimizes premature off-target toxicity.	Clinical trial results showed improved PFS compared to T-DM1; approved as second-line for HER2+ and for HER2-low breast cancer patients (DESTINY-Breast 03 and 04).
Sacituzumab Govitecan*	TROP-2	Sacituzumab (humanized antibody)	SN-38 (active metabolite of irinotecan, topoisomerase I inhibitor)	Cleavable linker (details not specified)	Targets TROP-2, expressed in ~80% of breast cancers; exerts cytotoxic effect by inhibiting topoisomerase I, leading to DNA damage.	In clinical trials, PFS and OS significantly improved in TNBC and HR+/HER2− breast cancer; approved for metastatic breast cancer.
Datopotamab Deruxtecan (Dato-DXd) *	TROP-2	Humanized anti-TROP2 antibody (IgG1)	Deruxtecan (topoisomerase I inhibitor)	Cleavable tetrapeptide	Shares potent payload with T-DXd, but targets TROP-2; demonstrated specificity and efficacy in intracellular delivery, promoting DNA damage and apoptosis.	Preliminary results (TROPION-PanTumor01) show promising response; phase III trials (TROPION-Breast02 and Breast01) ongoing for TNBC and HR+/HER2− breast cancer.
Disitamab Vedotin (RC48)	HER2	Disitamab (with higher affinity than trastuzumab)	MMAE (synthetic auristatin derivative, microtubule inhibitor)	Cleavable valine-citrulline	DAR of 4; high affinity for HER2 receptor; studies indicate efficacy in both HER2-positive and HER2-low populations.	Initially approved in China for HER2+ gastric cancer; clinical trials show promising responses in both subgroups, with satisfactory ORR and PFS data; under evaluation for breast cancer.
ARX-788	HER2	New anti-HER2 antibody	AS269	Site-specific conjugation via synthetic amino acid pAF	Conjugated via para-acetylphenylalanine (pAF) insertion, ensuring high stability and low systemic toxicity; active in HER2+, HER2-low, and T-DM1–resistant tumors.	Phase I trials show high response and disease control rates; phase III trials (ACE-Breast-02 and others) underway to confirm efficacy and safety.
Patritumab Deruxtecan (HER3-DXd)	HER3	Patritumab (fully human IgG1 antibody)	Deruxtecan (topoisomerase I inhibitor)	Cleavable tetrapeptide	Targets HER3-expressing tumors, associated with therapeutic resistance; active in HR+/HER2−, TNBC, and HER2+ subtypes; induces immune responses and proliferation suppression.	Phase I/II trials showed ORR ranging from 22.6% to 42.9% and responses across multiple subgroups; common adverse events include myelosuppression and some ILD cases; multiple clinical investigations ongoing.
Ladiratuzumab Vedotin	LIV-1	Antibody targeting LIV-1	MMAE (microtubule-disrupting agent)	Cleavable protease-sensitive	Targets LIV-1, associated with epithelial–mesenchymal transition; shows promising activity in breast cancer, both in monotherapy and in combination with immunotherapies.	Early TNBC studies showed ORR of 28% (monotherapy) and 35% with pembrolizumab; most common adverse events include nausea, fatigue, neuropathy, and neutropenia; trials are ongoing.

* Approved for breast cancer treatment until March 2025. Adapted from Mark et al., 2023 [39].

Clinical Studies with ADCs in Breast Cancer

In 2013, the FDA approved the first ADC directed against HER2-overexpressing breast cancer, the T-DM1, which combines the antibody trastuzumab with the cytotoxic agent emtansine. Since then, new ADCs have been evaluated in clinical trials, demonstrating significant advances and providing optimistic perspectives on current breast cancer management [40].

The phase III TROPiCS-02 study evaluated 517 patients with hormone receptor–positive, HER2-negative metastatic breast cancer treated at centers in the United States and Europe with sacituzumab govitecan (SG). Despite a high frequency of adverse events (neutropenia, diarrhea, nausea, hair loss, and anemia, including one fatal case of septic shock due to neutropenic colitis), SG reduced the relative risk of death by 21% and increased overall survival by 3.2 months, along with an improved quality of life compared to standard chemotherapy [41].

Similarly, the phase III ASCENT multicenter international study evaluated SG in 468 women with metastatic triple-negative breast cancer (TNBC) without brain metastases. Among the participants, 235 received SG (10 mg/kg on days 1 and 8 of a 21-day cycle) and 233 were treated with capecitabine, eribulin, vinorelbine, or gemcitabine. Patients treated with SG had a median progression-free survival (PFS) of 5.6 months versus 1.7 months for those receiving standard chemotherapy. Additionally, the median overall survival was 12.1 months for the ADC group compared to 6.7 months in the chemotherapy group. Although the objective response rate was much higher with SG (35% vs. 5%), serious adverse events such as febrile neutropenia, diarrhea, and anemia were reported [42].

Based on ASCENT study, Loibl (2023) evaluated the quality of life in 236 patients treated with SG and 183 receiving standard chemotherapy for advanced, refractory, or recurrent inoperable TNBC. Results showed improvements in overall health, reduced fatigue, better functional performance, and lower pain intensity in patients treated with SG, despite higher rates of nausea, vomiting, and diarrhea. Quality of life was assessed using the EORTC QLQ-C30 questionnaire. Thus, the study demonstrated a positive profile for SG in metastatic TNBC, with significant benefits and delayed clinical deterioration compared to chemotherapy [43].

TROPION-PanTumor01, is a two-part, multicenter, open-label phase I trial designed to evaluate the effects of datopotamab deruxtecan (Dato-DXd) in 82 patients with advanced solid tumors, including breast cancer in USA. Of these, 41 patients had advanced, inoperable, or metastatic hormone receptor–positive, HER2-negative breast cancer, while 44 had TNBC. In the HR+/HER2– group, the objective response rate was 26.8% with a PFS of 8.3 months, compared to 31.8% response and 4.4 months PFS in the TNBC group. Although 100% of patients experienced degree ≥3 adverse events, most commonly stomatitis, the results indicated that the ADC has promising clinical activity with a manageable safety profile [44]. This ADC was approved by the FDA in January 2025 for the treatment of adult patients with unresectable or metastatic breast cancer that is hormone receptor-positive (HR+) and human epidermal growth factor receptor 2-negative (HER2−; IHC 0, IHC 1+, or IHC 2+/ISH−), who have previously received endocrine therapy and chemotherapy for advanced diseases (FDA, 2025 (https://www.fda.gov/).

An additional trial, known as BEGONIA (NCT03742102) is an international multicenter study ongoing Phase Ib/II open-label research platform evaluating the safety and efficacy of novel first-line therapies for metastatic triple-negative breast cancer (TNBC). One of the project's branches investigates the combination of

the antibody-drug conjugate Dato-DXd with the immunotherapy durvalumab. As of February 2023, 62 patients with advanced, metastatic, and unresectable TNBC had been enrolled. Preliminary results were promising, with an objective response rate (ORR) of 79% and a progression-free survival (PFS) of 13.8 months. Regarding safety, the most common adverse events were nausea and stomatitis, with 57% of patients experiencing grade 3 or 4 events and 23% experiencing serious effects. Notably, there was a lower incidence of anemia, diarrhea, and neutropenia, highlighting the safety profile and therapeutic potential of this combination in advanced TNBC [45].

Other studies with trastuzumab deruxtecan (T-DXd), disitamab vedotin (DV), FS-1502, and ESG401 have also shown antitumor potential in various breast cancer subtypes, though these treatments have been associated with significant adverse events—including hematological and gastrointestinal toxicities, and cases of fatal interstitial lung disease [46-48].

Despite ADCs revolutionizing targeted anticancer therapy by delivering potent cytotoxic agents directly to antigen-marked tumor cells, not all patients respond favorably. Many develop either primary or acquired resistance. Key resistance mechanisms include loss of the target antigen (such as decreased HER2 expression following T-DM1 use), failures in ADC internalization or recycling, and resistance to the payload through efflux pumps, altered signaling pathways, or therapy-induced mutations. Ongoing research seeks to better understand these failures and develop strategies to overcome them [40].

Choosing the ideal target remains a major challenge in ADC development. For treatment to be both effective and safe, it is essential that the antigen is highly expressed on tumor cells and minimally or not at all on healthy tissues, a task complicated by significant inter- and intratumoral heterogeneity [17].

High investments are also required for ADC development and application. Production is complex, demanding advanced technology, specialized infrastructure, and qualified personnel. Moreover, indirect costs related to continuous patient monitoring and management of side effects further complicate the process. These factors must be carefully considered to ensure that treatments are both viable and accessible [31].

Regulatory issues, reimbursement policies, and pricing strategies also directly influence the availability of these medications, as has been observed with therapies for HER2-positive breast cancer [49].

In Brazil, the production of biological drugs faces significant challenges, including complex manufacturing processes, reliance on imported inputs, high costs, and regulatory hurdles. The concentration of production in São Paulo, market preference for foreign products, and insufficient local infrastructure and technical support are major barriers. Overcoming these obstacles requires investment in infrastructure, technical training, and modernization of regulatory standards to foster innovation and access to biological therapies [50].

With ongoing research, new strategies are being developed to overcome the limitations of first-generation ADCs. One approach involves identifying new therapeutic targets beyond traditional tumor antigens, such as proteins in the tumor microenvironment (TME) and cancer stem cells (CSCs), to enhance treatment efficacy. Another promising innovation is the development of Probody ADCs, which remain inactive in circulation and are activated only in the presence of specific TME proteases. This increases treatment selectivity and significantly reduces off-target toxicity.

Furthermore, preclinical models are exploring biparatopic, bispecific, and even Tri specific antibodies capable of recognizing multiple targets simultaneously. Although this strategy may broaden therapeutic efficacy, it poses challenges such as a narrower therapeutic window and a higher risk of toxicity [31,34].

Among the most innovative approaches in development are nanobodies, antibody fragments derived from humans or animals. Their small size, high stability, and specificity offer several advantages: a lower risk of unwanted immune responses, enhanced tumor penetration, and faster clearance from the bloodstream, all contributing to reduced systemic side effects [31,34].

Currently, several clinical studies are investigating combination therapies involving chemotherapy, radiotherapy, immunotherapy, and new ADCs. The goal is to explore synergistic effects to enhance clinical benefits. However, managing the toxicity of these combinations remains a significant challenge that requires careful control [51].

Conclusions

ADCs have marked a milestone in anticancer therapy by selectively targeting tumor cells with potent cytotoxic agents that are delivered via monoclonal antibodies which recognize specific antigens. The progress of this concept over the years reached a significant milestone with the FDA's approval of the first ADC in 2000. Since that time, extensive research has been undertaken to investigate the therapeutic potential of ADCs across various types of neoplasms, with a particular focus on breast cancer.

ADCs embody a novel and advancing strategy for the treatment of metastatic and advanced breast cancer, which is especially critical considering that a substantial number of patients either do not respond to or develop resistance against conventional therapies.

Successful outcomes in trials such as TROPiCS-02, ASCENT, TROPION, and BEGONIA confirm the efficacy of ADCs in patients with different disease subtypes (HER2+; HER2–; HR+; TNBC), demonstrating their potential to transform the oncologic therapeutic landscape.

However, the use of ADCs requires constant attention to safety, as they can cause serious adverse effects, such as neutropenia, anemia, gastrointestinal and pulmonary toxicity. Strict monitoring is essential to ensure patient safety and the appropriate selection of treatment candidates.

Aiming to improve clinical outcomes and minimize risks, there is ongoing effort to develop therapeutic tissues involving ADCs, immunotherapy, and chemotherapy, in addition to incorporating technological innovations such as Probody Drug Conjugates (PDCs), biparatopic and bispecific antibodies, and nanobodies. Continuous advancements in the fields of bioengineering and pharmacological design project a promising future, with increasingly effective, safe, and personalized therapeutic alternatives, bringing renewed hope to people facing advanced breast cancer.

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