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MINI-REVIEW ARTICLE

Immunotherapy in Combination with Chemotherapy for Triple-negative Breast Cancer

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Abstract: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer that lacks estrogen and progesterone receptors and does not overexpress the human epidermal growth factor receptor 2 (HER2). Previous treatment options for TNBC were limited to chemotherapy alone, resulting in a poor patient prognosis. In 2018, an estimated 2.1 million new cases of breast cancer were diagnosed globally, with the incidence increasing by 0.5% annually from 2014 to 2018. The exact prevalence of TNBC is difficult to determine because it is based on the absence of certain receptors and overexpression of HER2. Treatment options for TNBC include surgery, chemotherapy, radiation therapy, and targeted therapy. The available evidence suggests that combination immunotherapy using PD-1/PD-L1 inhibitors may be a promising treatment option for metastatic TNBC. In this review, we evaluated the efficacy and safety of different immunotherapies regimens for the treatment of TNBC. In many clinical trials, the overall response rate and survival were better in patients treated with these drug combinations than those treated with chemotherapy alone. Although definitive treatments are not within reach, efforts to gain a deeper understanding of combination immunotherapy have the potential to overcome the urge for safe and effective treatments.

Keywords: Cancer, breast, triple-negative breast cancer, immunotherapy, efficacy, safety, atezolizumab, camrelizumab, paclitaxel, gemcitabine.

1. INTRODUCTION

Triple-negative breast cancer (TNBC) is one of the most aggressive subtypes of breast cancer, representing 10-15% of all breast cancers [1-7]. It is associated with a poor prognosis for patients due to the lack of estrogen and progesterone receptors and the absence of overexpression of the human epidermal growth factor receptor 2 (HER2). Until recently, the only treatment for TNBC was chemotherapy alone, which resulted in a shorter life expectancy for patients. According to the World Health Organization, breast cancer is the most common cancer in women worldwide, accounting for 25% of all cancer cases. In 2018, an estimated 2.1 million new cases of breast cancer were diagnosed globally. The incidence of female breast cancer increased by 0.5% each year from 2014 to 2018 [8]. The exact statistics for triple-negative breast cancer (TNBC) are more difficult to determine because the classification of TNBC is based on the absence of estrogen and progesterone receptors and the absence of overexpression of the HER 2. While current treatment strategies for triple-negative breast cancer (TNBC) are predominantly determined by the absence of estrogen and progesterone receptors and overexpression of HER2, recent research suggests that HER3 and HER4 may play a more significant role in TNBC than previously thought, beyond simply acting as heterodimerization partners. Consequently, the expression patterns of these ErbB receptors could serve as valuable predictors of how responsive TNBC patients may be to combination treatments [9].

TNBC is very difficult to treat. Nonetheless, efforts continue to advance the understanding of the phenomena associated with its diagnosis and treatment. The results of gene ontology and clustering analysis, using DAVID and BioLattice, have demonstrated that there is a strong association between decreased immune system activity and the presence of highly suspicious microcalcifications in TNBC patients [10, 11]. This information should be considered when designing treatment strategies involving the combination of immune checkpoint inhibitors and chemotherapeutics for advanced TNBC. The specific treatment plan will depend on the individual patient's age, overall health, and the stage and characteristics of their cancer. The main treatment options are sur-

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gery, chemotherapy, radiation therapy, and targeted therapy. In 2019, the FDA approved the first immune checkpoint inhibitor regimen for breast cancer. The regimen, which consists of the PD-L1 targeted antibody atezolizumab in combination with nab-paclitaxel, is intended for patients with locally advanced or metastatic triple-negative breast cancer that expresses PD-L1[12]. The approval of this therapeutic agent for the treatment of TNBC using immune checkpoint inhibitors in combination with chemotherapies represents a significant milestone in the field of cancer research. This approval indicates that the combination of these two types of treatment has been shown to be effective and safe in clinical trials, and it provides a new option for treating patients with TNBC. This approval also opens the door for further research into the use of immune checkpoint inhibitors in combination with chemotherapies for the treatment of other types of cancer.

2. TARGETING CHECKPOINT PROTEINS

Immunotherapy offers new expectations for the treatment of TNBC [13-19]. Immunotherapy, which involves using the body's own immune system to fight cancer, has shown promising results in treating a variety of cancers, such as brain cancer [20], small cell lung cancer [21], non-small cell lung cancer (NSCLC) [22, 23], melanoma [24, 25], and colorectal cancer (CRC) with microsatellite-high (MSI-H) or mismatch repair deficiency (dMMR) status [26-28] and gynecologic malignancies [29]. Immune checkpoint blockers for CTLA-4 (cytotoxic T lymphocyte antigen 4), PD-1 (Programmed Death Receptor 1) and PD-L1 (Programmed Death Ligand 1) have generated a benefit in terms of overall survival rate [19] and are the main immunotherapy agents [13]. The B7 protein family, which PDL1 is a member of, also consists of six other proteins (CD80, CD86, ICOS-L, PDL2, B7H3, and B7H4). As shown by the autoimmune pathologies and immune deficiency disorders produced in mice with a knockout of B7 family genes, the primary function of this family is to regulate the immune response. All members of the B7 family are transmembrane proteins with extracellular IgV and IgC domains, a transmembrane domain, and a cytoplasmic tail, with the exception of B7H4, which is a glycosylphosphatidylinositol [GPI] linked protein. Although the cytoplasmic tail's precise role is unknown, given that it contains serine and threonine, it is possible that it plays a role in signaling and phosphorylation. The B7 family probably forms homodimers at the cell surface.

PD-L1-targeted therapeutic agents are a type of cancer treatment that works by blocking the PD-L1 protein. This protein is often found on the surface of cancer cells, and it can help them evade the immune system. By blocking PD-L1, these therapeutic agents can help the immune system recognize and attack cancer cells more effectively. The immune checkpoint CTLA-4 functions by regulating T-cell activation. Its ligands CD80 and CD86 act by inhibiting T-cell activity which facilitates tumor progression, preventing CTLA-4 from binding to its ligands causes T-cell recognition and elimination of tumor cells. Similar occurs with PD-1 and PD-L1; in this case, when T cells are activated, they express PD-1 causing recognition of cancer cells. However, cancer cells express PD-L1, which appears to block this recognition and, consequently, elimination [30].

3. COMBINATION IMMUNOTHERAPY IS THE NEW PARADIGM

Over the past few years, promising outcomes have been associated with cancer immunotherapy. Through regulating T-cell activity, activating apoptosis in antigen-specific T cells, and inhibiting apoptosis in regulatory T cells, Programmed Cell Death Protein 1 (PD-1) is essential for suppressing immune responses and fostering self-tolerance. Programmed Cell Death Ligand 1 (PD-L1) is a trans-membrane protein that is thought to be a co-inhibitory element of the immune response. When combined with PD-1, it can lower the proliferation of PD-1-positive cells, obstruct their cytokine secretion, and trigger apoptosis. With its ability to reduce the host immune system's response to tumor cells, PD-L1 is also crucial in a number of cancers. According to these viewpoints, the PD-1/PD-L1 axis plays a major role in cancer immunotherapy and is responsible for cancer immune escape.

Promising outcomes have been observed with cancer immunotherapy over the past few years. But current research on immunotherapy shows that targeting immune checkpoints is the most effective way to stimulate positive antitumor immune responses. Previous research on immunotherapy, however, was mainly focused on targeting immune checkpoints. By reducing T cell activity and encouraging the differentiation of regulatory T cells, the programmed cell death protein 1 (PD-1) contributes significantly to taming immune responses, promoting self-tolerance. Inducing apoptosis in T cells that are specific for an antigen and inhibiting apoptosis in regulatory T cells are two ways that the immune checkpoint known as PD-1 prevents autoimmune reactions. Successive clinical trials using immune-checkpoint blockades and PD-1 monoclonal antibodies have expanded the field of tumor immunotherapy and provided promising results. However, a large percentage of patients did not benefit from these recently developed immune-based approaches, and the survival rate was not satisfactory. There have been some newly developed and extremely promising additional strategies, particularly combination therapies. There are also efforts to find new, suitable predictive biomarkers.

Combination immunotherapy using PD-1/PD-L1 inhibitors is being proposed as a potential treatment option for metastatic TNBC [31], but further studies are needed to compare its effectiveness and safety to other treatments. The studies should focus on improving overall survival rates and reducing the incidence of adverse events in relation to PD-L1 expression. Currently, researchers are developing treatments related to PD-L1 expression, and this could be related to safety and efficacy. PD-L1 is a protein that can help cancer cells evade the immune system, and targeting it with therapies in combination with chemotherapy could be an effective way to treat TNBC (Fig. **1**). There is literature focused on evaluating the efficacy and safety after neoadjuvant chemotherapy with an immune checkpoint inhibitor is performed in patients with early TNBC [32]. Thus, the question arises Which PD-L1-related treatment is safest and most effective in patients with triple-negative breast cancer? Therefore, this review aims to provide a conceptual synthesis of recent developments about the combinations of different drugs for the treatment of triple-negative breast cancer, where it will be

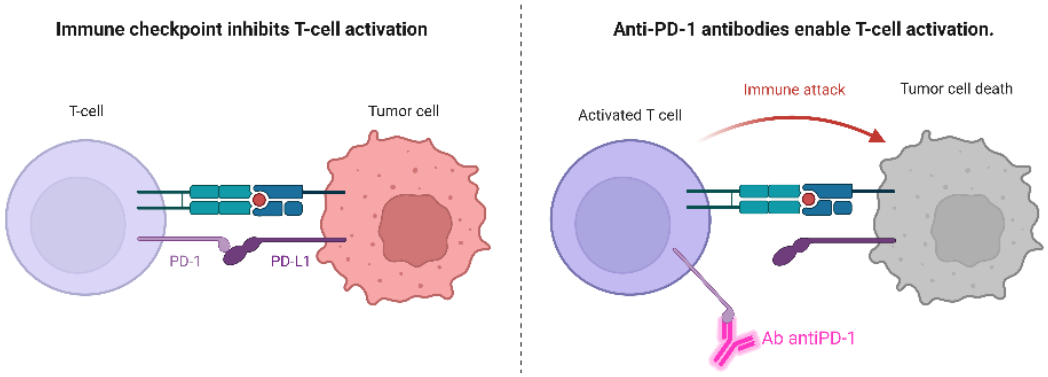

Fig. (1). PD-L1 inhibitors enable immune cell action on cancer cells. This figure was created based on the tools provided by Biorender.com (accessed on 12/14/2022). (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

concluded which treatment has the highest overall survival rate for patients with this type of cancer. The next few years of research will be key to treating this cancer and, ultimately, overcoming the challenges and adverse effects it can bring. Therefore, analysis of recent findings of immunotherapies targeting PD-L1 in combination with chemotherapy for TNBC will be of interest to researchers and clinicians concerned with current data and ongoing efforts to establish the safety and efficacy of immunotherapeutic approaches in TNBC.

4. EFFICACY TRIALS AND STUDY RESULTS

Combination immunotherapy has been approached as the most promising option for the treatment of triple-negative breast cancer. Several trials have been published recently, and their results should serve as a guide in the search for alternatives for this type of cancer [33-39]. The ORR and OS are shown in Table **1**. The table shows the results of different clinical trials investigating the use of chemotherapy combinations in the treatment of cancer. The trials include information on the number of patients, the drug regimen and dose used, the number of PD-L1 positive or negative patients, the overall response rate (ORR) and median overall survival (mOS). mOS in [35] is higher than in the rest of the studies, obtaining a mOS of 25.4 months in PD-L1-positive patients. It is important to note that median overall survival does not necessarily reflect the quality of life of the individuals involved in the study and may not consider factors, such as side effects of the treatment. On the other hand, the mOS of the chemotherapy combination trials in [36] was significantly lower than that observed in [33]. In [36], the mOS was only 8 months in the continuous dosing cohort and 9.5 months in the intermittent dosing cohort. The most frequent adverse effect in both cohorts was increased aspartate aminotransferase, with rates of 70% in the intermittent dosing cohort and 80% in the continuous dosing cohort.

In the trial by L.A. Emens et al. (2021), a regimen of atezolizumab 840 mg and nab-paclitaxel 100 mg/m^2 was used in 451 cancer patients. The overall response rate was 25.4%, and overall survival was 25.4 months. In the trial by D.A. Yardley et al. (2018), different chemotherapy regimens were used in 64, 61, and 66 patients, and overall response rates of 73%, 39%, and 44%, respectively, were observed. Median overall survival was 16.8 months, 12.1 months, and 12.6 months in each group, respectively. One of the most effective treatments, according to the data in the table, is a combination of atezolizumab 840 mg and nab-paclitaxel 100 mg/m^2, which was administered to 451 patients in a study by L. A. Emens et al. (2021). Among the 185 patients who tested positive for PD-L1, the overall response rate was 25.4 months. Another effective treatment regimen appears to be pembrolizumab 200 mg, which was administered to 84 patients in a study by S. Adams et al. (2019). In this study, all of the patients tested positive for PD-L1, and the overall response rate was 21%.

In [34], D. A. Yardley et al. found that treatment with nab-paclitaxel plus carboplatin (nab-P/C) resulted in a longer mOS compared to nab-paclitaxel plus gemcitabine (nab-P/G) [16.8 vs. 12.1 months], and the combination of gemcitabine plus carboplatin (G/C) had a lower mOS than the nab-P/G combination [12.6 vs. 12.1 months]. The most common adverse effects included thrombocytopenia, neutropenia, drug hypersensitivity, and fatigue (Table **2**). In [35], the mOS was 14.7 months, and the most common adverse effects were neutropenia, fatigue, alopecia, diarrhea, peripheral sensory neuropathy, peripheral neuropathy, and nausea (Table **2**).

Median overall survival was also reported in early-stage TNBC using carboplatin. P. Schmid et al. [40] reported an mOS of 1.7 months, and the most frequent adverse effect was neutropenia. Adverse events are any negative or unintended effects of a treatment that occur during a clinical trial. These can include side effects of a drug or other intervention, as well as complications that may arise from the administration of the treatment. Adverse events are closely monitored in clinical trials to ensure the safety of the participants and to assess the overall risks and benefits of the treatment being tested. In the monotherapy trials, mOS was higher in [38] than in [37] [18 vs. 9 months], and the most common adverse effects in both trials were fatigue and nausea (Table **2**).

The use of combination immune checkpoint inhibitor (ICI) therapy is linked to a significantly higher incidence of severe adverse events compared to ICI monotherapy [39]. The risk of certain adverse events is also considerably higher than others. As ongoing trials on combination ICI therapy

Table 1. Anti-PD-1/L1 monotherapy and chemotherapy trials in advanced or metastatic TNBC.

Reference	Number of Patients Included in the Study	Regimen / Dosage	Number of Patients with Positive or Negative PD-L1 (+ / -) Tumor Proportion Score	Overall Response Rate (ORR, %)	Median Overall Survival (mOS, months)
Trials Combining Chemotherapy					
[33]	451	Atezolizumab 840 mg, nab-paclitaxel 100 mg/m^2	185 + TPS ≥1%	No data	25.4
			266 -		19.7
[34]	64	nab-Paclitaxel 125 mg/m2 intravenous (VI), carboplatin	-	46(73%)	16.8
	61	nab-Paclitaxel 125 mg/m2, gemcitabine 1000 mg/m2	-	23(39%)	12.1
	66	Gemcitabine 1000 mg/m2, carboplatin	-	29(44%)	12.6
[35]	33	Atezolizumab 800 mg, nab-paclitaxel 125 mg/m^2	-	13(39.4%)	14.7
[36]	10	Camrelizumab 200 mg, Apatinib 250 mg orally (intermittent).	2 + TPS ≥1%	0	9.5
			8 -		
	30	Camrelizumab 200 mg VI, Apatinib 250mg por vía oral (Continuo).	12 + TPS ≥1%	13 (43.3%)	8.0
			18 -		
Monotherapy					
[37]	84	Pembrolizumab 200 mg	84 + TPS not reported. Combined positive score (CPS) ≥1.0	18(21%)	18
			0 -		
[38]	170	Pembrolizumab 200 mg	105 + TPS	9(5.3%)	9
		-	64 -		
		-	1 (Unknown)		

and new toxicity data continue to emerge, it is important for future studies to control for treatment dosages to establish cancer-specific differences in toxicity and clarify toxicity related to regimens containing PD-L1. The clinical safety profile of the combination therapy is an important consideration, as treatment-related adverse events (TRAEs) can significantly impact patients' quality of life and overall health outcomes. In clinical trials, TRAEs are typically graded according to their severity, with grade 1 and 2 events being less severe and more manageable than grade 3 or higher events. Clinicians and researchers are particularly concerned about potential neurotoxicity associated with the combination of CPIs and chemotherapy. Therefore, in Table **2**, we have included information on the grade of TRAEs reported in clinical trials of the combination therapy.

The objective of this review was to identify the most effective treatment for patients with triple-negative breast cancer (TNBC) and to evaluate the associated adverse effects of each regimen. For this comparison, we detected seven published studies, applying a search strategy [40]. Among them, 4 of the studies were trials of Anti-PD-1/L1 chemotherapy in advanced or metastatic TNBC, 2 were trials of Anti-PD-1/L1 monotherapy in advanced or metastatic TNBC, and 1 was a trial of Anti-PD-1/L1 combination therapy in early stage TNBC. The results of the IMpassion130 trial [33] showed that the combination of atezolizumab plus nab-paclitaxel had

Table 2. Adverse events from Anti-PD-1/L1 monotherapy and chemotherapy trials in advanced or metastatic TNBC.

Adverse Events (%)	Trials Combining Chemotherapy									Monotherapy					
	[33]		[34]			[35]		[36]				[37]		[38]	
	AG	G≥3	nab-P/C G≥3	nab-P/G G≥3	G/C G≥3	AG	G≥3	IDC AG	IDC G≥3	CDC AG	CDC G ≥3	AAG	G≥3	AG	G ≥3
Alopecia	57.2	0.4	-	-	-	-	-	-	-	-	-	-	-	-	-
Abdominal pain	11.5	0.4	-	-	-	-	-	-	-	-	-	-	-	-	-
Adrenal insufficiency	-	-	-	-	-	-	-	-	-	-	-	1.2	-	1.2	0
Alanine aminotransfer-ase increase	11.7	2.2	-	-	-	-	-	70	10	63.3	0	-	-	-	-
Anemia	28.3	3.5	13	12	27	24	6	20	0	16.7	0	-	-	6	1.2
Arthralgia	19.3	0.2	-	-	-	-	-	-	-	-	-	5.9	0	5.9	-
Asthenia	13	0.7	-	-	-	-	-	-	-	-	-	6.5	0	6.5	-
Back pain	16.1	1.3	-	-	-	-	-	-	-	-	-	-	-	-	-
Bone pain	-	-	-	-	-	12	3	-	-	-	-	-	-	-	-
Capillary hemangioma	-	-	-	-	-	-	-	30	0	10	0	-	-	-	-
Colitis	-	-	-	-	-	3	3	-	-	-	-	1.2	0	1.2	0
Constipation	25.4	0.7	-	-	-	-	-	-	-	-	-	-	-	-	-
Cough	27.4	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Decreased appetite	20	0.7	-	-	-	-	-	-	-	-	-	7.6	0	6	0
Decreased neutrophil count	12.4	3.7	-	-	-	-	-	-	-	-	-	-	-	-	-
Diabetes Mellitus Type 1	-	-	-	-	-	3	3	-	-	-	-	0.6	0.6	0.6	-
Diarrhea	32.8	1.7	-	-	-	39	6	10	0	20	0	7.1	1.8	11.9	1.2
Dizziness	15	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Dysgeusia	11.3	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Dyspnea	16.3	0.7	-	-	-	-	-	-	-	-	-	-	-	-	-
Edema peripheral	15.9	0.2	-	-	-	-	-	-	-	-	-	-	-	-	-
Fatigue	47	3.9	3	15	3	-	-	90	0	46.7	0	20.6	0.6	26.2	1.2
Febrile neutropenia	-	-	5	2	0	3	3	-	-	-	-	-	-	-	-
Gingival hemorrhage	-	-	-	-	-	-	-	20	0	3.3	0	-	-	-	-
Hand-foot syndrome	-	-	-	-	-	-	-	50	0	56.7	6.7	-	-	-	-
Headache	25.2	0.7	-	-	-	-	-	30	0	26.7	0	-	-	-	-
Hematochezia	-	-	-	-	-	-	-	10	0	0	0	-	-	-	-
Hepatitis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

(Table 2) Contd…

Adverse Events (%)	Trials Combining Chemotherapy									Monotherapy					
	[33]		[34]			[35]		[36]				[37]		[38]	
	AG	G≥3	nab-P/C G≥3	nab-P/G G≥3	G/C G≥3	AG	G≥3	IDC AG	IDC G≥3	CDC AG	CDC G ≥3	AAG	G≥3	AG	G ≥3
Hypertension	5.4	1.1	-	-	-	-	-	30	0	36.7	0	-	-	-	-
Hyperthyroidism	-	-	-	-	-	-	-	0	0	16.7	0	5.3	0	4.8	-
Hypokalemia	6.5	1.5	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypothyroidism	14.3	0	-	-	-	-	-	10	0	26.7	0	11.8	0	9.5	0
Increased aspartate aminotransferase	10.9	1.7	-	-	-	9	3	70	10	80	10	-	-	-	-
Increased bilirubin in the blood	-	-	-	-	-	-	-	10	0	20	0	-	-	-	-
Infusion-related reaction	-	-	-	-	-	-	-	-	-	-	-	1.8	0	1.2	0
Insomnia	11.7	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Leukopenia	-	-	6	3	11	12	6	30	0	30	3.3	-	-	-	-
Myalgia	15.4	0.4	-	-	-	15	3	-	-	-	-	-	-	-	-
Mycoplasma pneumonia	-	-	-	-	-	3	-	-	-	-	-	-	-	-	-
Myocarditis	-	-	-	-	-	-	-	-	-	-	-	0.6	0	0.6	-
Nasopharyngitis	11.3	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Nausea	46.7	1.1	-	-	-	-	-	20	0	13.3	0	11.2	0.6	13.1	0
Neutropenia	22.2	6.3	42	27	52	70	46	-	-	-	-	-	-	-	-
Pain in extremity	12	0.4	-	-	-	-	-	-	-	-	-	-	-	-	-
Paronychia	-	-	-	-	-	3	3	-	-	-	-	-	-	-	-
Peripheral neuropathy	21.7	5.7	5	7	2	30	3	-	-	-	-	-	-	-	-
Peripheral sensory neuropathy	16.3	2	-	-	-	-	-	-	-	-	-	-	-	-	-
Pneumonia	7	2.6	-	-	-	6	6	-	-	-	-	-	-	-	-
Pneumonitis	-	-	-	-	-	9	3	0	0	6.7	3.3	4.1	0.6	2.4	0
Proteinuria	-	-	-	-	-	-	-	50	0	53.3	3.3	-	-	-	-
Pruritus	15.9	0	-	-	-	-	-	-	-	-	-	6.5	0	7.1	0
Pyrexia	20.2	0.7	-	-	-	-	-	-	-	-	-	-	-	-	-
Skin rash	18.3	0.4	-	-	-	-	-	10	0	30	0	1.2	-	6	0
Stomatitis	10.7	0.2	-	-	-	-	-	-	-	-	-	-	-	-	-
Syncope	-	-	-	-	-	3	3	-	-	-	-	-	-	-	-
Thrombocytopenia	-	-	9	7	28	15	9	10	0	10	0	-	-	-	-
Upper respiratory tract infection	12	1.1	-	-	-	-	-	-	-	-	-	-	-	-	-
Urinary tract infection	13	0.9	-	-	-	-	-	-	-	-	-	-	-	-	-
Vomiting	20	1.1	-	-	-	-	-	20	0	13.3	0	-	-	6	0

Abbreviations: AG Any grade; IDC Intermittent dosing cohort; CDC Continuous dosing cohort.

a median overall survival (mOS) rate of 25.4 months in the PD-L1 positive population, compared to 19.7 months in the PD-L1 negative population. Adverse effects were consistent with those known for each drug, and the combination was considered safe and tolerable. The tnAcity trial [34] found that the nab-P/C combination resulted in a longer mOS and higher overall response rate (ORR) compared to the nab-P/G and G/C combinations. In the nab-paclitaxel plus carboplatin (nab-P/C), nab-paclitaxel plus gemcitabine (nab-P/G), and gemcitabine plus carboplatin (G/C) groups, 80%, 77%, and 84% of patients, respectively, reported at least one adverse event of grade ≥3. Grade ≥3 adverse events were mainly hematologic. Twenty-four (73%) patients experienced grade 3/4 adverse events in [35] attributed at least in part to atezolizumab, as shown in Table 2. The most frequent events were neutropenia and decreased neutrophil count. The most common grade 3/4 AEs exclusively attributed to atezolizumab were diarrhea (6%) and colitis (3%). In [38], the safety of all patients was evaluated, and it was found that 53 (63.1%) patients experienced at least one adverse event related to the treatment, with eight (9.5%) of them experiencing a grade 3 event, as shown in Table 2. No adverse events of grade ≥3 severity occurred in two or more patients. Combination therapies demonstrated a better response than single agents, indicating that this type of combination may be optimal for TNBC patients.

CONCLUDING REMARKS

After reviewing the results of several clinical trials, it was shown that combination chemotherapy with drugs, such as atezolizumab, nab-paclitaxel, carboplatin, gemcitabine and camrelizumab could be effective in the treatment of advanced triple-negative breast cancer. The overall response rate and median overall survival were better in many patients treated with these drug combinations than those treated with chemotherapy alone. In addition, the PD-L1 status of the cancer also appeared to have an impact on treatment effectiveness. However, further studies are needed to confirm these findings and determine the better use of these drugs in the treatment of advanced breast cancer. This review could provide valuable insights and help inform treatment decisions. However, it is important for patients to discuss their treatment options with their doctor, who can provide more personalized recommendations based on the specific characteristics of their cancer and their overall health. In general, the safety and effectiveness of any treatment will depend on a variety of factors, such as the stage of cancer and the overall health of the patient.

AUTHORS' CONTRIBUTIONS

E.M.S contributed to the conceptualisation, data curation, formal analysis, investigation, and methodology. J.C.S.B contributed to writing the original draft and review, and editing. C.C.G contributed to the conceptualisation, data curation, formal analysis, investigation, methodology, project administration, supervision, validation, writing of the original draft and the review, and editing.

LIST OF ABBREVIATIONS

TNBC	=	Triple-Negative Breast Cancer
HER2 2	=	Human Epidermal Growth Factor Receptor
NSCLC	=	Non-small Cell Lung Cancer
CRC	=	Colorectal Cancer
MSI-H	=	Microsatellite-high
GPI	=	Glycosylphosphatidylinositol
PD-L1	=	Programmed Cell Death Ligand 1
ORR	=	Overall Response Rate
mOS	=	Median Overall Survival
ICI	=	Immune Checkpoint Inhibitor
TRAEs	=	Treatment-related Adverse Events

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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