FARMÁCIA GENERALISTA

Artigo de Revisão

ATEZOLIZUMAB AS IMMUNOTHERAPEUTIC APPROACH FOR CLINICAL MANAGEMENT OF TRIPLE NEGATIVE BREAST CANCER - LITERATURE REVIEW

ATEZOLIZUMABE COMO ABORDAGEM IMUNOTERAPÊUTICA PARA O MANEJO CLÍNICO DO CÂNCER DE MAMA TRIPLO NEGATIVO - REVISÃO DA LITERATURA

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ABSTRACT

Breast cancer has elevated mortality rates and is the most common tumor in women worldwide. Among the types, the triple negative breast cancer (TNBC) has the worst prognostic and is highly incident in young women. In such context, the objective of this study was to associate the characteristics of TNBC and prognostic factors of immunotherapy when atezolizumab was applied for its clinical management. A systematic review was carried out following the PRISMA guidelines, using PubMed, LILACS, Web of Science and SCOPUS databases by selecting articles published over the last 10 years in Portuguese and English languages. The bibliographic survey revealed that TNCB is an exceptionally heterogeneous and aggressive group of breast cancer, presenting the highest metastatic rates and the lowest overall survival when compared to other molecular breast cancer subtypes. In front of this, the immunotherapy has emerged as a promising treatment strategy for TNBC. The research found 10 articles that reported the atezolizumab as new approach to management the TNBC. The atezolizumab, an anti-PD-L1 drug has been studied in association with nab-paclitaxel and it has already shown benefits for patients affected by TNBC. In this sense, this systematic review shows that the approval of the atezolizumab immunotherapy brings a new and promising treatment option against TNBC.

Keywords: Immunotherapy, Breast cancer, Atezolizumab; Anit-PD-L1

RESUMO

O câncer de mama apresenta taxas de mortalidade elevadas e é o tumor mais comum em mulheres em todo o mundo. Dentre os tipos, o câncer de mama triplo negativo (CMTN) tem o pior prognóstico e é altamente incidente em mulheres jovens. Nesse contexto, o objetivo deste

estudo foi associar as características do CMTN e os fatores prognósticos da imunoterapia quando o atezolizumabe foi aplicado para seu manejo clínico. Realizou-se revisão sistemática segundo as diretrizes do PRISMA, nas bases de dados PubMed, LILACS, Web of Science e SCOPUS, selecionando artigos publicados nos últimos 10 anos nos idiomas português e inglês. O levantamento bibliográfico revelou que o CMTN é um grupo excepcionalmente heterogêneo e agressivo de câncer de mama, apresentando as maiores taxas metastáticas e a menor sobrevida global quando comparado a outros subtipos moleculares de câncer de mama. Diante disso, a imunoterapia surgiu como uma estratégia de tratamento promissora para o CMTN. A pesquisa encontrou 10 artigos que relataram o atezolizumabe como nova abordagem para o manejo do CMTN. O atezolizumabe, um fármaco anti-PD-L1, tem sido estudado em associação com o nab-paclitaxel e já demonstrou benefícios para pacientes afetados pelo CMTN. Nesse sentido, esta revisão sistemática mostra que a aprovação da imunoterapia com atezolizumabe traz uma nova e promissora opção de tratamento contra o CMTN.

Palavras-chave: Imunoterapia; Câncer de mama; Atezolizumabe; Anti-PD-L1

INTRODUCTION

Breast cancer is the most common cancer in women worldwide and is considered an important public health problem because of the substantial humanistic and economic burden (TAO *et al.*, 2015; TORRE *et al.*, 2015). It is one of the few types of tumor in which the molecular classification has been successfully used for developing individualized therapeutic models (FENG *et al.*, 2018). Breast tumors that do not express estrogen receptors (ER), progesterone receptors (PR) and the HER2 oncogene are classified as triple negative breast cancer (TNBC). TNBC frequently affects young women (less than 40 years old), it has a generally larger tumor size than the other cancers, it is biologically more aggressive and involves the lymph node in the diagnosis (FENG *et al.*, 2018; TAO *et al.*, 2015). Importantly, despite having higher rates of clinical response to chemotherapy and a metastatic potential similar to that of other breast cancer subtypes, these tumors are associated with a shorter average time of recurrence and death (HUDIS; GIANNI, 2011; LEHMANN *et al.*, 2011). The lack of targeted therapies and the poor prognosis of TNBC patients have been motivating a great effort to pursue new actionable molecular targets to treat patients with these tumors (BIANCHINI *et al.*, 2016).

Among the several available types of treatments, the cytotoxic chemotherapy, as anthracyclines, taxanes and platinium compounds, remains the basis of treatment for TNBC (TORRE *et al.*, 2015). Despite the choice of the ideal therapeutic regimen, less than 30 % of women with metastatic breast cancer survive 5 years after diagnosis and practically all women with metastatic TNBC end up dying from their disease. Additionally, the treatment of TNBC

patients represents an important clinical challenge due to the molecular heterogeneity of the disease and the absence of well-defined molecular targets, since this breast cancer subtype does not respond to endocrine therapy or other available targeted agents (BIANCHINI *et al.*, 2016). In this sense, the immunotherapy has been proved to be a promising clinical strategy for different kinds of cancers, mainly because it reactivates human immune system and reduces adverse effects over the therapy (LI *et al.*, 2018). Clinical tests indicate that it is possible for patients with TNBC to achieve better results with immunotherapy than patients with other subtypes of the disease (BIANCHINI *et al.*, 2016). In such context, atezolizumab is a G1 immunoglobulin monoclonal antibody that may increase the survival of TNBC patients who have few treatment options (SAHA; NANDA, 2016). The aim of this review was to perform a bibliographic survey associating the epidemiological characteristics and prognostic factors to TNBC and to demonstrate the atezolizumab role as immunotherapy for TNBC management.

METHODS

Study design

The following steps were carried out following the PRISMA guidelines (GALVÃO *et al.*, 2015; GALVÃO; PEREIRA, 2014): (**I**) identification of the research theme and guiding question elaboration; (**II**) inclusion and exclusion criteria definition; (**III**) selection of articles by reading the title and summary. Lastly, after a detailed revision of the selected studies, (**IV**) it was collected the main information of the studies to evaluate the results and elaborate the review.

Research strategy

After delimiting the study theme, the following guiding question was asked: *"What is the impact of using the atezolizumab as immunotherapy in triple negative breast cancer treatment?"*. The inclusion criteria considered were listed:

A) Studies that address the subject of characteristics and prognostic factors to TNBC as well as the atezolizumab efficacy as immunotherapy;

B) Publications resulting from original articles, case reports, randomized clinical trials and cohort studies published in the last ten years;

C) Scientific reports published in Portuguese and English language.

Publications that do not respect the theme delimitation and the purpose of the study were excluded. The data survey was carried out in the PubMed, LILACS, Web of Science and SCOPUS databases. The following search terms were used: “triple negative breast cancer” and

"atezolizumab". Article's selection was carried out by reading the title and abstract. Following, the articles that were eligible according to the inclusion and exclusion criteria were selected and classified based on the methodological design (MELNYK; FONEOUT-OVERHOLT, 2005).

RESULTS

Identification and selection of studies

The electronic search yielded 133 citations identified from reference lists of found studies. After removal of duplicates, a total of 47 titles and abstracts were screened for inclusion. A total of 22 full articles were screened of which 10 were included in this review (Figure 1).

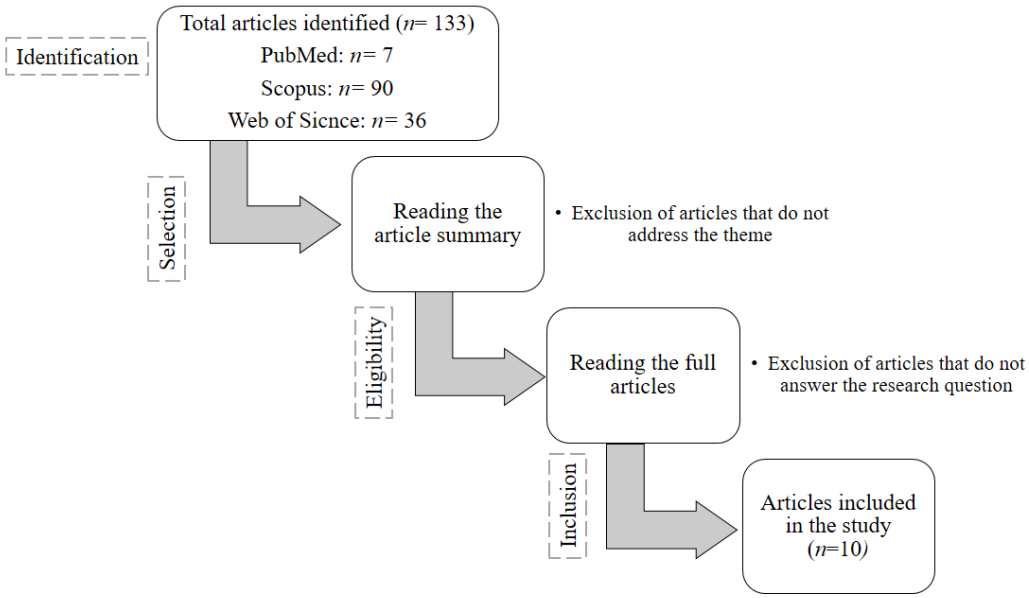

Figure 1 Flowchart for the selection of publications

Characteristics of included studies

Major characteristics of the included studies are presented in Table 1. Of the 10 studies included, 7 were about safe and clinical efficacy of atezolizumab as treatment in patients with TNBC (ADAMS *et al.*, 2019; CORTÉS *et al.*, 2019; EMENS *et al.*, 2019; IWATA *et al.*, 2019; KYTE *et al.*, 2020; SCHMID *et al.*, 2018; SCHMID *et al.*, 2020) and 3 presented the cost-effectiveness by adding atezolizumab to nab-paclitaxel therapy (PHUA *et al.*, 2020; WENG *et al.*, 2020; WU; MA, 2020). Besides, by methodological design the studies were classified in

randomized studies (CORTÉS *et al.*, 2019; IWATA *et al.*, 2019; KYTE *et al.*, 2020; SCHMID *et al.*, 2018; SCHMID *et al.*, 2020) and cohort study (ADAMS *et al.*, 2019; EMENS *et al.*, 2019). The majority of the studies involved the usage of atezolizumab plus nab-paclitaxel (*n* = 5) (ADAMS *et al.*, 2019; CORTÉS *et al.*, 2019; IWATA *et al.*, 2019; KYTE *et al.*, 2020; PHUA *et al.*, 2020; SCHMID *et al.*, 2018; WENG *et al.*, 2020; WU; MA, 2020) while one of them evaluated the efficacy of atezolizumab + pegylated liposomal doxorubicin + cyclophosphamide (SCHMID *et al.*, 2020), and only one study reported the atezolizumab as monotherapy (EMENS *et al.*, 2019).

Table 1. Characterization of articles eligible for the review

*NabP: Nab-Paclitaxel; Atezo: Atozolizumab; PLD: pegylated liposomal doxorubicin; CF: Ciclophosphamide

Author	Year	Journal	Study design	Therapy
Safety and Clinical Activity				
Schmid et al.	2018	The New England Journal of Medicine	Randomized study	NabP + Atezo
Adams et al.	2018	JAMA Oncology	Cohort study	NabP + Atezo
Emens et al.	2019	JAMA Oncology	Cohort study	Atezo
Cortés et al.	2019	Future Oncology	Clinical Trial Protocol – Randomized study	NabP + Atezo
Iwata et al.	2019	Japanese Journal of Clinical Oncology	Randomized study	NabP + Atezo
Kyte et al.	2020	Journal of Translational Medicine	Clinical Trial Protocol - Randomized study	PLD + CF + Atezo
Schmid et al.	2020	The Lancet Oncology	Randomized study	NabP + Atezo
Cost - Effectiveness				
Phua et al.	2020	BMC Health Services Research	-	NabP + Atezo x NabP
Weng et al.	2020	American Journal of Clinical Oncology	-	NabP + Atezo x NabP
Wu and Ma	2020	Therapeutic Advances in Medical Oncology	-	NabP + Atezo x NabP

DISCUSSION

Triple negative breast cancer: general aspects

The majority of TNBC is histologically classified as ductal invasive carcinomas with no specific type and lacks distinct histological characteristics. They are characterized by low

differentiation, elevated proliferative capacity and immune infiltrate, the occurrence of necrosis process and larger tumor size (DENKERT *et al.*, 2017; HUDIS; GIANNI, 2011). TNBC presents a strong positive tropism to metastasize to the hematological tissue instead of the lymphatic route, developing less axillary lymph node metastases than non-TNBC (LAURENTIIS *et al.*, 2010). Importantly, while other breast cancer subtypes usually spread to bones and soft tissues, TNBC often affects lungs and brain (KALIMUTHO *et al.*, 2015; LEHMANN *et al.*, 2011).

The molecular classification is based on the expression of distinct elements and oncogenic cell signaling, suggesting possible clinically useful molecular targets within these pathways (DENKERT *et al.*, 2017; KALIMUTHO *et al.*, 2015; LEE; DJAMGOZ, 2018). This division was recently restructured into four subtypes: basal like 1 (BL1), basal like 2 (BL2), receptor type of luminal androgen (RAL) and mesenchymal (M) (LEE; DJAMGOZ, 2018). These subclasses exhibit different therapeutic responses and genomic analysis indicates that these subtypes can coexist in the same tumor, which could explain the heterogeneity of the TN and reinforces the need of evaluating each patient individually (DENKERT *et al.*, 2017; LEE; DJAMGOZ, 2018).

TN tumors are characterized mainly by tumor protein 53 (TP53) and retinoblastoma 1 (RB1) mutations or deletion as well as amplification of myeloid leukemia cells 1 (MCL1) and the viral oncogene homolog of avian myelocytomatosis v-Myc (c-MYC). In addition, TN shows mutations in phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha (PIK3CA), phosphatase and tensin homologue (PTEN) and inositol polyphosphate-4-phosphatase type II (INPP4B). TN cancers are also characterized by generalized chromosomal instability and are associated with the presence of mutations in the BRCA1 and BRCA2 gene, which considerably influence the treatment. The BRCA1 and BRCA2 genes are important elements to the homologous recombination and restorative processes when DNA damage leads to its double strands breaks (KALIMUTHO *et al.*, 2015; LEE; DJAMGOZ, 2018; LEHMANN *et al.*, 2011). These genes encode proteins responsible for repairing the double DNA strand, contributing to the maintenance of genomic stability. In addition, they have also been implicated in other fundamental cellular processes, such as cell cycle control and gene transcription (COLLIGNON *et al.*, 2016).

Currently, the knowledge regarding the defects in the DNA repair mechanisms leads to some specific treatment approaches against TNBC. It was demonstrated that these tumors are potentially more sensitive to harmful DNA agents, such as platinum salts. The development of drugs that selectively inhibit poly ADP-ribose polymerase (PARP), such as olaparib, has been

considered a promising proposal for TNBC pharmacological management (COLLIGNON *et al.*, 2016; KALIMUTHO *et al.*, 2015). Patients with TNBC initially respond to conventional chemotherapy, but the disease often relapses, leading to a worse outcome than patients with other breast cancer subtypes. Chemotherapy remains the primary systemic treatment, and usually involves the administration of anthracyclines, taxanes, and / or platinum compounds aiming at disrupting the functions of cancer cells (BIANCHINI *et al.*, 2016; SCHMID *et al.*, 2018).

Until now, optimal chemotherapy regimens to treat TNBC were not established. Although the association of multiple chemotherapeutic agents provided better response rates compared to single agent administration, such an approach caused higher toxic effects without increasing patients' survival rate (BIANCHINI *et al.*, 2016). In spite of this, novel therapeutic targets for the treatment of this tumor type were recently identified, suggesting a possible advancement in the clinical management of TNBC (LEBERT *et al.*, 2018). Some potentially important targets include DNA damage and repair, immunomodulation, hormone receptor modulation and inhibition of some elements of signaling pathway. These new approaches may lead to better long-term patient outcomes (COLLIGNON *et al.*, 2016), which will require further clinical observation and monitoring.

Immunotherapy: The era of atezolizumab

The immunotherapy modified the treatment regimen for various cancer types, providing clinical responses improvement even in advanced and untreatable cancers as well as significantly increasing the chances of survival for patients (KALIMUTHO *et al.*, 2015). The immunotherapy applies monoclonal antibodies to stimulate the immune system. In a non-transformed tissue, the healthy cells present a homeostatic immune system, which regulates the cell proliferation and cytotoxic events in order to prevent autoimmune reactions. Such a scenario is not observed in the tumor environment, in which these mechanisms are adopted by the tumor to nullify immune cells anergic, avoiding tumor cells elimination (STOVGAARD *et al.*, 2018).

Immunotherapy has been emerging as a promising new alternative for the treatment of TNBC, which mainly focuses on blocking the synthesis and release of immune regulatory proteins, suppressing the tumor response (ESTEVA *et al.*, 2019). There are some scientific reports supporting that the interaction between tumor cells and the immune system can lead to clinically useful biomarkers (LEE; DJAMGOZ, 2018; STOVGAARD *et al.*, 2018), such as the tumor lymphocyte infiltrate (TIL), the prevalence of other immune system cells as well as

biomarkers related to immune/tumor interaction as the programmed death-ligand 1 (PD-L1). However, in breast cancer, there are important differences in the prognostic significance of immune cells according to the breast cancer subtype (LEE; DJAMGOZ, 2018; STOVGAARD *et al.*, 2018).

Currently, there are several clinical studies in progress that monitor patients with breast cancer and distinct immunotherapeutic treatment strategies. The most studied approaches of immunotherapy are focused on programmed cell death protein 1 (PD-1) and its ligand PD-L1 (ESTEVA *et al.*, 2019). PD-1 is a cell membrane surface protein expressed in several cell types, including T cells; is activated by its ligands PD-L1 and PD-L2. When PD-1 binds to PD-L1 it negatively modulates T cell activity. It was already demonstrated that high levels of PD-L1 expression in tumors lead to immune evasion and cancer progression (ESTEVA *et al.*, 2019; LEE; DJAMGOZ, 2018; STOVGAARD *et al.*, 2018). The PD-L1 expression in breast cancer was directly correlated with tumor size, differentiation degree, lymph node involvement and worse patients' survival rates. The protein PD-1 stands out as an important molecular target in antitumor activity regulation, since it has been observed in several types of TIL and is linked to poor prognosis and tumor recurrence (DENKERT *et al.*, 2017; OHAEGBULAM *et al.*, 2015). Mittendorf and collaborators (2014) reported PD-L1 overexpression in TNBC patients and its positive correlation with TIL quantify. In this sense, the poor prognosis indicated by the PD-1 overexpression in TIL and PD-L1 in tumor cells support the hypothesis of using these cellular elements as possible targets for pharmacological management of TNBC. The immunomodulatory agents are mainly represented by the pembrolizumab (targeting PD-1) and atezolizumab (targeting PD-L1) monoclonal antibodies (MITTENDORF *et al.*, 2014; OHAEGBULAM *et al.*, 2015).

Atezolizumab is a human-derived immunoglobulin G1 (IgG1), a monoclonal antibody produced through genetic engineering that selectively targets the PD-L1 in the tumor microenvironment. Atezolizumab acts by inhibiting PD-L1, which is produced by cancer cells to bypass the immune system and negatively modulates T lymphocytes responsiveness against cancer cells, as can be seen in **figure 2**. Atezolizumab as a single agent was already approved for the metastatic urothelial lesions and non-small cell lung cancer treatment. Additionally, this agent presented a safety profile and clinical effectiveness in patients with other solid tumors, including TNBC (SCHMID *et al.*, 2018).

The FDA has granted accelerated approval of atezolizumab in combination with nab-paclitaxel for TNBC patients that present locally advanced or metastatic unresectable positive PD-L1 expression tumors. Schmid et al. (2018) demonstrated by a phase 3 trial study

(IMpassion130 trial) that the treatment with atezolizumab associated with nab-paclitaxel prolonged the survival of PD-L1 positive metastatic TNBC patients of 5.0 to 7.5 months, without triggering additional adverse reactions in comparison to those observed in a single treatment schedule. Besides, in the intention-to-treat (ITT) analysis, the median overall survival (OS) was 21.3 months with atezolizumab plus nab-paclitaxel and 17.6 months with placebo plus nab-paclitaxel; among patients with PD-L1–positive tumors, the median OS was 25.0 months and 15.5 months, respectively (SCHMID *et al.*, 2018). These results were updated in a second interim analysis (data cutoff Jan 2, 2019), in which median OS in the ITT patients was 21.0 months with atezolizumab and 18.7 months with placebo. In the exploratory OS analysis of patients with PD-L1 immune cell-positive tumors, median OS was 25.0 months with atezolizumab versus 18.0 months with placebo. No new treatment-related deaths have been reported since the primary clinical data cutoff date (April 17, 2018) (SCHMID *et al.*, 2020).

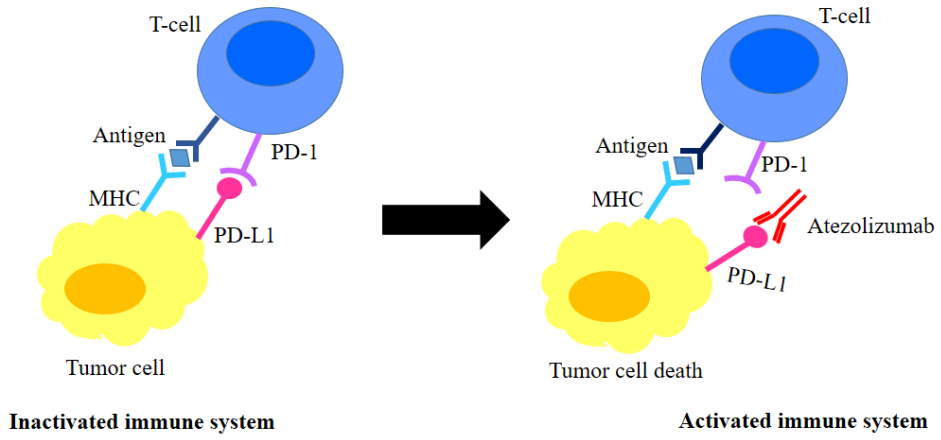

Figure 2 Illustration of atezolizumab anti-PD-L1 activity. Adapted from Kagihara et al. (KAGIHARA *et al.*, 2020). *MHC: Major Histocompatibility Complex; PD-1: Programmed Cell Death-1; PD-L1: Programmed Death-Ligand 1

Iwata et al. (2019) assessed the efficacy and safety of atezolizumab plus nab-paclitaxel in the IMpassion130 Japanese subpopulation. The study enrolled 65 patients whose co-primary endpoints evaluated were progression-free survival (PFS) and OS (ITT population and PD-L1 immune cell-positive subgroup). The median PFS was 7.4 months versus 4.6 months for

atezolizumab plus nab-paclitaxel and placebo plus nab-paclitaxel, respectively. In the PD-L1 immune cell-positive subgroup, median PFS was 10.8 months versus 3.8 months for atezolizumab plus nab-paclitaxel and placebo plus nab-paclitaxel, respectively. The incidence of all adverse events in Japanese patients was comparable to that in patients from the overall IMpassion130 population (IWATA *et al.*, 2019).

Adams et al. (2019) reported a phase 1b trial combining immune checkpoint blockade with chemotherapy in metastatic TNBC, in which safety, clinical activity, and biomarker analyses for 33 patients who received atezolizumab plus nab-paclitaxel were assessed. All patients experienced 1 or more treatment-related adverse effects; the most frequent were neutropenia, fatigue and alopecia. The objective response rate (ORR) was 39.4 % with duration of objective response (DOR) ranging from 2.9 to 20.9 months. The PFS was 5.5 months and OS was 14.7 months. In exploratory subgroup analyses, clinical activity parameters were examined by line of therapy (first line 1L vs second line or later 2L +) and PD-L1 status (PD-L1 positive defined as ≥1% of tumor-infiltrating immune cells (ICs) expressing PD-L1, and PD-L1 negative defined as <1% of ICs expressing PD-L1). Accordingly, to the authors, no statistically significant associations were found (ADAMS *et al.*, 2019).

Thus, taking into consideration these positive outcomes, the National Health Surveillance Agency (ANVISA) approved the first immunotherapy treatment for TNBC patients in Brazil on May 13, 2019 (BRASIL, 2019). As a single agent, atezolizumab was well tolerated and provided durable clinical benefit in patients with metastatic TNBC with stable or responding disease and in earlier lines of treatment. It was a multicenter phase 1 trial investigation of atezolizumab monotherapy in which 116 patients were enrolled for safety, and 115 were monitored for ORR. Treatment-related adverse effects occurred in 73 (63%) patients, with the majority being grade 1 to 2 (pyrexia, fatigue and nausea). Only 11 % of patients presented adverse effects classified as grade 3 or 4 (grade 3: pruritic rash, lichen planus, and adrenal insufficiency; and grade 4: pneumonitis). The study demonstrated a durable clinical activity and interesting survival benefit, particularly in first-line patients (OS: 1L – 17.6 months vs 2L+ - 7.3 months) or those with higher levels of ICs (12.6 months versus 6.7 months, respectively for >10% ICs and ≤10% ICs) and PD-L1 positive (10.1 months versus 6.9 months, respectively for PD-L1 positive and negative), suggesting a potential therapeutic benefit with atezolizumab in metastatic TNBC (EMENS *et al.*, 2019).

IMpassion132 is an ongoing multinational double-blind placebo-controlled two-arm randomized Phase III trial, which compared atezolizumab plus non-taxane chemotherapy (Carboplatin AUC 2 + gemcitabine 1000 mg/m^2, days 1 and 8, or Capecitabine 1000 mg/m^2

bid, days 1–14 every 21 days) versus placebo plus chemotherapy in early relapsing TNBC. All patients have received prior anthracycline and taxane therapy in the (neo)adjuvant setting (CORTÉS *et al.*, 2019). The primary end point that has been used is the OS and the estimated completed date is July 2023 (PÉREZ-GARCÍA *et al.*, 2020). It is important to mention that IMpassion131 is other ongoing randomized, placebo-controlled, phase 3 study, which compares the efficacy and safety of first-line atezolizumab plus paclitaxel versus placebo plus paclitaxel in previously untreated patients with recurrent, inoperable locally advanced or metastatic TNBC. The primary end point is PFS and the estimate date for completing the study is January 2021 (PÉREZ-GARCÍA *et al.*, 2020).

Importantly, the absence of any therapeutic answer of IMpassion130 against PD-L1 negative TNBC highlights the need of investigating if more immunogenic chemotherapy could induce an immunologically "cold" tumor response to PD-1/PD-L1-blockage. In such context, ALICE is an ongoing randomized, double-blind, placebo-controlled exploratory phase II study that evaluates the safety and efficacy of atezolizumab combined with immunogenic chemotherapy in patients with metastatic TNBC. The patients (75) enrolled in the study were randomly divided in two groups (2:3): A) pegylated liposomal doxorubicin (PLD 20 mg/m^2 intravenously every 2nd week) + cyclophosphamide (50 mg per day, first 2 weeks in each 4 week cycle) + placebo; B) pegylated liposomal doxorubicin (PLD 20 mg/m^2 intravenously every 2nd week) + cyclophosphamide (50 mg per day, first 2 weeks in each 4 week cycle) + atezolizumab (intravenously 840 mg every 2nd week until disease progression or for a maximum of 24 months). The primary objectives were toxicity and PFS assessment, while the secondary objectives include OS, tumor response rate, clinical benefit rate, patient reported outcomes, biomarkers and tumor-immune evolution over therapy assessment (KYTE *et al.*, 2020).

Regarding the financial cost, some studies were carried out in order to verify the cost-effectiveness by adding atezolizumab to nab-paclitaxel therapy. The results are still contradictory; Phua et al. and Weng et al. demonstrated that although the clinical benefits promoted by including atezolizumab in TNBC treatment, it still not an interesting cost-effective strategy (PHUA *et al.*, 2020; WENG *et al.*, 2020). On the other hand, the conclusions of Wu and Ma reported that the association of atezolizumab plus nab-paclitaxel has a beneficial cost-effectiveness, suggesting that the approach is a favorable economic alternative for TNBC patients that present PDL-1 increased levels (WU; MA, 2020).

CONCLUSIONS

Despite some ongoing studies, it is possible to conclude that inclusion of atezolizumab to conventional therapies for TNBC, mainly nab-paclitaxel, have been presenting satisfactory clinical benefits to the patients. In addition, the bibliographic review contributes to a joint performance of the health team in the management of therapy and adverse effects, seeking a safe and effective treatment for patients with TNBC.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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