Meta Narrative Review of PD-L1 by Immunotherapy on Triple-Negative Breast Cancer

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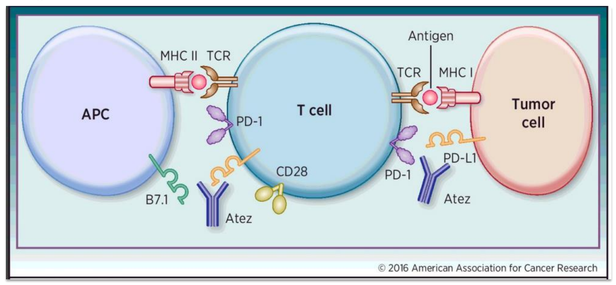
Introduction

PD-1/PD-L1 is a transmembrane protein found on a wide range of cells, including immune, epithelial, and endothelial cells. It has recently been discovered that these proteins are being used by cancer cells as an adaptive immunity mechanism to avoid immune responses. PD-1 is expressed in our T cells, whereas PD-L1 is used to block T-cells from fighting off the cancer cells in patients, so immunotherapy uses PD-1 and PD-L1 inhibitors to help T cells fight off cancer cells and are signified as “immune checkpoint inhibitors". This meta-narrative will work to review the current research that is trying to understand the connection of using PD-L1 biomarkers to detect breast cancer. The material evaluates the prognosis of the relationship between PD-L1 and the different types of breast cancers that have aided in experimental results analyzing the data that PD-L1 drugs such as Atezolizumab have on breast cancer patients. There will be further information in the meta-narrative exploring the complement treatments of PD-L1 and drugs as a method of alternative treatment. Using information such as case studies and immunostaining lab data to observe the evaluation of the relationship between PD-L1 and breast cancer. (Mediratta, 2020)

Figure 1: Mechanism of Atezolizumab



Significant of the Research

PD-L1 IHC helps healthcare professionals indicate how the patient responds to treatment with PD-L1 inhibitors with specific tumor types such as triple-negative breast cancer(TNBC). There are continuing research on monotherapy and combined PD-L1 + chemotherapy to contrast the effectiveness on patients with TNBC.

Guiding Research Question/Hypothesis

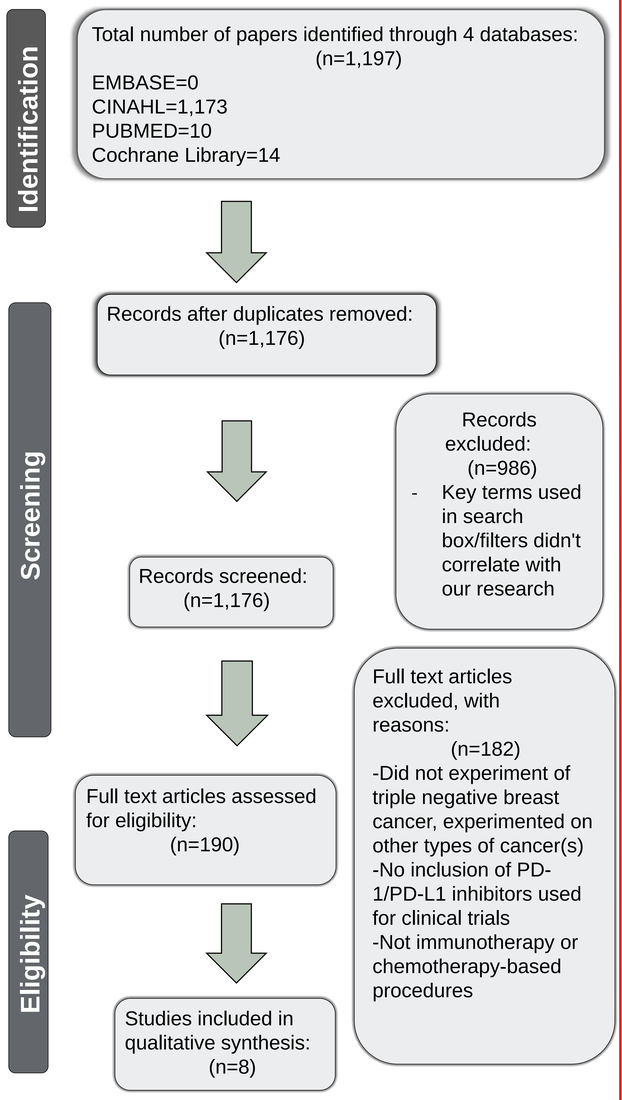
How do PD-L1 inhibitor drugs compare to other treatment methods in patients' response to treatment who are diagnosed with triple-negative breast cancer and how does it affect the prognosis?

Methodology

- Articles published within 5 years to date (2018-2023)
- Search conducted to evaluate different PD-L1 inhibitor drug effects
- Other cancer trials other than triple-negative breast cancer were excluded
- Search terms; "PD-L1 immunotherapy on triple-negative breast cancer", "atezolizumab", "pembrolizumab"
- Survival rates collected for data to support hypothesis

Articles Selection Flow Chart

Figure 2.



Note. Flow diagram of analysis of articles searched leading to our studies that are used in our qualitative for our research.

Result and Implications

Figure 3.

Study Name	Author	Year	Phase of Trial	Condition	Inhibitor	Result
Combine immunotherapy for metastatic triple-negative Breast cancer	He.R	2022	Phase 3	mTNBC	pembrolizumab	mOS: 12.7 months with pembrolizumab. 11.6 with chemotherapy
Current progress and challenges of immunotherapy	M.Kara	2020	Phase 3	TNBC	Atezolizumab/ placebo + Nab placlitaxel	mOS: 21.3 months
			Phase 3	Previous untreated mTNBC	1. Atezolizumab+ Nab-Paclitaxel 2. Placebo+ Nab-Paclitaxel	mOS: 21.3 months for arm (1); 17.6 for arm (2).
			Phase 3	mTNBC	Pembrolizumab	mOS: 9.0 months for past treatment; 18.0 months for PD-L1 tumor.
			Phase 3	Previous untreated/ recurrent, inoperable mTNBC stage IV	1. Pembrolizumab + chemotherapy 2. Placebo + chemotherapy	ORR: 53% for arm (1); 40% for arm (2)
			Phase 3	mTNBC	1. Pembrolizumab 2. Chemotherapy	mOS: 9.9 months for arm (1); 10.8 months for arm (2)
Rationale and clinical search progress on PD-1/PD-L1	Ren. Y	2022	Phase 3	mTNBC	1. Placebo + Nab-Pabclitaxel 2. Atezolizumab + Nab-Pabclitaxel	mOS: 18.0 months (1); 25.0 months (2).

Note: Table analysis of articles collected, and results summarized in findings. PD-L1: programmed death-ligand 1, PD1: program death 1, mOS: median overall survival, mTNBC: metastatic breast cancer, TNBC: triple-negative breast cancer, ORR: objective response rate.

Strength and Limitations

Strengths:

- Pembrolizumab-chemotherapy showed meaningful results in progression-free survival(PFS) as compared to placebo-chemotherapy among patients with metastatic triple-negative breast cancer.

- Atezolizumab prevented interaction with PD-L1 receptors and B7-1 reversing T-cell suppression.
- Atezolizumab plus nab-paclitaxel lengthened progression-free survival among patients with metastatic triple-negative breast cancer in both the intention-to-treat population and the PD-L1 positive subgroup.
- Efficacy in immunotherapy provides evidence of benefits using Atezolizumab–nab-paclitaxel in patients with PD-L1 positive tumors

Limitations:

- Tumor sizes and cancer stage for each patient varied, most common was early stages however, tumor sizes may affect the results on inhibitor drugs distributed.
- Small samples of patients were used during clinical trials and many came from a single institution therefore, the range of diversity was low and not running into problems due to the heterogeneity of PD-L1 expression may be unavoidable.
- One article stated that pathologists in the research trial were not trained using CPS to detect TNBC
- One article focused primarily on the immunohistochemistry assay. Not discussing the PFS, Overall survival(OS), or adverse events(AE) of the trial participants comparing adjuvant therapy to monotherapy of PD-L1 inhibitors.

Conclusions

The articles included in the meta-analysis focused on comparing the current practice of monotherapy treatment of chemotherapy to adjuvant therapy of chemotherapy and immunotherapy for the treatment of TNBC and metastatic TNBC. The resources used recently accepted FDA-approved PD-L1 inhibitors, such as Pembrolizumab and Atezolizumab, in conjunction with frequently used chemotherapy drugs, such as Paclitaxel and Niraparib. The compiled results showed a slightly positive result of progression-free survival and overall survivability (OS) in adjuvant therapy of chemotherapy and immunotherapy. The results were significantly more prevalent in patients who exhibited PD-L1 positive tumors compared to PD-L1 negative tumors. This is to be expected, as the immunotherapy treatment is designed to target the PD-L1 receptors. The AE results were in line with the standard toxic effects of such medications, and no significant, out of the ordinary, AE effects were documented. However, a significant number of studies had participants who had received prior neoadjuvant therapy before the trial, which may have severely impacted the trial results. The age range was consistent between the articles, ranging from 49 to 53 years of age for women. More research studies need to be performed highlighting the effects of PD-L1 inhibitors on PD-L1 positive tumor cells comparing monotherapy of immunotherapy treatment, versus adjuvant therapy of immunotherapy + chemotherapy, and immunotherapy + radiotherapy.

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