

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## INTRODUCTION

**Review question / Objective:** In recent years, controversial results have emerged from studies on the use of pembrolizumab in combination with chemotherapy in the treatment of triple-negative breast cancer

## Pembrolizumab in combination with chemotherapy vs. placebo in combination with chemotherapy for triple-negative breast cancer: a systematic review and meta-analysis

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**Review question / Objective:** In recent years, controversial results have emerged from studies on the use of pembrolizumab in combination with chemotherapy in the treatment of triple-negative breast cancer (TNBC). Therefore, we performed a meta-analysis to investigate the value of pembrolizumab in combination with chemotherapy in the treatment of TNBC.

**Eligibility criteria:** We set the following exclusion criteria: a) study type: retrospective studies, cohort studies, case reviews, and case reports; b) participants: patients with other forms of breast cancer; c) controls: active controls (i.e., known, effective treatments compared to placebo that are experimental).

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 September 2022 and was last updated on 03 September 2022 (registration number INPLASY202290015).

(TNBC). Therefore, we performed a meta-analysis to investigate the value of pembrolizumab in combination with chemotherapy in the treatment of TNBC.

**Condition being studied:** Pembrolizumab in combination with chemotherapy vs. placebo in combination with chemotherapy for triple-negative breast cancer.

## METHODS

**Search strategy:** A total of 1053 studies were systematically investigated by two researchers (SL and FJ) from Pubmed, Embase and the Cochrane Library to meet the consistency between results searched and our goal of identifying till July 2022. The keywords for searching were as follows: "pembrolizumab"[Title/Abstract] AND ("triple-negative breast cancer"[Title/Abstract] OR "triple-negative breast carcinoma"[Title/Abstract] OR "triple-negative breast tumor"[Title/Abstract] OR "triple-negative mammary cancer"[Title/Abstract] OR "TNBC"[Title/Abstract]). In addition, relevant systematic reviews and meta-analyses of RCTs were independently and manually screened to ensure a more comprehensive search.

**Participant or population:** Participants: patients aged 18-65 years diagnosed with TNBC; intervention: Patients were treated with conventional chemotherapy drugs plus pembrolizumab and conventional chemotherapy drugs plus placebo (pembrolizumab +chemotherapy Vs. placebo +chemotherapy); clinical outcomes: end points collected were pathologic complete response (PCR), events-free survival (EFS),and overall survival (OS).

**Intervention:** Patients were treated with conventional chemotherapy drugs plus pembrolizumab and conventional chemotherapy drugs plus placebo (pembrolizumab +chemotherapy Vs. placebo +chemotherapy).

**Comparator:** Patients were treated with conventional chemotherapy drugs plus pembrolizumab and conventional chemotherapy drugs plus placebo (pembrolizumab +chemotherapy Vs. placebo +chemotherapy).

**Study designs to be included:** All the selected 4 RCTs enrolled a total of 2751 patients were provided for efficacy and safety outcome analysis.

**Eligibility criteria:** We set the following exclusion criteria: a) study type: retrospective studies, cohort studies, case reviews, and case reports; b) participants: patients with other forms of breast cancer; c) controls: active controls (i.e., known, effective treatments compared to placebo that are experimental).

**Information sources:** Databases such as Pubmed, Embase and the Cochrane Library were searched for randomized controlled trials (RCTs) on pembrolizumab in combination with chemotherapy (PBC Group) and placebo in combination with chemotherapy (PLC Group) for TNBC by July2022.

**Main outcome(s):** End points collected were pathologic complete response (PCR), events-free survival (EFS),and overall survival (OS). The PCR in TNBC shows that patients treated with pembrolizumab in combination with chemotherapy were better than those treated by placebo in combination with chemotherapy(OR=2.69, 95% CI: 1.24–5.84, p=0.009) (Figure 2A). As shown in the figure (PCR), the combined result  $I^2=78.9\%$ , so we performed a sensitivity analysis.

**Quality assessment / Risk of bias analysis:** Risk of bias maps for individual studies were assessed using Review Manager 5.4 software. The Cochrane Collaboration's uniform criteria for assessing the risk of bias in RCTs were used, which included: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential bias. Each bias criterion was categorized as classified as "low", "high", or "unclear".

**Strategy of data synthesis:** None.

**Subgroup analysis:** None.

**Sensitivity analysis:** None.

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**Keywords:** pembrolizumab, combination chemotherapy, triple-negative breast cancer, PD-1/PD-L1, meta-analysis.

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