INPLASY PROTOCOL

To cite: Zhang et al. Efficacy and Safety of PD-1/PD-L1 Inhibitors in Triple-Negative Breast Cancer: A Systematic Review and Meta-Analysis. Inplasy protocol 202250128. doi: 10.37766/inplasy2022.5.0128

Received: 21 May 2022

Published: 21 May 2022

Corresponding author:
Ang Zheng

812144104@qq.com

Author Affiliation:
Department of Burn Plastic Surgery, Chaoyang Central Hospital, Chaoyang, Liaoning Province, China.

Support: **NSFC.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

Efficacy and Safety of PD-1/PD-L1 Inhibitors in Triple-Negative Breast Cancer: A Systematic Review and Meta-Analysis

Zhang, ML[1]; Song, J[2]; Yang, HG[3]; Jin, F[4]; Zheng, A[5].

Review question / Objective: **Breast cancer threatens women's health seriously, and triple-negative breast cancer (TNBC) is the subtype of breast cancer with poor prognosis. There is still a lack of effective therapeutic target in TNBC. We conducted a meta-analysis to evaluate the efficacy and safety of programmed cell death protein1 (PD-1)/ programmed death protein ligand 1 (PD-L1) inhibitors in combination with chemotherapy for TNBC patients.**
Condition being studied: **Several clinical trials focusing on immunotherapy in combination with chemotherapy have achieved promising outcomes in TNBC, nevertheless, the results of clinical trials have been inconsistent. In this meta-analysis, we included all available randomized controlled trials (RCTs) and investigated early-stage and advanced TNBC, respectively. The meta-analysis aims to evaluate the efficacy and safety of PD-1/PD-L1 inhibitors combined with chemotherapy and provide effective strategies for clinical diagnosis and treatment.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 May 2022 and was last updated on 21 May 2022 (registration number INPLASY202250128).

INTRODUCTION

Review question / Objective: **Breast cancer threatens women's health seriously, and triple-negative breast cancer (TNBC) is the subtype of breast cancer with poor prognosis. There is still a lack of effective therapeutic target in TNBC. We conducted a meta-analysis to evaluate the efficacy and safety of programmed cell death protein1 (PD-1)/ programmed death protein ligand 1 (PD-L1) inhibitors in combination with chemotherapy for TNBC patients.**

Condition being studied: **Several clinical trials focusing on immunotherapy in**

combination with chemotherapy have achieved promising outcomes in TNBC, nevertheless, the results of clinical trials have been inconsistent. In this meta-analysis, we included all available randomized controlled trials (RCTs) and investigated early-stage and advanced TNBC, respectively. The meta-analysis aims to evaluate the efficacy and safety of PD-1/PD-L1 inhibitors combined with chemotherapy and provide effective strategies for clinical diagnosis and treatment.

METHODS

Participant or population: Triple-negative breast cancer patients

Intervention: The experimental group was PD-1/PD-L1 inhibitors in combination with chemotherapy.

Comparator: Chemotherapy combined with or without placebo was in the control group.

Study designs to be included: II. study type was randomized controlled trial (RCT).

Eligibility criteria: I. patients were confirmed TNBC by pathology; II. study type was randomized controlled trial (RCT); III. the experimental group was PD-1/PD-L1 inhibitors in combination with chemotherapy, and chemotherapy combined with or without placebo was in the control group; IV. end points were pathological complete response (pCR), event free survival (EFS), progress free survival (PFS) or overall survival (OS); V. AEs associated with ICIs plus chemotherapy could be extracted.

Information sources: We searched PubMed, EMBASE, the Cochrane Library and Web of Science in November 2021. The search strategy combined subject words and free words. It included 'triple negative breast neoplasms' and free words, 'immune checkpoint inhibitors' and free words. In addition, specific drug names of PD-1/PD-L1 inhibitors were searched simultaneously, such as, 'pembrolizumab', 'atezolizumab', 'durvalumab', 'avelumab', and 'nivolumab'. According to the McMaster University's search formula, the retrieval strategy of study type was 'randomized controlled trial' OR 'randomized' OR 'placebo'. The search was conducted with an 'or' between the subject words and free words. 'And' was used to connect between subject words. Moreover, we also screened references of reviews and meta-analyses related to ICIs, to ensure the inclusion of all currently available RCTs.

Main outcome(s): Outcome indicators such as pCR, EFS, PFS, OS, hazard ratio (HR), 95% confidence interval (CI) and the occurrence of AEs.

Quality assessment / Risk of bias analysis: We performed quality evaluation of the RCTs through the Cochrane Collaboration's tool . The process was completed in the Review Manager 5.3 software. The criteria used to assess the quality of the literature included: I. random sequence; II. allocation concealment; III. blinding of participants and personnel; IV. blinding of outcome; V. incomplete outcome data; VI. selective reporting; VII. other bias. 'low risk', 'high risk' and 'unclear' were made for each item. Two researchers independently assessed the quality of the literature and resolved differences through discussion until the results were unified.

Strategy of data synthesis: Data analysis was carried out through the Review Manager 5.3 software. Odds risk (OR) and 95% CI were used to evaluate pCR and AEs between the two groups. We used HR and 95% CI to assess EFS, PFS and OS. $P < 0.05$ was considered statistically significant. We judged the heterogeneity according to Cochran Q and I^2 value. Cochran Q $P < 0.1$ or $I^2 \geq 50\%$ indicated that there was heterogeneity among the included studies. We further performed subgroup analysis or sensitivity analysis, otherwise random effect model was used. In addition, the fixed effect model was adopted when Cochran Q $P > 0.1$ and $I^2 < 50\%$.

Subgroup analysis: Data analysis was carried out through the Review Manager 5.3 software. We judged the heterogeneity according to Cochran Q and I^2 value. Cochran Q $P < 0.1$ or $I^2 \geq 50\%$ indicated that there was heterogeneity among the included studies. We further performed subgroup analysis or sensitivity analysis, otherwise random effect model was used.

Sensitivity analysis: Data analysis was carried out through the Review Manager 5.3 software. We judged the heterogeneity according to Cochran Q and I^2 value. Cochran Q $P < 0.1$ or $I^2 \geq 50\%$ indicated that there was heterogeneity among the included studies. We further performed subgroup analysis or sensitivity analysis, otherwise random effect model was used.

Country(ies) involved: China.

Keywords: triple-negative breast cancer, PD-1/PD-L1 inhibitors, immunotherapy, chemotherapy, meta-analysis.

Contributions of each author:
Author 1 - Meilin Zhang.
Author 2 - Jian Song.
Author 3 - Hongguang Yang.
Author 4 - Feng Jin.
Author 5 - Ang Zheng.