INPLASY PROTOCOL

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None declared.

Efficacy of immunotherapy plus chemotherapy in Advanced Triple-Negative Breast Cancer: A Systematic Review and Meta-analysis

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Review question / Objective: **To explore the efficacy of adding immune checkpoint inhibitors to chemotherapy in advanced triple-negative breast cancer and whether it can prolong overall survival and progression-free survival in relevant populations.**
Information sources: **(triple-negative breast cancer[MeSH Terms]) AND （Immunotherapy OR PD-1 inhibitor OR PD-L1 inhibitor OR anti-PD-1 OR anti-PDL-1 OR Atezolizumab OR Durvalumab OR Pembrolizumab OR immune checkpoint inhibitor）.In EMBASE the search algorithm was: Term(s): PD-1 inhibitor OR PD-L1 inhibitor OR anti-PD-1 OR anti-PDL-1 OR Atezolizumab OR Durvalumab OR Pembrolizumab OR immune checkpoint inhibitor; Year(s): 2010-2022; Title, abstract or author-specified keywords: Immunotherapy; Title: triple-negative breast cancer. And The Cochrane Library was (triple-negative breast cancer in Record Title) AND (Immunotherapy in All Text OR PD-L1 inhibitor in All Text OR PD-1 inhibitor in All Text - in Trials) (Word variations have been searched).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 August 2022 and was last updated on 07 August 2022 (registration number INPLASY202280026).

INTRODUCTION

Review question / Objective: **To explore the efficacy of adding immune checkpoint inhibitors to chemotherapy in advanced triple-negative breast cancer and whether it can prolong overall survival and progression-free survival in relevant populations.**

Condition being studied: **Breast cancer accounts for 30% of all cancers in women and will surpass lung cancer as the number one cancer worldwide by 20201. It has grown at a rate of 0.5% per year since 20142. Triple-negative breast cancer is a type of breast cancer that is negative for estrogen, progesterone, and human epidermal growth factor 2 (HER2). It**

accounts for only 15% of all types of breast cancer and is the type with a poor prognosis. Due to its specific molecular phenotype, TNBC is insensitive to endocrine therapy or molecularly targeted therapy. Chemotherapy is often used in clinical treatment to prolong the life of patients.Anti-PD-1/PD-L1 drugs have become the focus of current immunotherapy. Programmed death receptor 1 (PD-1) is an immunosuppressive molecule that targets PD-1 for tumor immunity, and its binding to its ligand (PD-L1) triggers the programmed death of T cells, resulting in Tumor cells gaining immune escape. The U.S. FDA approved atezolizumab and pembrolizumab for unresectable locally advanced or metastatic PD-L1-positive TNBC in 2019 and 2020, respectively. Immunotherapy has trans-generational significance. At present, relevant studies have shown that PD-1 inhibitors have clinical effects on TNBC survival.

METHODS

Participant or population: Includes females with recurrent, metastatic, inoperable, or advanced triple-negative breast cancer. These women received chemotherapy combined with immune checkpoint inhibitors (including pembrolizumab, atezolizumab, and durvalumab)1. as second-line or third-line therapy2. in single arm study or parallel-group study with placebo/ any chemotherapeutic3. as rescue advanced triple-negative breast cancer treatment.

Intervention: Immunotherapy plus Chemotherapy, including but not limited to Atezolizumab, Pembrolizumab, Durvalumab.

Comparator: Chemotherapy alone or plus placebo, including nab-paclitaxel; paclitaxel; or gemcitabine plus carboplatin.

Study designs to be included: As second-line or third-line therapy, public randomised controlled trials to access full text and extract raw data.

Eligibility criteria: Literature inclusion criteria were:(1)risk ratios (HRs) and 95% confidence intervals (CIs) for reported OS and PFS feasibility studies. Exclude the following criteria:(1)literature for which full text and raw data are not available. (4) repeated publications, reviews, and other non-RCT literature.

Information sources: (triple-negative breast cancer[MeSH Terms]) AND (Immunotherapy OR PD-1 inhibitor OR PD-L1 inhibitor OR anti-PD-1 OR anti-PDL-1 OR Atezolizumab OR Durvalumab OR Pembrolizumab OR immune checkpoint inhibitor) .In EMBASE the search algorithm was: Term(s): PD-1 inhibitor OR PD-L1 inhibitor OR anti-PD-1 OR anti-PDL-1 OR Atezolizumab OR Durvalumab OR Pembrolizumab OR immune checkpoint inhibitor; Year(s): 2010-2022; Title, abstract or author-specified keywords: Immunotherapy; Title: triple-negative breast cancer. And The Cochrane Library was (triple-negative breast cancer in Record Title) AND (Immunotherapy in All Text OR PD-L1 inhibitor in All Text OR PD-1 inhibitor in All Text - in Trials) (Word variations have been searched).

Main outcome(s): Overall survival(OS); Progression-Free-Survival(PFS).

Additional outcome(s): 1.PD-L1 positive populations OS and PFS 2. adverse events of grade 3 or 4.

Quality assessment / Risk of bias analysis: The risk of bias will be assessed using the Cochrane risk of bias.

Strategy of data synthesis: Analyses comparing overall survival and progression-free survival of immunotherapy plus chemotherapy versus chemotherapy alone or with placebo, calculating reported hazard ratios (HR) and 95% confidence intervals (CI) for each outcome, followed by meta-analysis using Revman 5.4. For adverse events, we used a

dichotomy, odds or risk ratio (OR/RR) with 95% confidence intervals (CI) will be calculated. If we are unable to pool the data statistically using meta-analysis we will conduct a narrative synthesis of the results.

Subgroup analysis: Comparing OS and PFS for different PD-L1 combined positive score.

Sensitivity analysis: None.

Country(ies) involved: Chine.

Keywords: Triple-Negative Breast Cancer, Immunotherapy, immune checkpoint inhibitors, chemotherapy, Atezolizumab, Pembrolizumab, Durvalumab.

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