

INPLASY PROTOCOL

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None declared.

Impact of platinum-based chemotherapy on the prognosis of early triple-negative breast cancer: a Systematic review and Meta-analysis

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Review question / Objective: Our meta-analysis aimed at analyzing survival with platinum-based neoadjuvant and adjuvant chemotherapy in patients with TNBC.

Condition being studied: Whether platinum-based chemotherapy can improve survival of neoadjuvant and adjuvant chemotherapy in patients with triple-negative breast cancer (TNBC) is still controversial, though it can improve pCR. Our meta-analysis aimed at analyzing survival with platinum-based neoadjuvant and adjuvant chemotherapy in patients with TNBC.

Information sources: PubMed, EMBASE, MEDLINE, and Cochrane for studies up to December 2021.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 February 2022 and was last updated on 14 February 2022 (registration number INPLASY202220050).

INTRODUCTION

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based neoadjuvant and adjuvant chemotherapy in patients with TNBC.

METHODS

Search strategy: We searched PubMed, EMBASE, MEDLINE, Cochrane databases, and several major conferences up to December 2021. Fixed and random models were used for our meta-analysis. Disease-free survival (DFS), overall survival (OS), and side effects data were extracted from the included literature in addition to the corresponding pooled hazard ratio (HR) and odds ratio (OR) with 95% confidence intervals (CIs). The following keywords were used in our literature search: (a) breast neoplasm OR breast cancer OR breast carcinoma OR breast tumor OR breast tumor OR mammary cancer (b) triple-negative OR TNBC; (c) platinum compounds OR cisplatin OR carboplatin OR platinum; (d) NACT OR neoadjuvant chemotherapy OR NCT OR neoadjuvant chemotherapy OR preoperative chemotherapy OR primary chemotherapy OR preoperative chemotherapy; and (e) adjuvant chemotherapy.

Participant or population: The inclusion criteria were organized using the PICO strategy. The study inclusion criteria were (a) women with early TNBC; (b) having received adjuvant or neoadjuvant chemotherapy based on platinum or other chemotherapy drugs (patients in the experimental group received platinum-based neoadjuvant or adjuvant chemotherapy, whereas patients in the control group received chemotherapy without platinum); (c) survival after neoadjuvant or adjuvant chemotherapy was followed, and (d) pCR after neoadjuvant chemotherapy was evaluated. All the included studies were randomized controlled trials (RCTs) with available survival data, including DFS and OS. We also summarized the detailed information of each study, including study name, year of publication, author, patient grouping, basic patient information, neoadjuvant and adjuvant chemotherapy regimens, pCR, and median follow-up. We searched the databases PubMed, EMBASE, MEDLINE,

and Cochrane for studies up to January 2021. These studies compared the differences in survival between platinum-based and non-platinum-based chemotherapy in neoadjuvant and adjuvant regimens. We also searched major conferences, including the European Society of medical oncology (ESMO), the American Society of Clinical Oncology (ASCO), and the San Antonio Breast Cancer Symposium (SABCS). The following keywords were used in our literature search: (a) breast neoplasm OR breast cancer OR breast carcinoma OR breast tumor OR breast tumor OR mammary cancer (b) triple-negative OR TNBC; (c) platinum compounds OR cisplatin OR carboplatin OR platinum; (d) NACT OR neoadjuvant chemotherapy OR NCT OR neoadjuvant chemotherapy OR preoperative chemotherapy OR primary chemotherapy OR preoperative chemotherapy; and (e) adjuvant chemotherapy.

Intervention: Data extraction and quality assessment The first author's name, the year of publication, the type of study design, the total number of patients receiving platinum-based and anthracycline and/or paclitaxel based chemotherapy, DFS and OS of patients receiving platinum-based and anthracycline and/or paclitaxel based chemotherapy, and the side effects of platinum-based and anthracycline and/or paclitaxel based chemotherapy were extracted from all included studies. We also extracted the number of TNBC patients who achieved pCR after neoadjuvant chemotherapy with or without platinum-based compounds. Study objectives We extracted DFS and OS data from the studies and the corresponding hazard ratio (HR) and 95% confidence interval (CI). If the HR and 95% CI were not provided in the study, we extracted the HR and 95% CI from the survival curve using Engauge Digitizer software or contacted the corresponding author to ask for the original data. We extracted the side effects of platinum-based and anthracycline and/or paclitaxel based chemotherapy in TNBC patients and the corresponding odds ratio

(OR) and 95% CI according to the number of people with side effects. The OR and the 95% CI of pCR were also extracted. We compared DFS and OS in platinum-based and anthracycline and/or paclitaxel based chemotherapy.

Comparator: We compared DFS and OS in platinum-based and anthracycline and/or paclitaxel based chemotherapy.

Study designs to be included: Randomized controlled study

Eligibility criteria: 1. women with early TNBC; 2. having received adjuvant or neoadjuvant chemotherapy based on platinum or other chemotherapy drugs (patients in the experimental group received platinum-based neoadjuvant or adjuvant chemotherapy, whereas patients in the control group received chemotherapy without platinum); 3. survival after neoadjuvant or adjuvant chemotherapy was followed, and 4. pCR after neoadjuvant chemotherapy was evaluated.

Information sources: PubMed, EMBASE, MEDLINE, and Cochrane for studies up to December 2021.

Main outcome(s): Pooled analysis of DFS in patients with TNBC who received platinum-based or platinum-free anthracycline and/or paclitaxel based chemotherapy.

Additional outcome(s): 1. Pooled analysis of OS and the subgroup analysis of DFS and OS. 2. The subgroup analysis was conducted considering neoadjuvant and adjuvant and platinum-based chemotherapy with or without anthracycline in the experimental group. 3. Side effects of chemotherapy were also secondary outcomes.

Data management: We used Stata 12.0, Review Manager 5.4, and Engauge Digitizer software for our meta-analysis. An HR > 1 indicates higher ORR and grade 3 and 4 AEs rates in the platinum-based neoadjuvant chemotherapy group. An OR < 1 indicates lower pCR, ORR and grade 3

and 4 AEs rates in the platinum-based neoadjuvant chemotherapy group.

Quality assessment / Risk of bias analysis:

The heterogeneity of our meta-analysis was judged by the p-value and the forest plot I². If I² < 50% and p > 0.1, we used the fixed-effects model. If I² > 50% and P < 0.1, we used the random-effects model. Publication bias was analyzed with Begg's test. A p-value of <0.05 was statistically significant.

Strategy of data synthesis: We extracted DFS and OS data of TNBC patients had received platinum-based and platinum-free neoadjuvant/adjuvant chemotherapy. HRs and 95% CI were calculated for the effect of platinum-based versus platinum-free neoadjuvant/adjuvant chemotherapy for DFS and OS. HR < 1 indicates improved DFS and OS with platinum-based neoadjuvant/adjuvant chemotherapy. HR > 1 indicates reduced DFS and OS with platinum-based neoadjuvant chemotherapy. ORs and 95% CI were calculated for the effect of platinum-based versus platinum-free neoadjuvant/adjuvant chemotherapy for side effects. OR > 1 indicates higher side effect rates in the platinum-based neoadjuvant/adjuvant chemotherapy group. An OR < 1 indicates lower side effect rates in the platinum-based neoadjuvant chemotherapy group.

Subgroup analysis: The subgroup analysis was conducted according to neoadjuvant and adjuvant chemotherapy. Moreover, side effects of chemotherapy were also secondary outcomes.

Sensitivity analysis: We conducted a sensitivity analysis to analyze whether the different characteristics of these studies have an impact on the meta-analysis results. We excluded each study sequentially, and the results showed stable pooled HR estimates.

Country(ies) involved: China.

Keywords: triple-negative breast cancer; platinum; prognosis.

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