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Efficacy and safety of perioperative (neoadjuvant plus adjuvant) immunotherapies for resectable non–small cell Lung Cancer: A systematic review and meta-analysis of phase 3 trials

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 April 2024 and was last updated on 01 April 2024.

INTRODUCTION

Review question / Objective Meta-analysis based on phase III trials which investigated the efficacy and safety of perioperative (neoadjuvant plus adjuvant) immunotherapy in resectable non–small cell lung cancer (NSCLC) patients are lacking. In addition, existing phase III studies have described inconsistent results of perioperative immunotherapies in some important subgroups of patients and requires further investigation.

Rationale This meta-analysis was designed to provide a comparison between the efficacy and safety profiles of perioperative immunotherapies versus perioperative chemotherapy in resectable NSCLC.

Condition being studied Despite the chance of radical resection, stage II-III NSCLC has a high risk of postoperative recurrence, with 52%-75% of patients experiencing local recurrence or distant metastasis within 5 years of surgery. Neoadjuvant/adjuvant chemo can only improve the 5-year survival rate by 5%, which is limited for clinical needs. There is an urgent need to explore better perioperative treatment options to improve the prognosis of stage II-III NSCLC patients. Several phase III trials have been published and demonstrated the efficacy of perioperative immunotherapies in resectable NSCLC, which is expected to hold great promise for these patients. However, no meta-analysis based on phase III studies have comprehensively assessed the association of perioperative immunotherapies with clinical outcomes in resectable NSCLC. Moreover, efficacy of perioperative immunotherapies in some important subgroups of patients were inconsistent

across trails. We attempt to answer these questions through a systematic review and meta-analysis.

METHODS

Search strategy We systematically searched PubMed, Embase and Cochrane Library for relevant articles published in English before March 23, 2024.

Participant or population (1) Patients with resectable non-small cell lung cancer. (2) No prior therapy.

Intervention Perioperative (neoadjuvant plus adjuvant) immunotherapy.

Comparator Perioperative chemotherapy.

Study designs to be included Inclusion criteria: (1) Randomized controlled trials that investigated perioperative (neoadjuvant plus adjuvant) immunotherapy in resectable NSCLC. (2) Phase III trial. Exclusion criteria: (1) Trail that investigated neoadjuvant-only or adjuvant-only immunotherapy in resectable NSCLC. (2) Unpublished gray literature, commentaries, letters, reviews and editorials.

Eligibility criteria Phase III trials that investigated perioperative (neoadjuvant plus adjuvant) immunotherapy in resectable NSCLC.

Information sources PubMed, Embase, Cochrane Library.

Main outcome(s) Event-free survival (EFS); Major pathological response (MPR); pathological complete response (pCR).

Additional outcome(s) Objective response rate(ORR); Overall survival (OS); Incidence rate of adverse event (AE); Surgery outcomes.

Quality assessment / Risk of bias analysis The quality of included RCT studies will be assessed using the Cochrane "Risk of Bias" Tool according to the following items: (1) random allocation method; (2) allocation concealment; (3) whether to adopt a blind method for the participants and researchers; (4) whether the outcome was assessed by a blind method; (5) completeness of outcome data; (6) selective reporting of outcomes; (7) other bias. Each item will be scored as low, high, or unclear risk of bias.

Strategy of data synthesis Literature search, data extraction and quality assessment for eligible articles will be performed by two authors independently. All analyses will be conducted using the software R (version 4.1.1, R Foundation for Statistical Computing) via the meta package. The pooled hazard ratios (HRs) for both EFS and OS of perioperative immunotherapy and perioperative chemotherapy were determined through the generic inverse-variance methods model. Pooled risk difference (RD) for ORR, MPR, PCR, safety and surgery outcomes were derived through the inverse variance method. The heterogeneity among studies will be estimated by the χ^2 and I^2 test. When P value was less than 0.10 or I^2 was greater than 50%, the studies were considered to be heterogeneous and the random-effect model will be applied. Otherwise, a fixed-effect model will be applied.

Subgroup analysis Subgroup analyses were performed according to stage, histology, PD-L1 expression and pCR/MPR status. The analysis method was the same as the strategy for data synthesis.

Sensitivity analysis The stability of the results will be assessed by sensitivity analysis.

Language restriction English.

Country(ies) involved China.

Keywords perioperative, immunotherapy, resectable Non-Small Cell Lung Cancer.

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