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Efficacy and Safety of Neoadjuvant, Adjuvant, and Perioperative Immune Checkpoint Inhibitors Single Agent or with Chemotherapy in Resectable NSCLC: Indirect Comparison and Clinicopathological Impact

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Corresponding author:
Hongbing Liu

ycmeng_nmu@163.com

Author Affiliation:
Department of Respiratory Medicine, Jinling Hospital, Nanjing Medical University.

Meng, YC[1]; Zhang, QF[2]; Wu, RP[3]; Wang, ZF[4]; Li, HJ[5]; Yao, Y[6]; Li, XJ[7]; Gong, YZ[8]; Chen, ZX[9]; Liu, HB[10].

ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

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 06 February 2024 and was last updated on 06 February 2024.

INTRODUCTION

Review question / Objective Resectable non-small cell lung cancer (NSCLC) undergoing surgical resection carries a high risk of cancer recurrence. Several randomized clinical trials (RCTs) have investigated adjuvant, neoadjuvant, and perioperative immunotherapies. Understanding the clinical efficacy and safety of these regimens is necessary for clinical care. OBJECTIVE: To assess the efficacy and safety of neoadjuvant, adjuvant, and perioperative immunotherapies and to indirectly compare the differences among the three.

Condition being studied Lung cancer remains the deadliest cancer in the world. The primary goal for these patients with early and locally advanced resectable NSCLC is cure, and there are currently neoadjuvant, adjuvant, and perioperative immunotherapies available for patients with resectable lung cancer. Therefore, there is an urgent need to explore more desirable treatment options through meta-analysis to guide clinical work and clinical study design.

METHODS

Participant or population Patients with early or locally advanced non-small cell lung carcinoma.

Intervention Neoadjuvant and perioperative immune checkpoint inhibitors plus chemotherapy; Adjuvant immune checkpoint inhibitors.

Comparator Chemotherapy or observation.

Study designs to be included All randomized controlled trials reporting neoadjuvant, adjuvant, and perioperative immune checkpoint inhibitor combined wtih chemotherapy.

Eligibility criteria Studies were included if they satisfied these criteria: (1) Randomized controlled trials (RCTs); (2) comparisons of neoadjuvant, adjuvant, or perioperative immune checkpoint inhibitors (ICIs) with chemotherapy (CT) against CT alone or observation; (3) inclusion of adult patients with early-stage I-III non-small cell lung cancer (NSCLC); (4) reporting of outcomes such as pathologic complete response (pCR), major pathologic response (MPR), adverse events (AEs) of any grade, AEs of grade ≥3, immune-related adverse events (irAEs) of any grade, irAEs of grade ≥3, event-free survival (EFS), and overall survival (OS).Exclusions applied to studies involving patients with prior systemic immunosuppressive therapy or active autoimmune disease, those lacking relevant outcomes, and research incorporating radiotherapy or dual immunotherapy.

Information sources Pubmed, the Cochrane Library, Embase, grey literature.

Main outcome(s) Event-free survival; Major pathologic response; pathologic complete response.

Quality assessment / Risk of bias analysis Risk of bias was assessed using the Cochrane Collaboration tool (RoB 2), and publication bias was assessed using funnel plots, egger's test, and begg's test.

Strategy of data synthesis Dichotomous variables were analyzed using odds ratios (ORs) with 95% confidence intervals (CIs), while survival outcomes were assessed through hazard ratios (HRs) with 95% CIs. Due to heterogeneity among studies, a random effects model was employed. Network meta-analysis facilitated indirect comparisons between neoadjuvant therapy and perioperative therapy within a Bayesian framework.

Subgroup analysis Analyses were conducted considering factors such as PD-L1 expression, initial disease stage, histological type, epidermal growth factor receptor mutation status, gender, and the occurrence of MPR/pCR.

Sensitivity analysis Sensitivity analyses, conducted by sequentially excluding individual studies, confirmed the robustness of the meta-analysis findings.

Country(ies) involved China.

Keywords Neoadjuvant; perioperative; adjuvant; immune checkpoint inhibitor; Non-small cell lung cancer.

Contributions of each author

Author 1 - Yunchang Meng.
Email: ycmeng_nmu@163.com
Author 2 - Qingfeng Zhang.
Email: zhang1998qf@163.com
Author 3 - Ranpu Wu.
Email: wuranpu2532@163.com
Author 4 - Zhaofeng Wang.
Email: wangzhaofeng8811@163.com
Author 5 - Huijuan Li.
Email: lhj08282425@163.com
Author 6 - Yang Yao.
Email: yaoyang00818@163.com
Author 7 - Xinjing Li.
Email: 312626668@qq.com
Author 8 - Yanzhuo Gong.
Email: gongyanzhuo2022@126.com
Author 9 - Zhangxuan Chen.
Email: 2524432484@qq.com
Author 10 - Hongbing Liu.
Email: netlhb@126.com