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Abstract
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Peri-operative Immune Checkpoint Inhibitors and EGFR-Tyrosine Kinase Inhibitors in Resectable Non-Small Cell Lung Cancer: A Systematic Review and Network Meta-analysis of Randomized Controlled Trials

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Abstract

Objectives:

Peri-operative immune checkpoint inhibitors (ICIs) and epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitors (TKIs) have been shown to improve disease control in resectable non-small cell lung cancer. However, the optimal approach in terms of the choice of systemic agents and treatment sequence is unclear. This study aimed to investigate the efficacy of peri-operative ICIs and EGFR-TKIs in resectable non-small cell lung cancer.

Methods:

Scientific databases were searched for relevant randomized controlled trials (RCTs) comparing peri-operative (neoadjuvant or adjuvant) ICIs or EGFR-TKIs with standard treatment. Methodological quality of each trial was assessed using the revised Cochrane risk of bias tool. The outcome of interest was disease-free survival (DFS). Fixed effects frequentist network meta-analysis was performed.

Results:

Twelve RCTs including 5,799 patients were identified. All trials had low risk of bias. In EGFR-mutant patients, the most effective approach in improving DFS was adjuvant Osimertinib (hazard ratio (HR), 0.17; 95% confidence interval (CI), 0.11-0.26), followed by adjuvant Icotinib (HR, 0.36; 95% CI, 0.24-0.55) and adjuvant Pembrolizumab (HR, 0.44; 95% CI, 0.23-0.84). In EGFR-wildtype patients, the most effective approach in improving DFS was neoadjuvant Nivolumab (HR, 0.63; 95% CI, 0.43-0.92), followed by adjuvant Atezolizumab (HR, 0.67; 95% CI, 0.45-1.00) and adjuvant Pembrolizumab (HR, 0.78; 95% CI, 0.58-1.04). In patients with PD-L1 tumor proportion score (TPS) of at least 50% and 1-49%, neoadjuvant Nivolumab had the largest DFS improvement (HR, 24; 95% CI, 0.10-0.60 and HR, 0.58; 0.30-1.12, respectively); whereas in patients with PD-L1 TPS of less than 1%, adjuvant Pembrolizumab had the largest DFS improvement (HR, 0.78; 95% CI, 0.58-1.04).

Conclusion(s):

Among patients with resectable NSCLC, adjuvant Osimertinib confers the greatest DFS benefit in EGFR-mutant patients, whereas neoadjuvant Nivolumab is the most effective approach in EGFR-wildtype and PD-L1-positive (TPS of at least 1%) patients. Personalized approach based on molecular biomarkers should be considered when strategizing peri-operative therapy.