

## Efficacy of immunotherapy combined with chemotherapy in NSCLC patients with EGFR-TKI resistance: a meta-analysis of randomized clinical trials

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**ADMINISTRATIVE INFORMATION****Support** - QN RC2016363.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202420075**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 February 2024 and was last updated on 18 February 2024.**INTRODUCTION**

**Review question / Objective** The objective of this systematic review and meta-analysis was to assess the efficacy of immunotherapy combined with chemotherapy in EGFR-Mutant NSCLC patients with EGFR-TKI resistance.

**Condition being studied** We searched all the eligible studies of immunotherapy combined with chemotherapy in NSCLC patients with EGFR-TKI resistance versus control group with EGFR-TKI, which were retrieved from CNKI, Wanfang database, CBM, VIP, PubMed, EMBase, Cochrane Library, Web of Science. Quality evaluation was assessed by the Cochrane Collaboration's tool for randomized controlled trials and methodological index (MINORS) for non-randomized trials. Meta-analysis was conducted by RevMan5.3 software after data extraction.

**METHODS**

**Participant or population** Patients diagnosed with non-small-cell lung cancer by histopathology and cytology.

**Intervention** Immunotherapy combined with chemotherapy. Patients diagnosed with non-small-cell lung cancer by histopathology and cytology.

**Comparator** Epidermal Growth Factor Receptor (EGFR)-Tyrosine Kinase Inhibitor alone.

**Study designs to be included** Clinical trials (RCT).

**Eligibility criteria** NSCLC patients with disease progression after tyrosine-kinase inhibitor.

**Information sources** CNKI, Wanfang database, CBM, VIP, PubMed, EMBase, Cochrane Trials databases, Web of Science.

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**Main outcome(s)** Progression-free survival(PFS), Complete response rate(CR) , Objective response rate(ORR) , Disease control rate(DCR) , Survival rates, adverse reactions rate.

**Quality assessment / Risk of bias analysis** Two reviewers will independently assess the quality of the included studies. The Cochrane Collaboration's tool was for randomized controlled trials. Items will be evaluated in three categories: Low risk of bias, unclear bias and high risk of bias. The following characteristics will be evaluated: Random sequence generation (selection Bias) Allocation concealment (selection bias) Blinding of participants and personnel (performance bias) Incomplete outcome data (attrition bias) Selective reporting (reporting bias) Other biases. Results from these questions will be graphed and assessed using Review Manager 5.3. The methodological index (MINORS) was for non-randomized trials, Mainly from the following aspects of evaluation: The purpose of the study is clearly given. Patient coherence was included. Expected data collection. The end points appropriately reflect the purpose of the study. Objective evaluation of end points. Adequate follow-up time. The loss to follow-up was less than 5%. Was the sample size estimated.

**Strategy of data synthesis** All meta analyses were performed using Cochrane RevMan version 5.3 and Stata (version 16). The results were reported as pooled odds ratios (ORs) with 95% confidence intervals (95% CIs). We used Cochrane's Q test and I<sup>2</sup> statistics to evaluate the heterogeneity of all the studies. If the heterogeneity was significant (p > 50.0%), the random effects model was adopted; otherwise, the fixed effects model was used. Potential publication bias was assessed using funnel plots, Egger's test, and Begg's test. Results of this meta-analysis were presented by forest plots, and the p value less than 0.05 was considered significant. Publication bias was evaluated through funnel plots.

**Subgroup analysis** When we analyze the results, we can decide whether to do a subgroup analysis based on that factor.

**Sensitivity analysis** The sensitivity analysis was carried out by Stata software, and the sensitivity of the article was reflected by the change of effect size after deleting one of the articles.

**Language restriction** English and Chinese language.

**Country(ies) involved** China.

**Keywords** EGFR-Tyrosine Kinase Inhibitor, immunotherapy, chemotherapy, NSCLC, resistance.

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