International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

New Options for Advanced NSCLC Patients Resistant to EGFR Tyrosine Kinase Inhibitors – A Systematic Review and Network Meta-analysis

INPLASY202510014
doi: 10.37766/inplasy2025.1.0014
Received: 5 January 2025
Published: 5 January 2025

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ADMINISTRATIVE INFORMATION

Support - This study does not receive any financial support.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202510014

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 January 2025 and was last updated on 5 January 2025.

INTRODUCTION

Review question / Objective P: Patients with histologically or cytologically confirmed advanced EGFR-mutated NSCLC whose disease had progressed following at least one EGFR-TKI treatment.
I: Any treatment strategies including ADCs and bsAbs for this population.
C: The traditional stand-of-care chemotherapy.
O: Progression-free survival (PFS), overall survival (OS), objective response rate (ORR), any-grade adverse events (any-grade AEs), and severe-grade adverse events (severe-grade AEs).

Condition being studied While developments in targeted therapy have marked a new epoch for NSCLC patients harboring actionable genomic alterations, the management of individuals resistant to EGFR-TKIs remains a formidable challenge. We conducted this network meta-analysis and systematic review to find out the optimal treatment regimen for this difficult-to-treat refractory population, potentially guiding clinical decision.

METHODS

Participant or population Patients were classified as resistant if their disease progressed on first/second-generation EGFR-TKIs with a verified negative T790M mutation status or if they progressed on first-line third-generation EGFR-TKIs.

Intervention All the available treatment strategies being studied in EGFR-TKI-resistant NSCLC patients.

Comparator The conventional stand-of-care chemotherapy.

Study designs to be included Phase 2 or phase 3 randomized controlled trials.

Eligibility criteria Eligible studies comprised phase 2 or phase 3 RCTs from both published and gray literature sources. The included trials were required to involving patients with histologically or cytologically confirmed advanced (stage III, IV, or recurrent) EGFR-mutated NSCLC who exhibited

resistance to EGFR-TKIs. These studies must also report at least one efficacy or safety outcome of interest, such as objective response rate (ORR), progression-free survival (PFS), overall survival (OS), and adverse events (AEs) of any grade or severe grade (grade higher than or equal to 3).

Information sources Digital databases (PubMed, Embase, Cochrane Library, Web of Science, and ClinicalTrials.gov) and abstracts from relevant international conferences (AACR, ASCO, ESMO, WCLC, and CSCO). The reference lists of relevant meta-analyses and reviews were also manually screened to minimize the risk of omission.

Main outcome(s) Objective response rate (ORR), progression-free survival (PFS), overall survival (OS), and adverse events (AEs) of any grade or severe grade (grade higher than or equal to 3).

Quality assessment / Risk of bias analysis The Cochrane risk of bias tool for RCTs was utilized to evaluate the risk of bias across included trials.

Strategy of data synthesis We performed the data analysis using R software and the Markov chain Monte Carlo simulation technique was employed to conduct the network meta-analysis.

Subgroup analysis Dedicated comparisons within immunotherapy-based treatment strategies were performed.

Sensitivity analysis Global inconsistency of network meta-analyses was assessed by comparing consistency with inconsistency models according to the suitability of model fit, while local inconsistency of direct and indirect results was judged by comparing estimates from network meta-analyses and pairwise meta-analyses. In addition, Bayesian meta-regression analyses were conducted on potential effect modifiers.

Country(ies) involved China.

Keywords EGFR-TKI resistance; NSCLC; ADC; bispecific antibody.

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