INPLASY PROTOCOL

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None declared.

Comparison of bevacizumab and immune checkpoint inhibitors combined with chemotherapy in the first-line treatment of advanced non-squamous non-small cell lung cancer: a systematic review and network meta-analysis

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Review question / Objective: **Bevacizumab and immune checkpoint inhibitors (ICIs) are included in the first-line therapy of advanced non-squamous non-small cell lung cancer. However, the diversity of available treatments and the lack of direct comparisons make decision-making difficult.**
Condition being studied: **First-line treatment of advanced non-squamous non-small cell lung cancer. A solid foundation of mathematics knowledge and a clear, logical mind.**
Study designs to be included: **First, all included trials were phase II/III randomized controlled trials that enrolled patients with histologically or cytologically confirmed non-small cell lung cancer. Second, all included trials had to have compared any two or more different arms and reported at least one of the following clinical outcomes of non-squamous NSCLC: objective response rate (ORR), progression-free survival (PFS), overall survival (OS), or grade ≥ 3 adverse events (AEs).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 August 2021 and was last updated on 13 August 2021 (registration number INPLASY202180054).

INTRODUCTION

Review question / Objective: **Bevacizumab and immune checkpoint inhibitors (ICIs) are included in the first-line therapy of advanced non-squamous non-small cell lung cancer. However, the diversity of available treatments and the lack of direct comparisons make decision-making difficult.**

Condition being studied: First-line treatment of advanced non-squamous non-small cell lung cancer. A solid foundation of mathematics knowledge and a clear, logical mind.

METHODS

Participant or population: Patients with histologically or cytologically confirmed non-small cell lung cancer and treated with bevacizumab and immune checkpoint inhibitors.

Intervention: Bevacizumab and immune checkpoint inhibitors combination therapy or monotherapy.

Comparator: Bevacizumab, immune checkpoint inhibitors combination therapy or monotherapy.

Study designs to be included: First, all included trials were phase II/III randomized controlled trials that enrolled patients with histologically or cytologically confirmed non-small cell lung cancer. Second, all included trials had to have compared any two or more different arms and reported at least one of the following clinical outcomes of non-squamous NSCLC: objective response rate (ORR), progression-free survival (PFS), overall survival (OS), or grade ≥ 3 adverse events (AEs).

Eligibility criteria: All study periods and durations of follow-up were eligible for consideration, and some updated data from mature or long-term follow-up updates made to original articles were used. Titles and abstracts were screened, and the full texts of potentially eligible articles were sequentially assessed for final inclusion.First, all included trials were phase II/III randomized controlled trials that enrolled patients with histologically or cytologically confirmed non-small cell lung cancer. Second, all included trials had to have compared any two or more different arms and reported at least one of the following clinical outcomes of non-squamous NSCLC: objective response rate (ORR), progression-free survival (PFS), overall survival (OS), or grade ≥ 3 adverse events (AEs).

Information sources: Eligible studies were searched in the PubMed, Embase, and ClinicalTrials.gov databases.We also included complete and updated outcomes from important international conferences.

Main outcome(s): Objective response rate (ORR), progression-free survival (PFS), overall survival (OS), or grade ≥ 3 adverse events (AEs).

Quality assessment / Risk of bias analysis: We assessed the risk of bias of individual studies using the Cochrane Risk of Bias Tool.

Strategy of data synthesis: All the included studies were analyzed by two independent readers with the direction of a predefined protocol. Discrepancies were resolved by discussion with a third reader. The information extracted from the selected articles was as follows: study ID, sample size, sex, intervention arm, control arm, median PFS, and median OS. We gave preference to data from ITT populations and was evaluated by BICR to include more objective data. We also preferred to consider treatment-related adverse events as safety data, but if adverse events were not specified as treatment-related in a study, we included all adverse events.

Subgroup analysis: We chose PFS as the primary outcome of this study. Further subgroup analysis of PFS was conducted according to PD-L1 expression.

Sensitivity analysis: To assess the robustness and reliability of results, we planned severe sensitivity analyses, as squamous cell carcinoma patients were included in the GEMSTONE 302 and IMpower 110 studies. In addition, we excluded the CHECKMATE-9LA study and atezolizumab plus bevacizumab plus pemetrexed-free chemotherapy arm in the IMpower 150 study, as they both consisted of four-drug regimens.

Country(ies) involved: China.

Keywords: bevacizumab; immune checkpoint inhibitors; non-squamous non-small cell lung cancer.

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