INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Efficacy and safety of first-line PD-1/PD-L1 inhibitor combinations for extensive-stage small-cell lung cancer: A Bayesian network meta-analysis

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Review question / Objective: **A series of randomized controlled trials (RCTs) have indicated that first-line programmed cell death-1/death-ligand 1 inhibitors plus chemotherapy (PD-1/PD-L1+chemo) led to survival benefits in extensive-stage small cell lung cancer (ES-SCLC) compared with platinum-based chemotherapy, but the optimal combination strategy remains controversial. We included RCTs comparing PD-1/PD-L1+chemo versus chemo alone in ES-SCLC. Overall survival (OS), progression free survival (PFS), objective response rate (ORR), and grade ≥3 treatment-related adverse events (TRAEs) were considered. We aim to evaluate the efficacy and safety of all the currently available first-line PD-1/PD-L1 combinations for patients with ES-SCLC.**

Condition being studied: **Efficacy and safety of first-line PD-1/PD-L1 inhibitor combinations for extensive-stage small-cell lung cancer. The electronic databases, namely, PubMed, Cochrane Library, and ClinicalTrials.gov databases were systematically searched for relevant literatures conducted until July 6, 2022. To include the updated outcomes, we also explored online proceedings from annual conferences.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 September 2022 and was last updated on 28 September 2022 (registration number INPLASY202290121).

INTRODUCTION

Review question / Objective: **A series of randomized controlled trials (RCTs) have indicated that first-line programmed cell death-1/death-ligand 1 inhibitors plus chemotherapy (PD-1/PD-L1+chemo) led to survival benefits in extensive-stage small cell lung cancer (ES-SCLC) compared with platinum-based chemotherapy, but the optimal combination strategy remains controversial. We included RCTs comparing**

PD-1/PD-L1+chemo versus chemo alone in ES-SCLC. Overall survival (OS), progression free survival (PFS), objective response rate (ORR), and grade ≥3 treatment-related adverse events (TRAEs) were considered. We aim to evaluate the efficacy and safety of all the currently available first-line PD-1/PD-L1 combinations for patients with ES-SCLC.

Condition being studied: The electronic databases, namely, PubMed, Cochrane Library, and ClinicalTrials.gov databases were systematically searched for relevant literatures conducted until July 6, 2022. To include the updated outcomes, we also explored online proceedings from annual conferences.

METHODS

Participant or population: Patients with ES-SCLC confirmed by either histologically or cytologically.

Intervention: PD-1/PD-L1+chemo.

Comparator: Chemotherapy.

Study designs to be included: RCT.

Eligibility criteria: The inclusion criteria were as follows: (1) RCTs that enrolled patients with ES-SCLC confirmed by either histologically or cytologically; (2) RCTs that used PD-1/PD-L1 inhibitors combinations as first-line treatment settings; (3) RCTs comparing first-line combinations of PD-1/PD-L1 inhibitors with platinum-etoposide chemotherapy versus platinum-etoposide chemotherapy alone in ES-SCLC; (4) Phase II or III trials reporting at least one of the following clinical outcomes: OS, defined as the time from randomization until death from any cause; PFS, defined as the time from randomization to disease progression or death from any cause; ORR, defined as the proportion of patients who achieved an objective response; treatment-related adverse events (TRAEs) of any-grade or grade greater than or equal to 3 TRAEs, which were defined and graded according to the National Cancer Institute Common Terminology Criteria for AEs.The exclusion criteria were as follows: (1) RCTs that were based on overlapping patients; (2) RCTs with ambiguous clinical outcomes.

Information sources: The electronic databases, namely, PubMed, Cochrane Library, and ClinicalTrials.gov databases were systematically searched for relevant literatures conducted until July 6, 2022. To include the updated outcomes, we also explored online proceedings from annual conferences.

Main outcome(s): Overall survival (OS), progression free survival (PFS), objective response rate (ORR), and grade ≥3 treatment-related adverse events (TRAEs).

Quality assessment / Risk of bias analysis: Cochrane Risk of BiasTool.

Strategy of data synthesis: All statistical analyses were executed using R software (version 4.2.1) and R Studio software. If the P value for $\chi 2 > 0.1$ and I2 was <50%, a fixed-effects model would be used to count the pooled estimate. Otherwise, a random-effects model would be selected to combine the studies.

Subgroup analysis: According to used immunotherapy molecule.

Sensitivity analysis: Sensitivity analysis were executed using R software (version 4.2.1) and R Studio software.

Country(ies) involved: China.

Keywords: PD-1/PD-L1 + chemo, ES-SCLC, survival benefits.

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