International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

INPLASY2023110061

doi: 10.37766/inplasy2023.11.0061

Received: 15 November 2023

Published: 15 November 2023

**Corresponding author:**
Yun Fan

fanyun@zjcc.org.cn

**Author Affiliation:**
Zhejiang University of Traditional Chinese Medicine.

# Efficacy and safety of first-line PD-1/PD-L1 inhibitor combinations with or without Angiogenesis Inhibitors for extensive-stage small-cell lung cancer: a Bayesian network meta-analysis.

Zhou, LJ[1]; Li, YW[2]; Wang, L[3]; Jing, Y[4]; Fan, Y[5].

## ADMINISTRATIVE INFORMATION

**Support -** Not available.

**Review Stage at time of this submission -** The review has not yet started.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY2023110061

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 November 2023 and was last updated on 15 November 2023.

## INTRODUCTION

**Review question / Objective** A series of randomized controlled trials (RCTs) have indicated that PD-1/PD-L1 inhibitors plus chemotherapy with or without Angiogenesis Inhibitors 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 D-1/PD-L1 inhibitors plus chemotherapy versus D-1/PD-L1 inhibitors plus chemotherapy with Angiogenesis Inhibitors in ES-SCLC. Overall survival (OS), progression free survival (PFS), objective response rate (ORR), and grade ≥3 adverse events were considered. We aim to evaluate the efficacy and safety of all the currently available first-line PD-1/ PD-L1 combinations with or without angiogenesis Inhibitors for patients with ES-SCLC.

**Condition being studied** Efficacy and safety of PD-1/L1 inhibitors plus chemotherapy with or without angiogenesis inhibitors for extensive stage small cell lung cancer.The electronic databases, namely, PubMed, Cochrane Library, Embase and ClinicalTrials.gov databases were systematically searched for relevant literatures conducted until November 8, 2023. 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/L1 inhibitors plus chemotherapy with angiogenesis inhibitors.

**Comparator** PD-1/L1 inhibitors plus chemotherapy.

**Study designs to be included** Randomized controlled trials.

**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 with or without angiogenesis inhibitors as first-line treatment settings;(3)RCTs comparing first-line combinations of PD-1/ PD-L1 inhibitors plus platinum-etoposide chemotherapy with or without angiogenesis inhibitors versus platinum-etoposide chemotherapy alone in ES-SCLC; (4) Phase II and III trials reporting at least one of the following clinical outcomes: (5) OS, defined as the time from randomization until death from any cause; (6) PFS, defined as the time from randomization to disease progression or death from any cause; (7) Objective response rate (ORR), defined as the pro-portion of patients who achieved an objective response; (8) Adverse events (AEs) of any-grade or grade greater than or equal to 3 AEs, which were defined and graded according to the National Cancer Institute Common Terminology Criteria for AEs.

**Information sources** The electronic databases, namely, PubMed, Cochrane Library, Embase and ClinicalTrials.gov databases were systematically searched for relevant literatures conducted until November 8, 2023. 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 adverse events(AEs).

**Quality assessment / Risk of bias analysis** We will assess potential risks of bias of the included trials using the Cochrane risk-ofbias tool. Quality assessment consisted of random-sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective report (reporting bias), and other biases. Included studies will be categorized into three grades: low risk of bias (+), high risk of bias (–), and unclear (?). The quality assessment will be conducted by two independent investigators, and any discrepancy among investigators will be resolved by consensus.

**Strategy of data synthesis** Strategy of data synthesis: All statistical analyses were executed using R software and R Studio software. If the P value for $x2 > 0.1$ and was $I2<50\%$, a fixed-effects model would be used to count the pooled estimate. Otherwise, a randomeffects model would be selected to combine the studies.

**Subgroup analysis** Liver metastatis.

**Sensitivity analysis** Sensitivity analysis were executed using R software and R Studio software.

**Country(ies) involved** China.

**Keywords** PD-1/PD-L1 inhibitor combinations, Angiogenesis Inhibitors, extensive-stage small cell lung cancer.

**Contributions of each author**

Author 1 - Linjing Zhou.
Email: 939313190@qq.com
Author 2 - Yuwei Li.
Author 3 - Le Wang.
Author 4 - Ying Jin.
Author 5 - Yun Fan.