Original Article

Efficacy and safety of immune checkpoint inhibitors plus platinum-etoposide *vs.* platinum-etoposide in the first-line treatment of extensive-stage small cell lung cancer: a systematic review and a meta-analysis

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Background: Currently, immune checkpoint inhibitors (ICIs) combined with platinum-etoposide (EP) are gradually becoming the first-line standard treatment for extensive-stage small cell lung cancer (ES-SCLC). This meta-analysis aims to compare the efficacy and safety of ICIs combined with EP *vs.* EP alone in the first-line treatment of ES-SCLC.

Methods: We searched PubMed, Embase, and Cochrane Library databases for phase II/III randomized controlled trials (RCTs) that met inclusion criteria from January 2016 to November 2023. Outcome measures included progression-free survival (PFS), overall survival (OS), objective response rate (ORR), treatment-related adverse events (TRAEs), treatment-related serious adverse events (TRSAEs), and immune-related adverse events (IRAEs). The effect analysis statistics of the outcome indicators were expressed with hazard ratio (HR) and odds ratio (OR) and their 95% confidence interval (CI).

Results: This study included nine RCTs with a total of 4,711 patients. Compared to EP, ICIs plus EP improved patients' PFS (HR =0.71; 95% CI: 0.64–0.79; P<0.001), OS (HR =0.79; 95% CI: 0.74–0.84; P<0.001), and ORR (OR =1.27; 95% CI: 1.12–1.44; P=0.001), but increased the incidence of adverse events (AEs): TRAEs (OR =1.45; 95% CI: 1.20–1.76; P<0.001), IRAEs (OR =3.97; 95% CI: 2.49–6.32; P<0.001), and grade 3–4 IRAEs (OR =6.17; 95% CI: 2.36–16.15; P<0.001). However, there was no significant difference in the incidence of grade 3–4 TRAEs (OR =1.05; P=0.54), TRSAEs (OR =1.40; P=0.13), and grade 3–4 TRSAEs (OR =1.17; P=0.72). Subgroup analysis found that patients with brain metastasis did not benefit from ICIs combined with EP therapy, and patients with programmed cell death ligand 1 (PD-L1) expression ≥1% had poorer survival benefits compared to patients with PD-L1 expression <1%.

Conclusions: In the first-line treatment of ES-SCLC, compared to EP chemotherapy, ICIs with EP can benefit patients in terms of PFS, OS, and ORR, but it will increase the occurrence of AEs.

Keywords: Extensive-stage small cell lung cancer (ES-SCLC); immune checkpoint inhibitors (ICIs); platinum-etoposide (EP); efficacy; safety

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Introduction

The latest International Agency for Research on Cancer (IARC) data show that the incidence of lung cancer ranks second among all cancer types (accounts for 11.4% of all cancers), and it has the highest mortality rate (18.0% of all cancer deaths) (1). Small cell lung cancer (SCLC) is a type of lung malignancy originating from bronchial mucosa or glands with neuroendocrine function, accounting for about 15% of the total number of lung cancer cases (2). It is characterized by rapid growth and early extensive metastasis, with approximately 70% of patients having extensive-stage SCLC (ES-SCLC) at diagnosis (3). ES-SCLS is sensitive to chemotherapy, and the traditional first-line treatment is etoposide plus either cisplatin or carboplatin (4). The median progression-free survival (PFS) is 5.5 months, and the overall survival (OS) is only 10 months (5,6). With the breakthrough of immune checkpoint inhibitors (ICIs) in other cancer types, some success has also been achieved in ES-SCLC (7).

Among which, IMpower133 (8) and CASPIAN (9) studies represented by immunochemotherapy extended the median OS of patients to 12.3 and 12.9 months respectively. Although ICIs plus standard chemotherapy prolonged OS in ES-SCLC by 2–3 months, there is no breakthrough in the efficacy observed so far because of the limited OS benefit, limited population, and lack of effective clinical predictors and biomarkers. In addition, due to the high cost of immunotherapy and the high adverse reactions of combination therapy, it is particularly important to evaluate its efficacy and safety in clinical application. Therefore, we conducted a meta-analysis of ICIs plus platinum-etoposide (EP) regimens in the first-line treatment of ES-SCLC to evaluate its efficacy and safety, provide the dominant population and predictive biomarkers, and provide a more reliable evidence-based medical basis for the first-line treatment of patients with ES-SCLC. We present this article in accordance with the PRISMA reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-149/rc) (10).

Highlight box

Key findings

- Although immune checkpoint inhibitors (ICIs) with chemotherapy can improve the efficacy of patients in first-line treatment of extensive-stage small cell lung cancer (ES-SCLC), it will increase the occurrence of adverse events, and its beneficiary population and predictive biomarkers are failed to be effectively identified.

What is known and what is new?

- Immunotherapy can improve the prognosis of tumor patients, which may be closely related to the high expression of programmed cell death ligand 1 (PD-L1).
- This study showed that patients with PD-L1 expression ≥1% had poorer survival benefits compared to patients with PD-L1 expression <1%, suggesting that PD-L1 expression may not be a predictive biomarker for ICIs plus platinum-etoposide (EP) as first-line treatment for ES-SCLC. And patients with brain metastasis did not benefit from ICIs plus EP.

What is the implication, and what should change now?

- The efficacy of immunotherapy in the first-line treatment of ES-SCLC is indisputable. It is imperative to explore new effective predictors in future clinical trials.

Methods

Search strategy

Phase II–III randomized controlled trials (RCTs) from January 2016 to November 2023 were searched in PubMed, Embase, and Cochrane Library. Additionally, we reviewed conference reports from the American Society of Clinical Oncology (ASCO), the European Society of Medical Oncology (ESMO), and the World Conference on Lung Cancer (WCLC) to obtain further up-to-date research data. The search strategy was constructed based on the PICOS model, breaking down the clinical question and identifying relevant subject headings and free terms. The search strategy is provided in Appendix 1.

Inclusion and exclusion criteria

Inclusion criteria: (I) subjects: patients receiving first-line treatment with SCLC that extended beyond one thorax or had distant metastases. (II) Experimental group: treated with ICIs combined with EP, and the ICIs included programmed cell death 1 (PD-1)/programmed cell death ligand 1 (PD-

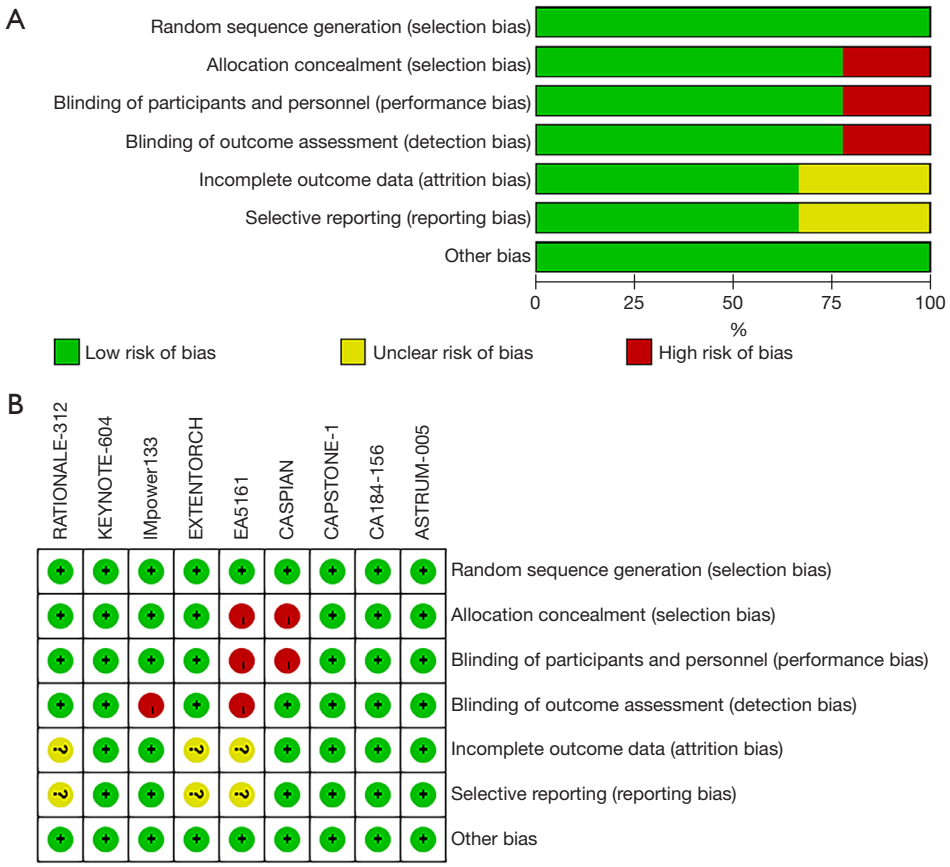

Figure 1 The Cochrane risk bias assessment tool. (A) Risk of bias graph; (B) risk of bias summary. Green "+" represents low risk; yellow "?" represents uncertainty; red "–" represents high risk.

L1) inhibitors, and cytotoxic T lymphocyte-associated antigen-4 (CTLA-4) inhibitors, and the platinum included cisplatin or carboplatin; control group: treated with EP. (III) Outcomes: efficacy: PFS, OS, objective response rate (ORR); safety: treatment-related adverse events (TRAEs), grade 3–4 TRAEs, treatment-related serious adverse effects (TRSAEs), grade 3–4 TRSAEs, immune-related adverse events (IRAEs), grade 3–4 IRAEs. (IV) Study type: II/III phase RCTs.

Exclusion criteria: reviews, non-RCTs, studies with unavailable or ineffective data, duplicate published studies, and non-first-line treatment research.

Literature quality evaluation

Two researchers independently searched and read literature, and selected literature that met the criteria. The Cochrane bias risk assessment tool was applied to evaluate the quality of RCTs in Review Manager 5.4.0 software (*Figure 1*).

Statistical analysis

STATA 17.0 software was used for data analysis. The hazard ratio (HR) and its 95% confidence interval (CI) were used as effect analysis statistics for PFS and OS. The odds ratio (OR) and its 95% CI were used as effect analysis statistics for ORR and adverse events (AEs). The results were presented using forest plots. Cochran's Q test and I^2 statistic were used to assess heterogeneity. If $P>0.05$ or $I^2<50\%$, a fixed-effect model was used. Otherwise, a random-effects model was used for analysis. The $\alpha=0.05$ and $P<0.05$ indicated a statistically significant difference.

Results

Literature screening

A total of 272 relevant studies were obtained through the above search. Endnote was used to exclude duplicate literature, and after reading the titles and abstracts,

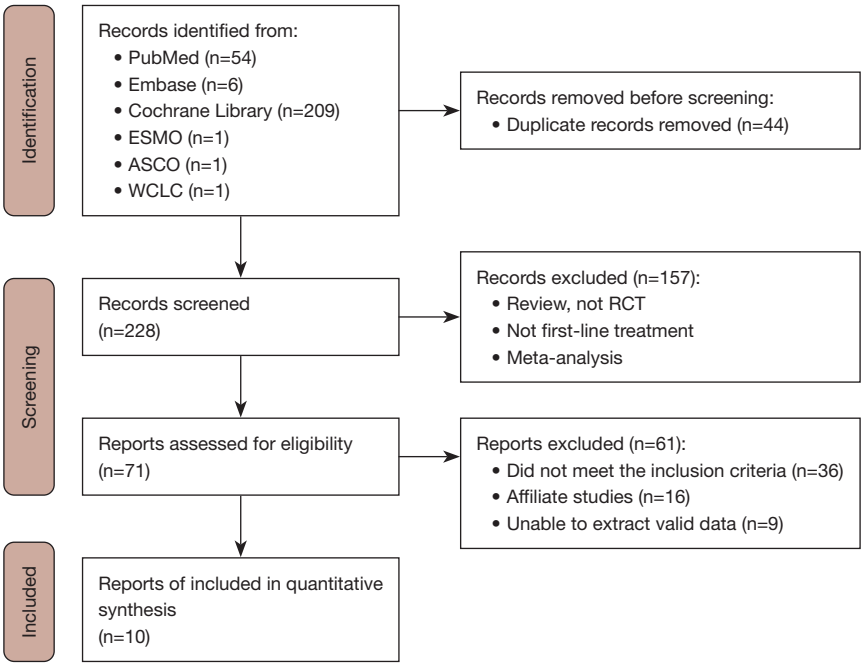

Figure 2 Flow diagram for selection of studies. ESMO, European Society of Medical Oncology; ASCO, American Society of Clinical Oncology; WCLC, World Conference on Lung Cancer; RCT, randomized controlled trial.

literature such as reviews, non-first-line treatments, and could not be used to extract valid data were excluded. Finally, after reading the full text, 10 articles were retained (*Figure 2*).

Basic characteristics of the studies

In the nine included experiments, ASTRUM-005 (11), EXTENTORCH (12), KEY-NOTE-604 (13), EA5161 (14), and RATIONALE-312 (15) studies reported the treatment of PD-1 plus EP regimen; IMpower133 (8,16) and CAPSTONE-1 (17) studies reported the treatment of PD-L1 plus EP regimen; CA184-156 (18) study reported the treatment of CTLA-4 plus EP regimen; CASPIAN (9) study reported PD-L1 and dual ICIs plus EP regimen (*Table 1*).

Results of meta-analysis

In the result of the forest map (*Figure 3*), we can see that PFS (I^2=65.8%; P=0.002) showed moderate heterogeneity, so a random-effect model was used. And, there was no significant heterogeneity in the results of OS (I^2=13.9%; P=0.32) and ORR (I^2=35.5%; P=0.13), so a fixed-effect model was used. ICIs plus EP can improve patients' PFS (HR =0.71; 95% CI: 0.64–0.79; P<0.001), OS (HR =0.79; 95% CI: 0.74–0.84; P<0.001), and ORR (OR =1.27; 95% CI: 1.12–1.44; P=0.001). This reduced the risk of disease progression by 29%, reduced the risk of death by 21%, and increased the ORR by 1.26 times.

Subgroup analysis

The study conducted the subgroup analysis of PFS, OS, and ORR according to the type of PD-1/PD-L1 inhibitors (*Figure 4*). There was no heterogeneity between groups of PFS (PD-1: HR =0.63 *vs.* PD-L1: HR =0.75, P=0.08), OS (PD-1: HR =0.75 *vs.* PD-L1: HR =0.74, P=0.96), and ORR (PD-1: OR =1.40 *vs.* PD-L1: OR =1.50, P=0.66). This suggests that the patient benefit is not related to the type of PD-1/PD-L1 inhibitor.

To further discover the advantageous population and clinical benefit indicators, post hoc exploratory subgroup analysis was conducted based on the clinical pathological characteristics of the patients. Three studies reported subgroup data on patients' PFS (*Figure 5*). The results showed that the benefit of PFS in patients was independent of the type of PD-1/PD-L1 inhibitors (P=0.08), type of

Table 1 Basic characteristics of literature

Study	Year	Phase	Number		Therapy		PFS, months (median)			OS, months (median)			ORR, %		TRAEs, %	
			EG	CG	EG	CG	EG	CG	HR (95% CI)	EG	CG	HR (95% CI)	EG	CG	EG	CG
ASTRUM-005 (11)	2022	III	389	186	Serplulimab + EC	EC	5.7	4.3	0.48 (0.38–0.59)	15.4	10.9	0.63 (0.49–0.82)	80	74.2	69.9	55.6
EXTENTORCH (12)	2023	III	223	219	Toripalimab + EC	EC	5.8	5.6	0.67 (0.54–0.82)	14.6	13.3	0.80 (0.65–0.98)	NR	NR	NR	NR
KEYNOTE-604 (13)	2020	III	228	225	Pembrolizumab + EP	EP	4.5	4.3	0.75 (0.61–0.91)	10.8	9.7	0.80 (0.64–0.98)	70.6	61.8	97.8	95.5
EA5161 (14)	2020	II	80	80	Nivolumab + EP	EP	5.5	4.6	0.65 (0.46–0.90)	11.3	8.5	0.67 (0.46–0.98)	52.3	47.7	NR	NR
RATIONALE-312 (15)	2023	III	227	230	Tislelizumab + EP	EP	4.8	4.3	0.63 (0.51–0.78)	15.5	13.5	0.75 (0.61–0.92)	68.3	61.7	NR	NR
IMpower133 (8,16)	2021/2018	III	201	202	Atezolizumab + EC	EC	5.2	4.3	0.77 (0.62–0.96)	12.3	10.3	0.76 (0.60–0.95)	60.2	64.4	94.9	92.3
CAPSTONE-1 (17)	2022	III	230	232	Adebrelimab + EC	EC	5.8	5.6	0.67 (0.54–0.83)	15.3	12.8	0.72 (0.58–0.90)	70.4	65.9	100	98.7
CASPIAN (9)	2021	III	268	269	Durvalumab + EP	EP	5.1	5.4	0.80 (0.66–0.96)	12.9	10.5	0.75 (0.62–0.91)	67.9	58	90.2	89.8
CA184-156 (18)	2016	III	478	476	Ipilimumab + EP	EP	4.6	4.4	0.85 (0.75–0.97)	11	10.9	0.94 (0.81–1.09)	62.1	62.2	81.8	75.8
CASPIAN (9)	2021	III	268	269	Durvalumab + tremelimumab + EP	EP	4.9	5.4	0.84 (0.70–1.01)	10.4	10.5	0.82 (0.68–1.00)	58.2	58	89.4	89.8

IMpower133 (8,16), the (16) updated OS and PD-L1 subgroup. EG, experimental group; CG, control group; PFS, progression-free survival; HR, hazard ratio; CI, confidence interval; OS, overall survival; ORR, objective response rate; TRAEs, treatment-related adverse events; EC, carboplatin-etoposide; NR, not reported; EP, platinum-etoposide; PD-L1, programmed cell death ligand 1.

platinum (P=0.64), gender (P=0.34), age (P=0.67), PD-L1 expression (P=0.67), brain metastasis (P=0.09), liver metastasis (P=0.09), Eastern Cooperative Oncology Group (ECOG) score (P=0.80), and lactate dehydrogenase (LDH) level (P=0.83). Patients with brain metastases do not benefit from PFS in ICIs combined with EP. Six studies reported subgroup data on patients' OS (*Figure 5*). According to the summary table, it can be seen that the benefit of patient OS is not related to the type of PD-1/PD-L1 inhibitors (P=0.96), type of platinum (P=0.94), gender (P=0.64), age (P=0.52), PD-L1 expression (P=0.08), brain metastasis (P=0.18), liver metastasis (P=0.10), ECOG score (P=0.93), LDH level (P=0.42), and smoking history (P=0.19). Patients with PD-L1 expression level ≥1%, brain metastasis, and ECOG score of 0 did not benefit from OS in ICIs combined with EP.

Security analysis

Six studies reported security events (*Figure 6*), the pooled results showed that ICIs plus EP increased the incidence of TRAEs (OR =1.45; 95% CI: 1.20–1.76; P<0.001), and increased the occurrence rate of IRAEs (OR =3.97; 95% CI: 2.49–6.32; P<0.001) and grade 3–4 IRAEs (OR =6.17; 95% CI: 2.36–16.15; P<0.001) by 3.97 times and 6.17 times, respectively. However, there is no difference in the occurrence rates of grade 3–4 TRAEs (OR =1.05; P=0.54), TRSAEs (OR =1.40; P=0.13), and grade 3–4 TRSAEs (OR =1.17; P=0.72) (*Figure 6A*). Among TRAEs, the incidence of alopecia (OR =0.85; P=0.048) was reduced, while the incidence of decreased appetite (OR =1.23; P=0.04), rash (OR =4.69; P=0.001), and hyperthyroidism (OR =5.92; P=0.01) were increased. Among grade 3–4 TRAEs, the incidence of decreased appetite (OR =0.58; P=0.005) and neutropenia (OR =0.77; P=0.001) were reduced, while the incidence of fatigue (OR =2.46; P=0.02), diarrhea (OR =4.94; P<0.001), and rash (OR =12.14; P=0.02) were increased (*Figure 6B*). No difference was observed in other specific TRAEs and grade 3–4 TRAEs (*Figure 6C*).

Sensitivity analysis

We conducted sensitivity analyses on PFS, OS, and ORR separately. In the included studies, removing any one study did not result in significant changes in the combined effect sizes and did not affect our conclusions. This suggests that the literature may come from the same population, indicating no obvious heterogeneity and demonstrating

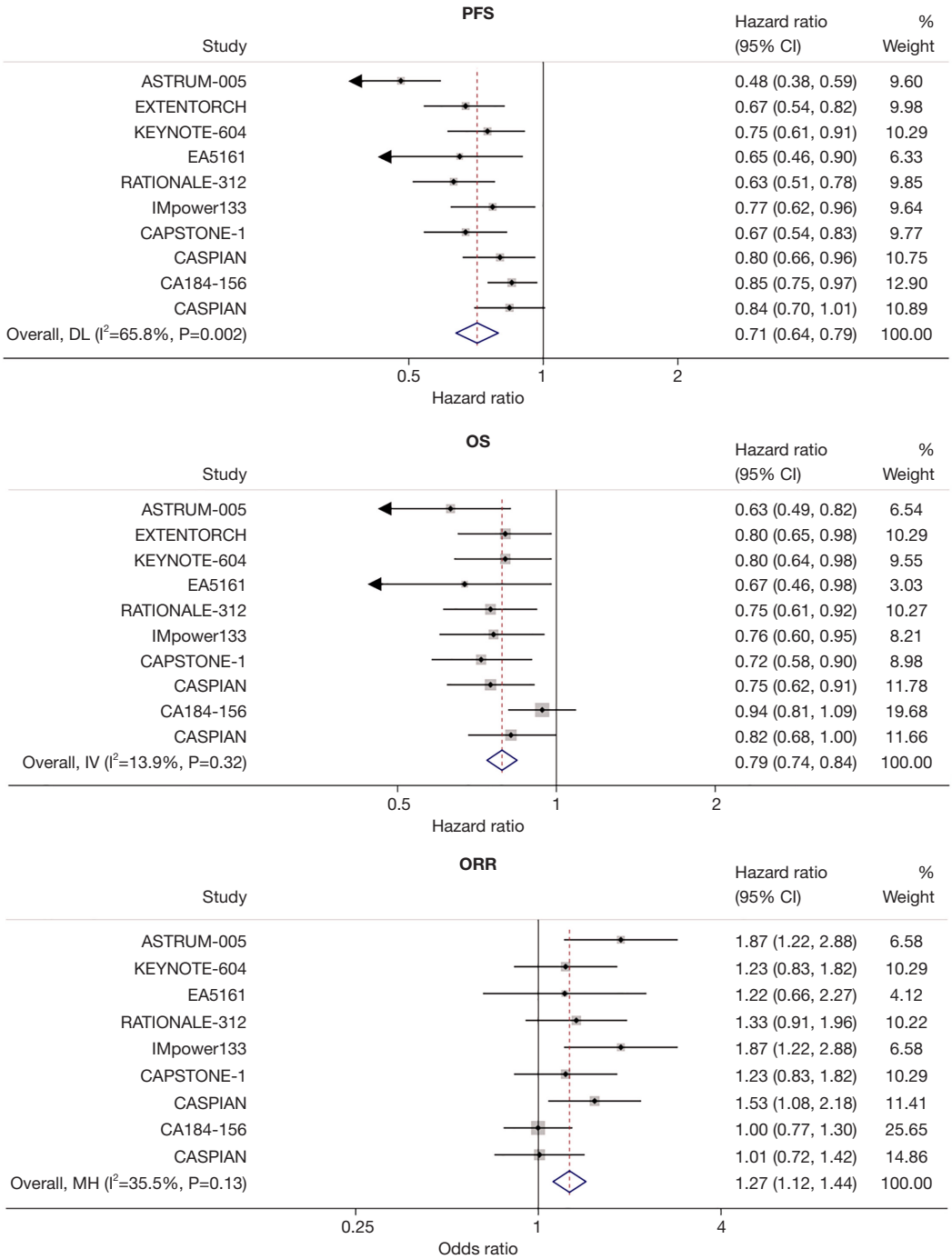

Figure 3 Survival analysis of PFS, OS, and ORR in ICIs plus EP *vs.* EP. PFS, progression-free survival; CI, confidence interval; DL, DerSimonian and Laird; OS, overall survival; IV, inverse variance; ORR, objective response rate; MH, Mantel-Haenszel; ICIs, immune checkpoint inhibitors; EP, platinum-etoposide.

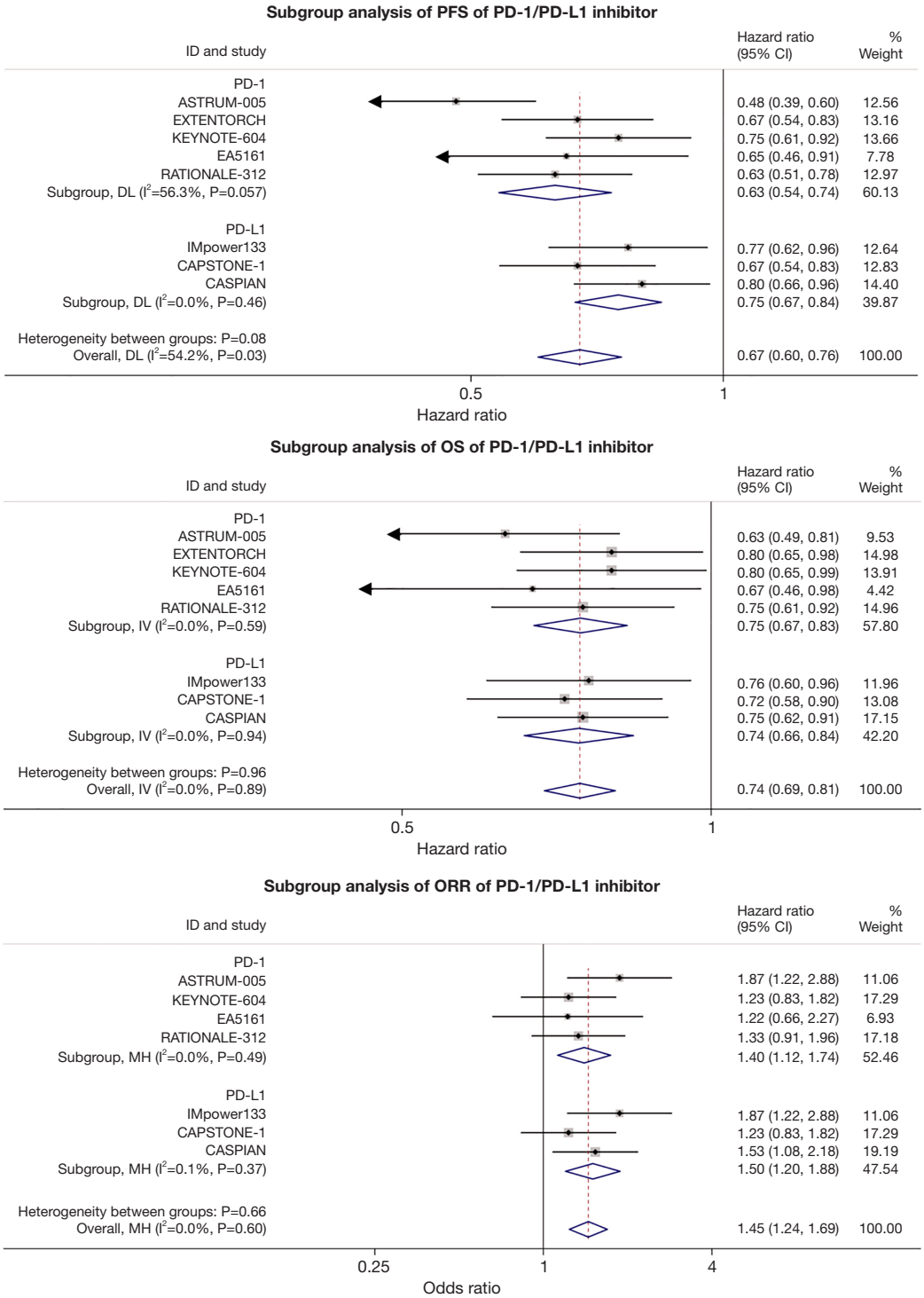

Figure 4 Subgroup analysis of PFS, OS, and ORR according to the type of PD-1/PD-L1 inhibitors. PFS, progression-free survival; PD-1, programmed cell death 1; PD-L1, programmed cell death ligand 1; CI, confidence interval; DL, DerSimonian and Laird; OS, overall survival; IV, inverse variance; ORR, objective response rate; MH, Mantel-Haenszel.

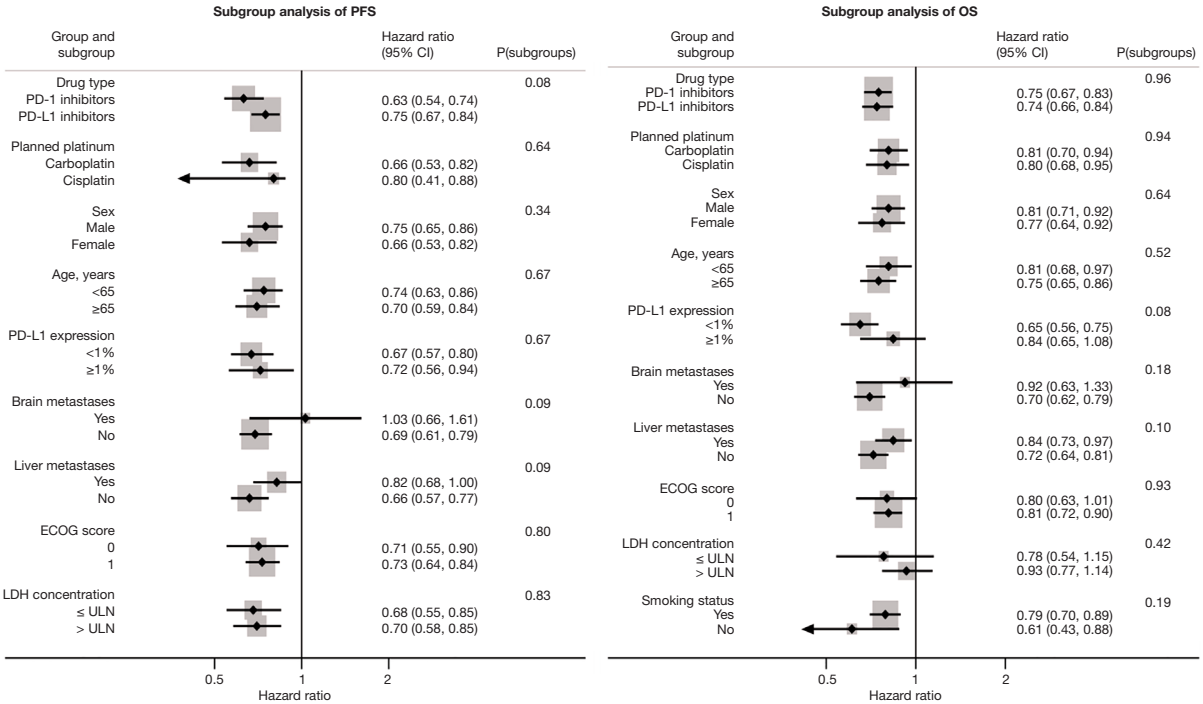

Figure 5 Subgroup analysis of PFS and OS in ICIs plus EP *vs.* EP. PFS, progression-free survival; OS, overall survival; CI, confidence interval; PD-1, programmed cell death 1; PD-L1, programmed cell death ligand 1; ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; ULN, upper normal limit; ICIs, immune checkpoint inhibitors; EP, platinum-etoposide.

robust and reliable results (*Figure 7*).

Publication bias

The results of Begg's test (PFS, P=0.03; OS, P=0.02; ORR, P=0.71) and Egger's test (PFS, P=0.058; OS, P=0.005; ORR, P=0.63) suggest that there may be publication bias in this study.

Discussion

Lung cancer is the main cause of human cancer incidence and death. SCLC accounts for about 15% of lung cancer types, it is highly malignant and aggressive, and most patients are in the stage of extensive metastasis when they are at their first diagnosis with a poor overall prognosis. Compared with the traditional EP regimen chemotherapy, the new treatment regimen of ICIs combined with EP can bring a certain degree of survival benefit for ES-SCLC. Meanwhile, we should also pay attention to its AEs. Different from the published meta-analyses (19-22), this meta-analysis included the most recent experiments, and conducted a subgroup analysis of outcome indicators PFS and OS to find the dominant population and predictive biomarkers, and also analyzed specific AEs to guide clinical prevention of adverse reactions caused by combined treatment.

This study included nine RCTs, with 4,711 patients (2,592 received ICIs combined with EP, and 2,119 received EP). The results showed that in first-line treatment of ES-SCLC, immunochemotherapy improved patients' PFS (HR =0.71; P<0.001), OS (HR =0.79; P<0.001), and ORR (OR =1.27; P=0.001). This is because tumor cells can escape the host immune response through various mechanisms, while ICIs can generate an anti-tumor immune response by activating the immune system (23,24), and ICIs can also change the tumor microenvironment (TME) by regulating the immune response, playing an anti-tumor therapeutic effect (25). However, not all populations benefit from immunotherapy, and the discovery of clinical predictive biomarkers is particularly important. So, we conducted a post-hoc exploratory subgroup analysis to look for benefit populations and predictive biomarkers.

In subgroup analysis, the benefits to patients were not

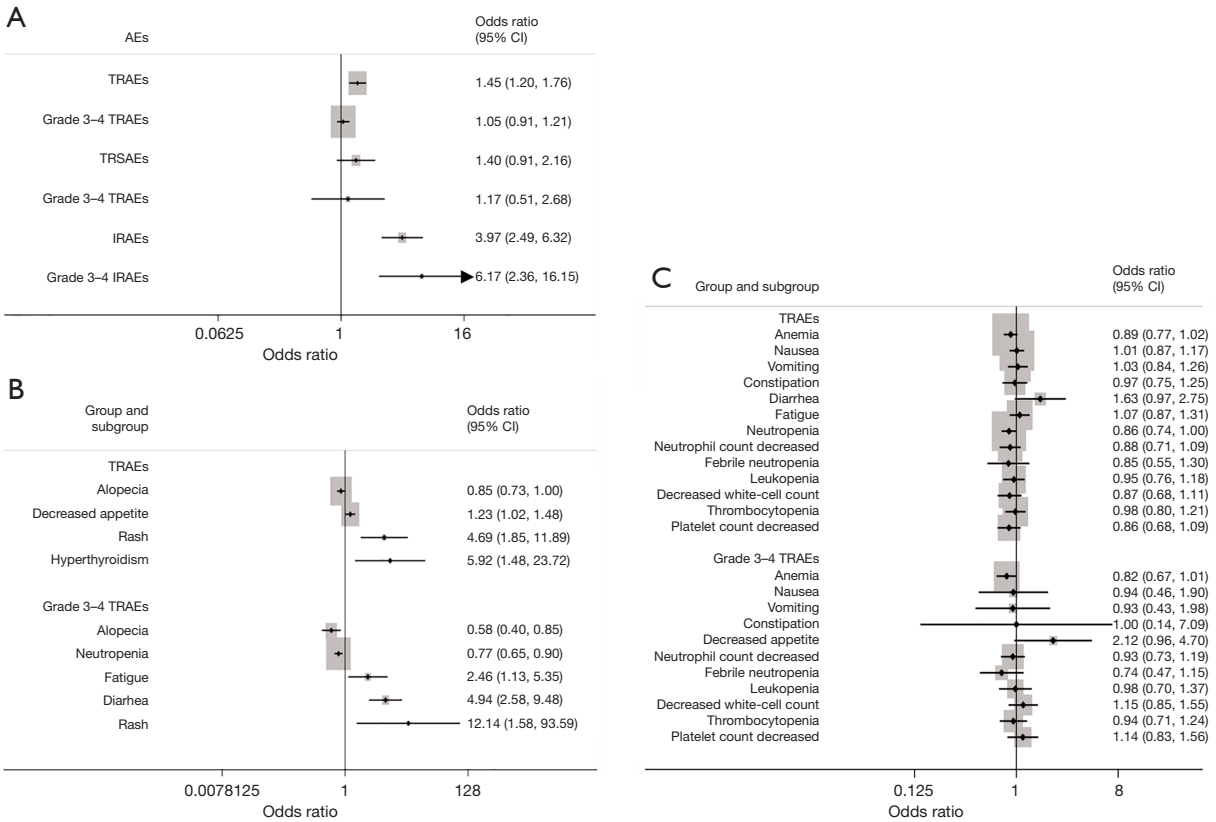

Figure 6 Safety analysis of ICIs plus EP *vs.* EP. (A) Summary of AEs; (B) summary of significant differences in TRAEs and grade 3–4 TRAEs; (C) summary of no differences in TRAEs and grade 3–4 TRAEs. AEs, adverse events; CI, confidence interval; TRAEs, treatment-related adverse events; TRSAEs, treatment-related serious adverse effects; IRAEs, immune-related adverse events; ICIs, immune checkpoint inhibitors; EP, platinum-etoposide.

affected by the type of PD-1/PD-L1, type of platinum, gender, age, PD-L1 expression, brain metastasis, liver metastasis, ECOG score, LDH level, or smoking history. However, the expression level of PD-L1 expression in PFS (<1%: HR =0.67 *vs.* ≥1%: HR =0.72) and OS (<1%: HR =0.65 *vs.* ≥1%: HR =0.84) subgroup analysis showed that patients with PD-L1 expression ≥1% had poorer survival benefits compared to patients with PD-L1 expression <1%. As described in the Skopelidou *et al.* (26) and Li *et al.* (27) studies, this meta-analysis also suggested that PD-L1 expression may not be a predictive biomarker for ICIs plus EP as first-line treatment for ES-SCLC. And similar results were seen in non-SCLC (NSCLC), where immunotherapy did not provide better benefits to patients with high PD-L1 expression (28,29). Brain metastasis is the most common distant metastasis type in SCLC, with 10% of patients having brain metastasis at initial diagnosis, which is the leading cause of death of patients with SCLC (30). Whole brain radiotherapy (WBRT) is the main treatment mode for SCLC brain metastases, but it can cause serious side effects such as neurotoxicity (31). Therefore, it is particularly important to explore the role of immunochemotherapy in patients with brain metastases. However, in first-line treatment of ES-SCLC, our subgroup analysis showed that ICIs combined with EP did not benefit PFS (HR =1.03; P=0.89) and OS (HR =0.92; P=0.65) in patients with brain metastases compared to EP regimen, and similar results were found in these studies (32,33). At the same time, we also analyzed specific data from the following studies on patients with brain metastases receiving radiation therapy. In the CASPIAN study, although only patients with brain metastases (8%) in the EP group received prophylactic cranial irradiation (PCI), the OS (HR =0.76; 95% CI: 0.43–1.33) benefit was more pronounced in the durvalumab plus EP group (34,35). A brief report of the CASPIAN study also showed that PFS and OS in ES-SCLC patients could

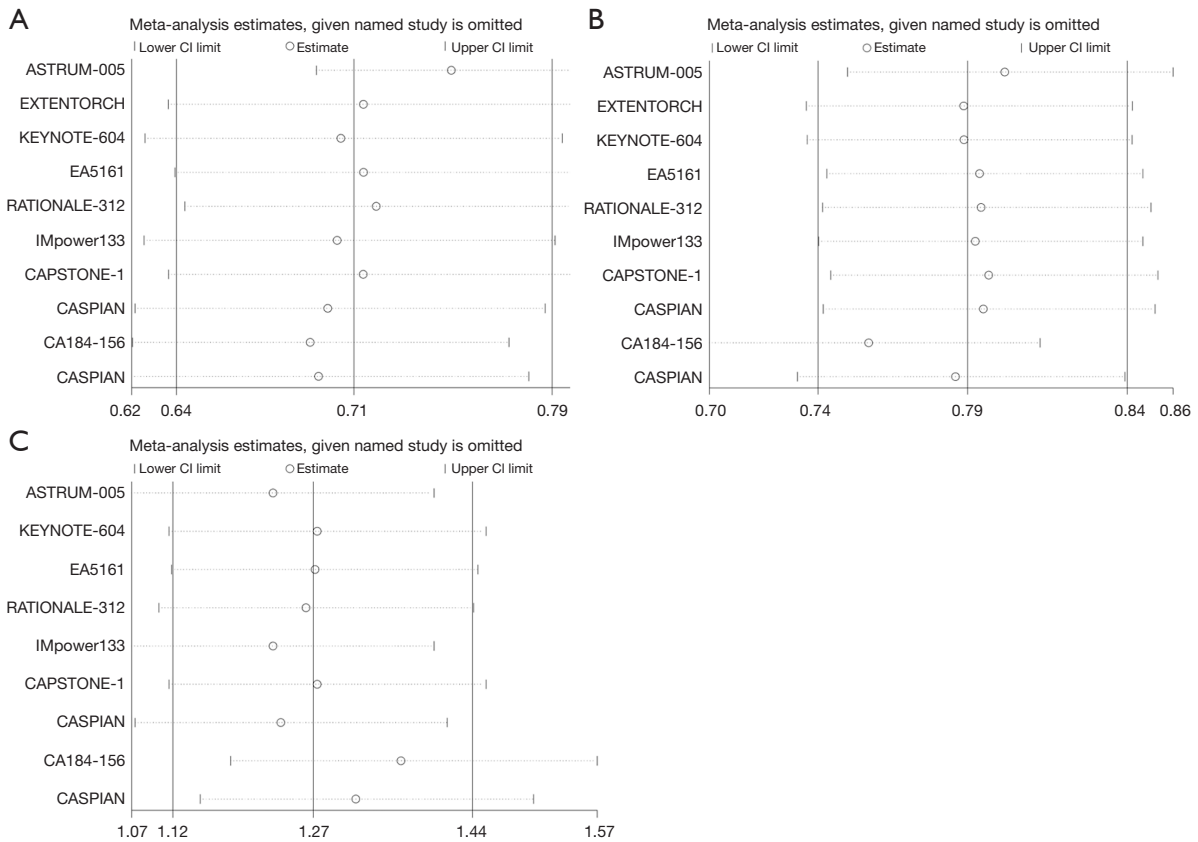

Figure 7 Sensitivity analysis of PFS (A), OS (B), and ORR (C) in ICIs plus EP *vs.* EP. CI, confidence interval; PFS, progression-free survival; OS, overall survival; ORR, objective response rate; ICIs, immune checkpoint inhibitors; EP, platinum-etoposide.

benefit from durvalumab plus EP regardless of the presence of brain metastases, and exploratory analysis suggested that immunotherapy could delay intracranial progression in patients (36). In the IMpower133 and CAPSTONE-1 study, the ICIs plus EP group (11.1% and 2%) and the EP group (11.2% and 1%) received a similar proportion of PCI intervention. The benefit of CAPSTONE-1 in the brain metastases population is still unknown due to the small number of patients enrolled (2%). However, in the IMpower133 study, patients with brain metastases ES-SCLC treated with atezolizumab plus EP showed no significant OS (HR =1.07; 95% CI: 0.47–2.43) benefit compared with the EP group (16). In summary, the efficacy of PCI in ES-SCLC is still controversial, and according to current guidelines, PCI is not commonly recommended for ES-SCLC (4). This may require a large number of prospective experimental studies and RCTs to further explore.

Although immunotherapy plays a crucial role in the field of cancer treatment, 50–80% of patients still do not benefit from it, mainly due to some patients not tolerating severe adverse reactions during treatment (37). This study results showed that compared to EP, ICIs with EP had no difference in the incidence of grade 3–4 TRAEs, TRSAEs, or grade 3–4 TRSAEs, but increased the incidence of TRAEs (OR =1.45; P<0.001), and the incidence of IRAEs and grade 3–4 IRAEs by 3.97 times and 6.17 times, respectively. We should pay attention to the occurrence of lack of appetite, and fatigue, especially diarrhea, rash, and hyperthyroidism.

There are some limitations in this study. Firstly, under the premise of having only one group of data on CTLA-4 and dual ICIs combined chemotherapy, this study failed to separately compare the efficacy and safety of CTLA-4 and dual ICIs combined chemotherapy. Secondly, although the results of sensitivity analysis showed that the included RCTs came from the same population, the results of PFS and OS tests indicated that there is publication bias in this study,

which may require the inclusion of more clinical trials to make the results more reliable.

Although this study conducted post-hoc exploratory subgroup analysis of clinical benefit indicators, it failed to effectively identify the beneficiary population and predictive biomarkers for ICIs combined with EP as first-line treatment for ES-SCLC. Therefore, it is particularly important to add new subgroup analyses in clinical research. Some experiments have shown that paraneoplastic neurological syndromes are associated with a good prognosis in SCLC (38); tumor mutational burden (TMB) has been proven to be a beneficial predictive factor for immunotherapy, mainly applicable to melanoma and NSCLC, and there are also studies suggesting that TMB may benefit SCLC (39), but an exploratory analysis with EXTENTORCH (12) and IMpower133 (8) showed that therapeutic effect was independent of TMB status; the predictive value of inflammatory cytokines for SCLC immunotherapy is gradually being evaluated (40). Although ICIs have improved the survival of ES-SCLC patients, new drugs are still needed in the future to achieve more precise and personalized treatment, such as neoantigen vaccines (41,42), lymphocyte activation gene-3 (43), immunoglobulin-like transcript 4 (44), and oncolytic viruses (45,46).

In summary, this meta-analysis data show that in first-line treatment of ES-SCLC, ICIs with EP can improve patients' survival benefits, reducing the risk of disease progression by 29%, reducing the risk of death by 21%, and increasing the ORR by 1.27 times compared with EP chemotherapy. However, it increases the incidence of TRAEs, IRAEs, and grade 3–4 IRAEs by 1.45, 3.97, and 6.17 times, respectively. Subgroup analysis found that patients with brain metastasis do not benefit from ICIs combined with EP therapy. All in all, these are only preliminary research results, and more clinical research and basic experiments are needed for further exploration and verification.

Conclusions

In first-line treatment of ES-SCLC, compared to EP chemotherapy, ICIs with EP can benefit patients' PFS, OS, and ORR, but it will increase the incidence of TRAEs, especially IRAEs and grade 3–4 IRAEs. Subgroup analysis results indicate that patients with brain metastasis will not benefit from ICIs combined with EP regimens.

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Footnote

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