Original Article

Effect of the number of induction chemotherapy cycles on the efficacy of first-line atezolizumab combined with chemotherapy in extensive-stage small cell lung cancer

Mengxing You[1#], Jiayu Liu[1#], Fei Teng[2#], Lige Wu[1], Haifeng Qin[3], Yan Zhang[4], Cuiying Zhang[5], Ziling Liu[6], Kewei Ma[6], Esteban C. Gabazza[7], Jacopo Vannucci[8], Xuezhi Hao[1], Junling Li[1], Puyuan Xing[1]

[1]Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [2]Department of Thoracic Surgery, Xuanwu Hospital, Capital Medical University, Beijing, China; [3]Department of Medical Oncology, Senior Department of Oncology, Chinese PLA General Hospital, The Fifth Medical Center, Beijing, China; [4]Department of Thoracic Oncology, Tumor Hospital Affiliated to Xinjiang Medical University, Urumqi, China; [5]Cancer Center, Inner Mongolia Autonomous Region People's Hospital, Huhhot, China; [6]Cancer Center, The First Hospital of Jilin University, Changchun, China; [7]Department of Pulmonary and Critical Care Medicine, Mie University Faculty and Graduate School of Medicine, Tsu, Mie, Japan; [8]Thoracic Surgery Unit, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy

Contributions: (I) Conception and design: P Xing, J Li; (II) Administrative support: J Liu, L Wu; (III) Provision of study materials or patients: F Teng, H Qin, Y Zhang, C Zhang, Z Liu, K Ma, X Hao; (IV) Collection and assembly of data: M You, J Liu, F Teng; (V) Data analysis and interpretation: M You; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Junling Li, MD; Puyuan Xing, MD. Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 17 Panjiayuan Nanli, Chaoyang District, Beijing 100021, China. Email: lijunling@cicams.ac.cn; xingpuyuan@cicams.ac.cn.

Background: Compared with chemotherapy alone, the addition of atezolizumab to the first-line treatment of extensive-stage small cell lung cancer (ES-SCLC) improves the overall survival (OS), but the benefit remains limited. This study aims at investigating the factors influencing prognosis and to assess the effect of the number of induction chemotherapy cycles on treatment efficacy.

Methods: We retrospectively analyzed the data of patients with ES-SCLC treated in five centers between March 2020 and September 2022. All 45 patients received first-line treatment with etoposide plus platinum combined with atezolizumab. The primary endpoints were progression-free survival (PFS) and OS in the total population and subpopulations based on the number of induction chemotherapy cycles. Least absolute shrinkage and selection operator (LASSO) regression were applied to identify the prognostic variables, and the effect of varying the number of induction chemotherapy cycles on the treatment efficacy was evaluated.

Results: A total of 45 patients were enrolled in the study. The median PFS for the first-line treatment was 7 months, and the median OS was 17.6 months. The following 10 variables were analyzed using LASSO regression: gender, age, liver metastasis, bone metastasis, brain metastasis, number of first-line induction chemotherapy cycles, first-line immunotherapy maintenance, receipt of cross-line immunotherapy, chest radiotherapy, and brain radiotherapy. The analysis revealed that receiving ≥6 cycles of induction chemotherapy was the most important variable affecting prognosis and the only one significant [concordance index: 0.658; hazard ratio: 0.32 (95% confidence interval: 0.17–0.63)]. Patients who received ≥6 cycles of induction chemotherapy (n=25) had a longer median PFS (8 *vs.* 5 months) and median OS (18.5 *vs.* 13.1 months) than those who received <6 cycles (n=20). Subgroup analyses indicated consistent survival benefits of ≥6 induction chemotherapy cycles across key subgroups, including males, patients aged ≤65 years, and those with or without brain metastasis (all P value <0.05).

Conclusions: Receiving ≥6 cycles of induction chemotherapy significantly prolonged the median PFS and median OS of patients, highlighting its crucial factor influencing the efficacy of first-line atezolizumab combined with chemotherapy in patients with ES-SCLC.

Keywords: Atezolizumab; extensive-stage small cell lung cancer (ES-SCLC); induction chemotherapy; cycles

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Introduction

Lung cancer is the most common cancer worldwide, and has the highest morbidity and mortality rates (1). Small cell lung cancer (SCLC) is a highly aggressive subtype of lung cancer that is recalcitrant to treatment, associated with a poor prognosis, and accounts for approximately 13–15% of all lung cancer cases (2). The majority of SCLC patients are diagnosed at the extensive stage (ES-SCLC). After more than 20 years of limited progress in systemic treatment, the introduction of immune checkpoint inhibitors has provided survival benefits to these patients in recent years (3).

Recently, several phase-III randomized controlled trials investigating first-line immunotherapy combined with chemotherapy for ES-SCLC have been conducted, including IMpower133, CASPIAN, CAPSTONE-1, ASTRUM-005, and EXTENTORCH (4-8). These studies have reported survival benefits for patients, and a median overall survival (mOS) of approximately 12.3–15.8 months. As a result, immunotherapy combined with chemotherapy is now the standard first-line treatment for ES-SCLC. The ETER701 study (9) investigated the combination of immunotherapy, chemotherapy, and the anti-angiogenic small molecule tyrosine kinase inhibitor, anlotinib, as a first-line treatment for ES-SCLC, and reported a mOS of 19.3 months, which can be compared to the mOS of 11.9 months reported for the chemotherapy group. This represents the longest overall survival (OS) reported among all large-scale studies. While the addition of first-line immunotherapy has provided survival benefits for patients, these benefits remain limited, and the disease continues to rapidly progress in most patients.

In view of the limited treatment options available, to identity predictive biomarkers of efficacy is crucial to further improve the survival outcomes of these patients. Programmed cell death-ligand 1 (PD-L1) expression has not been found to be a reliable predictor of the efficacy after first-line immunochemotherapy, which may be attributed to the low PD-L1 expression in SCLC and its predominance in immune cells (3). The tumor mutational burden is high in SCLC; however, there is no evidence to suggest that it can predict the efficacy of first-line immunotherapy combined with chemotherapy (10). Currently, SCLC is classified into four subtypes based on the differential expression of the transcription factors *ASCL1*, *NEUROD1*, and *POU2F3*, or the low expression of combined all three, accompanied by inflammatory gene signatures (SCLC-A, N, P, and I, respectively) (11,12). The SCLC-I subtype was more likely to benefit from immunotherapy combined with chemotherapy than the other subtypes (12). Currently, no accurate predictive factors have been identified to predict the efficacy of combined immunotherapy and chemotherapy in ES-SCLC.

Various clinical trials have employed different study designs; for example, some have used 4 cycles of induction chemotherapy while others have extended this scheme to a maximum of 6 cycles (5,6). Preliminary data from real-world studies suggest that more induction chemotherapy cycles may be correlated with improved OS (13,14). However, these studies had insufficient follow-up times.

Consequently, the present study retrospectively analyzed

Highlight box

Key findings

- The number of induction chemotherapy cycles affects the efficacy of first-line atezolizumab combined with chemotherapy in extensive-stage small cell lung cancer (ES-SCLC), with a greater number of cycles being correlated with improved progression-free survival (PFS) and overall survival (OS).

What is known, and what is new?

- Atezolizumab combined with chemotherapy is the standard treatment for ES-SCLC, but the optimal number of induction chemotherapy cycles remains unclear.
- In first-line immunochemotherapy for ES-SCLC, the patients who underwent ≥6 cycles of induction chemotherapy had prolonged PFS and OS.

What is the implication, and what should change now?

- Increasing the number of induction chemotherapy cycles is a modifiable factor that can optimize the efficacy of immunochemotherapy in ES-SCLC. In clinical trials, attention should be paid to the effect of the number of induction chemotherapy cycles on treatment efficacy.

the data from patients with ES-SCLC treated in five institutions with first-line atezolizumab in combination with chemotherapy. The aim was to identify prognostic factors influencing the efficacy of first-line immunotherapy combined with chemotherapy, and to evaluate the impact of different numbers of induction chemotherapy cycles on treatment outcomes and prognosis. We present this article in accordance with the STROBE reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-2025-207/rc).

Methods

Study patients

The data used in this retrospective study were collected from March 2020 to September 2022 from five tertiary medical facilities in China: National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College; Chinese PLA General Hospital (The Fifth Medical Center); Tumor Hospital Affiliated to Xinjiang Medical University; Inner Mongolia Autonomous Region People's Hospital; The First Hospital of Jilin University. All cases enrolled in this study were consecutive and not selected arbitrarily. To be eligible for inclusion in the study, the patients had to meet the following inclusion criteria: (I) a pathologically confirmed diagnosis of SCLC; (II) extensive-stage disease at diagnosis according to the Veterans Administration Lung Study Group staging system; (III) receipt of first-line systemic treatment with atezolizumab combined with chemotherapy; (IV) an induction chemotherapy regimen consisting of etoposide plus platinum; and (V) completion of at least 2 cycles of induction chemotherapy as first-line treatment. Patients were excluded from the study if they met any of the following criteria: (I) absence of measurable lesions according to the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v.1.1); and/or (II) missing critical information. The clinical pathological data of patients were obtained from the hospitals' electronic medical record system. In the study, the decision to extend the number of induction chemotherapy cycles beyond four was determined based on individual patient characteristics, including tumor response and treatment tolerance. Patient survival information was obtained through careful telephone follow-up calls, and the data collection cut-off date was September 27, 2024. If a loss to follow-up occurred, the date of the last follow-up was recorded as the data cut-off time. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (No. 2025032116232902) and the requirement of informed consent for this retrospective study was waived. All participating hospitals/centers were informed and agreed with this study.

Efficacy evaluation

The patient data were obtained from the inpatient and outpatient medical record systems. Efficacy was evaluated according to the RECIST v.1.1, which classified responses into four categories: complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). The objective response rate (ORR) included the patients with CR and PR, while the disease control rate (DCR) included the patients with CR, PR, and SD.

The study endpoints were the assessment of progression-free survival (PFS) and OS in the overall population and subpopulations based on the number of induction chemotherapy cycles. PFS was defined as the start of first-line systemic treatment (immunotherapy or chemotherapy) to disease progression, death, or the end of follow-up. OS was defined as the start of first-line systemic treatment (immunotherapy or chemotherapy) to death from any cause or the end of follow-up.

Statistical analysis

Descriptive statistics are used to summarize the distribution of patients, as well as their baseline demographic and clinical characteristics. PFS, OS, and the corresponding survival curves were analyzed using the Kaplan-Meier method. The median follow-up time was determined using the reverse Kaplan-Meier method. Least absolute shrinkage and selection operator (LASSO) regression was employed to select prognostic variables, and regularized path diagrams were used to visualize the relative importance of these variables. Cross-validation plots were applied to identify the optimal regularization parameters. Cox proportional hazards regression was used to identify critical variables within different subgroups, and forest plots were generated to visualize the effect of these variables across various subgroups. All statistical analyses were conducted using

Table 1 Demographic and clinical characteristics of the patients at the baseline

Characteristics	Values (N=45)
Age, n (%)	
>65 years	16 (35.6)
≤65 years	29 (64.4)
Gender, n (%)	
Female	13 (28.9)
Male	32 (71.1)
Smoking history, n (%)	
Current/former	31 (68.9)
Never	14 (31.1)
Largest size of lung lesion, n (%)	
>10 cm	12 (26.7)
≤10 cm	28 (62.2)
Unknown	5(11.1)
Liver metastases, n (%)	
Yes	4 (8.9)
No	41 (91.1)
Bone metastases, n (%)	
Yes	16 (35.6)
No	29 (64.4)
Brain metastases, n (%)	
Yes	13 (28.9)
No	32 (71.1)

RStudio software (version 4.3.1; R Core Team, Vienna, Austria). The statistical tests were two-tailed, and a P value <0.05 was considered statistically significant.

Results

Baseline patient characteristics

A total of 45 eligible patients were enrolled in the study between March 2020 and September 2022. The baseline characteristics of the patients are presented in *Table 1*. The mean age of the patients was 62.8±7.3 years, and approximately one-third of the patients were over 65 years old. Most of the patients were male (71.1%), and either former or current smokers (68.9%). Twelve patients (26.7%) had pulmonary lesions with a maximum diameter >10 cm. Additionally, 4 patients (8.9%) had liver metastasis, 16 (35.6%) had bone metastasis, and 13 (28.9%) presented with brain metastasis at the time of diagnosis.

Treatment and efficacy

All patients received atezolizumab combined with etoposide and platinum as the first-line systemic treatment. Among the platinum-based agents, 1 patient received nedaplatin, 6 received cisplatin, and the rest received carboplatin. Regarding the number of first-line induction chemotherapy cycles, 4 patients underwent 3 cycles, 9 patients underwent 4 cycles, 7 underwent 5 cycles, 1 underwent 8 cycles, and the remaining 24 patients underwent 6 cycles. Notably, 62.2% of the patients underwent maintenance therapy with atezolizumab following first-line combination chemotherapy. Additionally, approximately half of the patients (44.4%) received second-line immunotherapy following first-line treatment failure. Of those receiving second-line immunotherapy, 4 patients switched to other immune checkpoint inhibitors (sugemalimab, sintilimab, durvalumab, and serplulimab, 1 patient each), while the rest continued with atezolizumab. Further, 48.9% of the patients received chest radiotherapy, and 17.8% underwent brain radiotherapy (*Table 2*).

Among the patients receiving first-line immunochemotherapy, a CR was observed in 4 patients (8.9%), a PR in 35 patients (77.8%), SD in 5 patients (11.1%), and PD in 1 patient (2.2%). The ORR was 86.7%, and the DCR was 97.8%. The median follow-up time was 39.1 months [95% confidence interval (CI): 26.5–not attained (NA)], the median progression-free survival (mPFS) was 7.0 months (95% CI: 6.0–9.0) (*Figure 1A*), while the mOS was 17.6 months (95% CI: 15.9–18.9) (*Figure 1B*).

Safety

The overall safety profile of first-line immunochemotherapy was favorable. Among the 45 patients, 9 (20.0%) experienced immune-related adverse events, including 3 cases of rash, 2 cases of hypothyroidism, 3 cases of immune-related pneumonia, and 1 case of immune-related encephalitis. Five adverse events were classified as grades 1–2, while 4 were classified as grade 3 (1 case of rash, 2 cases of immune-related pneumonia, and 1 case of immune-related encephalitis). The case of immune-related encephalitis involved a 76-year-old patient with

Table 2 First-line systemic treatment with or without radiotherapy

Variables	Values (N=45)
Induction chemotherapy regimen (etoposide +), n (%)	
Cisplatin	6 (13.3)
Carboplatin	38 (84.4)
Nedaplatin	1 (2.2)
Induction chemotherapy cycles, n (%)	
<6	20 (44.4)
≥6	25 (55.6)
Immuno-maintenance, n (%)	
Yes	28 (62.2)
No	17 (37.8)
Cross-line immunotherapy, n (%)	
Yes	20 (44.4)
No	25 (55.6)
Best response to first-line immunochemotherapy, n (%)	
CR	4 (8.9)
PR	35 (77.8)
SD	5 (11.1)
PD	1 (2.2)
Progression after first-line immunochemotherapy, n (%)	
Yes	42 (93.3)
No	3 (6.7)
Chest radiotherapy, n (%)	
Yes	22 (48.9)
No	23 (51.1)
Brain radiotherapy, n (%)	
Yes	8 (17.8)
No	37 (82.2)

CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

brain metastasis, and the possibility that the neurological symptoms were tumor-related could not be ruled out. No grade 4 or fatal adverse events were observed.

Prognostic variables

For the prognostic analysis, we included 10 critical variables: gender, age, liver metastasis, bone metastasis, brain metastasis, number of first-line induction chemotherapy cycles, first-line immune maintenance, immune cross-line treatment, chest radiotherapy, and brain radiotherapy. LASSO regression analysis identified the best regularization parameter based on the cross-validation graph (*Figure 2A*). The regularization path graph (*Figure 2B*) showed that the most influential variable was receiving ≥6 cycles of induction chemotherapy with a concordance index (C-index) of 0.658, sensitivity of 0.038, and a hazard ratio (HR) of 0.32 (95% CI: 0.17–0.63).

Number of induction chemotherapy cycles

A total of 25 patients received ≥6 cycles of induction chemotherapy as part of their first-line treatment. The survival analysis indicated that both PFS (*Figure 3A*) and OS (*Figure 3B*) were significantly better in the group that received ≥6 cycles of induction chemotherapy than the group that received <6 cycles of induction chemotherapy. The mPFS was 8.0 months (95% CI: 7.0–15.0) in the ≥6-cycle group and 5.0 months (95% CI: 3.0–9.0) in the <6-cycle group while the mOS was 18.5 months (95% CI: 18.0–NA) and 13.1 months (95% CI: 9.2–18.9), respectively. The subgroup analysis using Cox proportional hazard regression (*Figure 4*) revealed that patients receiving ≥6 cycles of chemotherapy had significantly better survival outcomes than those receiving <6 cycles. This benefit was observed across various subgroups including men, patients aged ≤65 years those without liver metastasis, with or without brain metastasis, without bone metastasis, with or without first-line immune maintenance therapy, those receiving cross-line immune therapy, with or without chest radiotherapy, and those without brain radiotherapy. Conversely, in women, patients aged >65 years, those with bone metastasis, and those without cross-line immune therapy, the risk of death was reduced in the group receiving ≥6 cycles of induction chemotherapy. However, this difference was no statistically significant compared to the group receiving <6 cycles of induction chemotherapy. Due to the limited number of patients with liver metastasis and with brain radiotherapy, statistical analysis could not be performed of these subgroups. Therefore, the effect of the number of induction chemotherapy cycles in these groups remains unclear.

Discussion

This study found that the number of induction

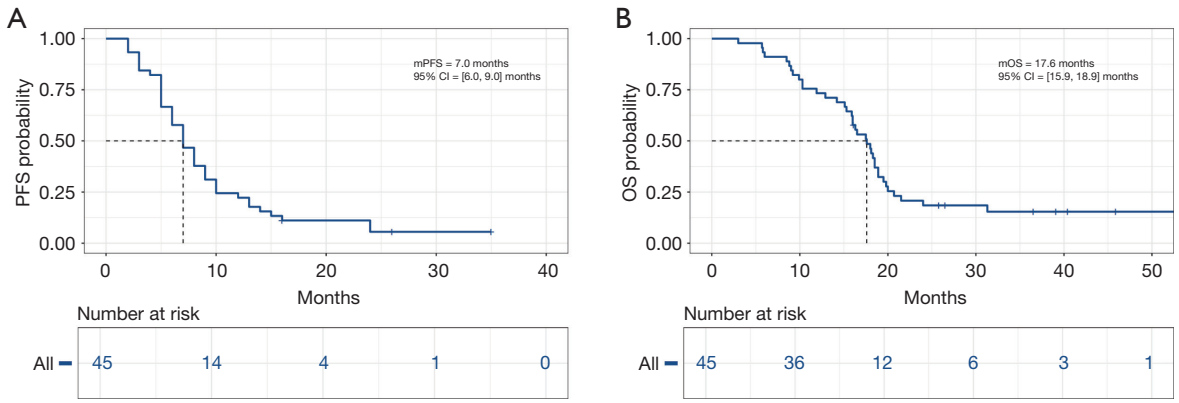

Figure 1 Kaplan-Meier plots for PFS (A) and OS (B) in the overall population. CI, confidence interval; mOS, median overall survival; mPFS, median progression-free survival; OS, overall survival; PFS, progression-free survival.

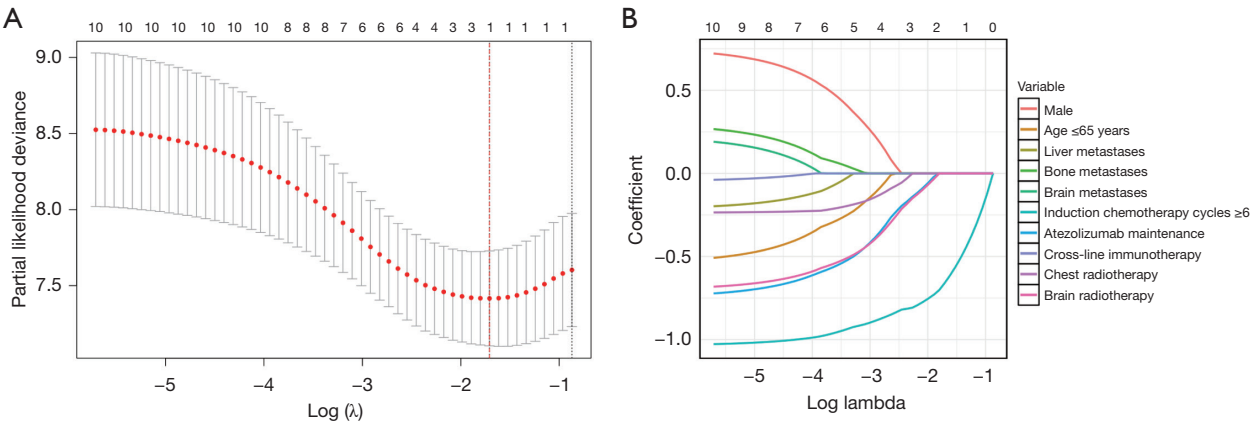

Figure 2 The LASSO regression analysis was employed to identify significant prognostic variables. The best regularization parameter (λ value) in the cross-validation graph (A). The regularization path graph (B) showed that ≥6 cycles of induction chemotherapy was the most crucial variable. LASSO, least absolute shrinkage and selection operator.

chemotherapy cycles in the first-line treatment of ES-SCLC patients plays a crucial role in both treatment efficacy and patient prognosis. This finding could significantly affect future treatment protocols for ES-SCLC. Patients that received ≥6 cycles of induction chemotherapy had a prolonged PFS and OS. In the IMpower133 study (6), the mOS of the atezolizumab plus chemotherapy group was 12.3 months. In our study, the mOS of the patients treated with first-line atezolizumab combined with chemotherapy reached 17.6 months, and the mOS of the patients that received ≥6 cycles of induction therapy reached 18.5 months, which can be compared to the mOS of 13.1 months of those that received <6 cycles. The mOS of the patients who received <6 cycles of induction chemotherapy is closely aligned with the results of the IMpower133 study (6), where the maximum number of induction chemotherapy cycles was limited to 4. These findings suggest that the prolonged survival observed in our study may be attributed to the increased number of induction chemotherapy cycles.

We employed LASSO regression to analyze 10 crucial variables related to demographics and treatment, and found that the number of induction chemotherapy cycles was the most significant and indeed the only variable to affect patient prognosis. The C-index for this single-variable model was 0.658, indicating a moderate prognostic predictive ability. Several previous studies have reported similar trends. The MAURIS study (13), a phase-III

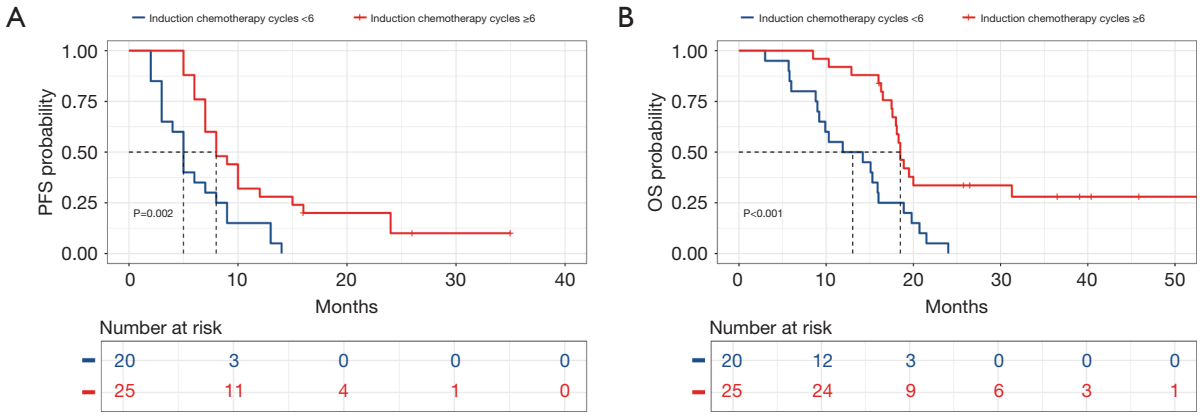

Figure 3 Kaplan-Meier plots showed that both PFS (A) and OS (B) were significantly better in the ≥6 cycles of induction chemotherapy group than the <6 cycles of induction chemotherapy group. OS, overall survival; PFS, progression-free survival.

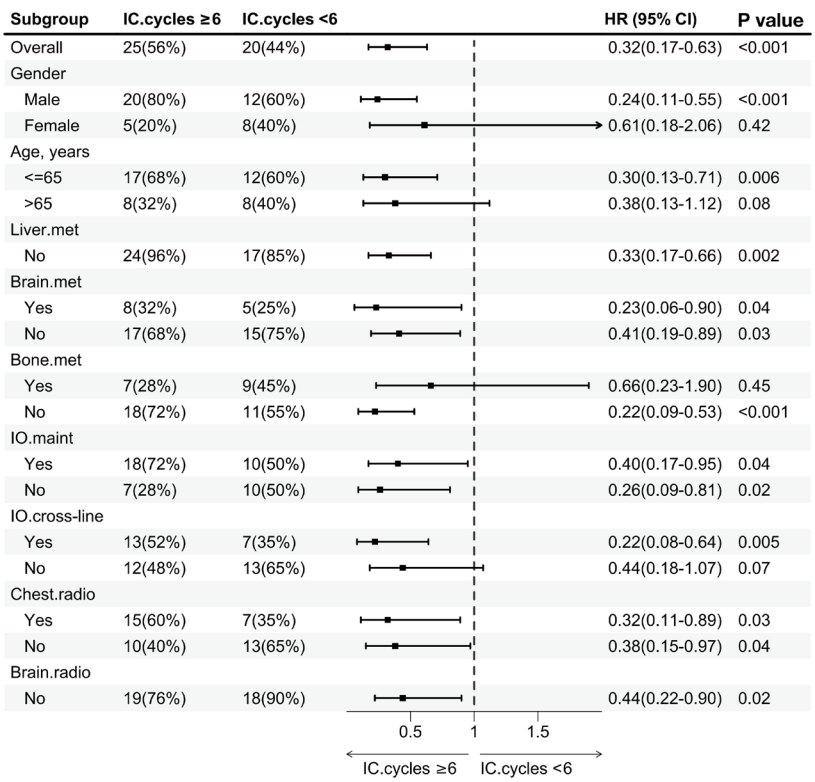

Figure 4 Forest plot showing that the patients who received ≥6 cycles of induction chemotherapy had better survival outcomes across most subgroups. Bone.met, bone metastasis; Brain.met, brain metastasis; Brain.radio, brain radiotherapy; Chest.radio, chest radiotherapy; CI, confidence interval; HR, hazard ratio; IC.cycles, induction chemotherapy cycles; IO.cross-line, cross-line immunotherapy; IO.maint, immunotherapy maintenance; Liver.met, liver metastasis.

multicenter trial conducted in Italy, reported that patients who received 5–6 cycles of induction chemotherapy had improved OS compared to those who received 4 or fewer cycles (≤3 cycles). However, it is important to note that, the median follow-up time for this study was relatively short, at only 10.5 months. Additionally, a multicenter, real-world study (14) from China reported that patients receiving ≥4 cycles of induction chemotherapy had significantly better PFS [HR: 0.54 (95% CI: 0.36–0.80)]. However, the OS data from this study are insufficient and further follow-up is required.

The IMpower133 (15) and CASPIAN (7) studies have established the role of immunotherapy as a first-line treatment for ES-SCLC. In both trials, PD-L1 inhibitors were used as immunotherapy agents, and patients received 4 cycles of induction chemotherapy, resulting in mOS of 12.3 months in IMpower133 and 13.0 months in CASPIAN. The ASTRUM-005 study (8), which also used 4 cycles of induction chemotherapy, was the first to show the efficacy of a PD-1 inhibitor in ES-SCLC, reporting a mOS of 15.4 months. In the CAPSTONE-1 study (5), the PD-L1 inhibitor, adebrelimab was administered with 4–6 cycles of induction chemotherapy, resulting in a reported mOS of 15.3 months. In the IMpower133 study (6), only 8.5% of patients in the immunochemotherapy group had brain metastasis, whereas in our study, 28.9% of patients had brain metastasis, all of whom were treated with atezolizumab combined with chemotherapy. Despite this higher incidence of brain metastasis, our study achieved superior OS, especially in the subgroup that received ≥6 cycles of induction chemotherapy, which had a mOS of 18.5 months, compared to the 12.3 months reported in the IMpower133 study (6). Although direct comparisons between studies should be made cautiously, our findings suggest that receiving ≥6 cycles of induction chemotherapy may be a critical prognostic factor. SCLC exhibits a high degree of sensitivity to chemotherapy, and emerging evidence (16) suggests that the combination of chemotherapy and immunotherapy may exert a synergistic effect.

Besides, there was no significant difference in OS in the chemotherapy groups between patients receiving 4 and 6 cycles of etoposide plus cisplatin (17). These results underscore the need for further prospective trials to explore the potential benefits of increasing the number of induction chemotherapy cycles in patients treated with immunochemotherapy.

Our study also showed that immune maintenance therapy following first-line chemoimmunotherapy did not confer any OS benefits, which confirms the findings of previous studies (18,19). Immune rechallenge refers to the use of immunotherapy after the failure of prior immunotherapy. This study showed that continuing immunotherapy after first-line treatment failure did not improve OS. However, a trend toward an extension in OS was observed [mOS 18.1 (95% CI: 16.0–31.3) *vs.* 16.5 (95% CI: 15.1–19.8) months, P=0.17]. This finding was not entirely consistent with previous studies. Shang *et al.* (20) found that cross-line immunotherapy improved survival in ES-SCLC patients with fewer than four metastatic sites. However, another study (21) found that while cross-line immunotherapy improved PFS, it did not significantly improve OS. An OS benefit was observed in the subgroup of patients whose initial response to immunotherapy was SD or PD. These inconsistent results may be attributed to the limited sample size, as only 4 patients in our study who received cross-line immunotherapy had an initial treatment response of SD or PD. This observation requires further investigation in studies with a larger sample size.

The use of chest radiotherapy and prophylactic cranial irradiation (PCI) in ES-SCLC remains controversial (22-24). In this study, 22 patients received chest radiotherapy, 8 received brain radiotherapy, and 4 received PCI. The results revealed that both treatments were associated with reduced risk of death, although the difference was not statistically significant. Further studies with larger sample sizes need to be performed to validate the potential role of concurrent chest and brain radiotherapy in ES-SCLC.

In the subgroup analysis, we found that patients who received ≥6 cycles of induction chemotherapy demonstrated improved survival outcomes across most subgroups, particularly among males, patients aged ≤65 years, and those without liver metastasis, with or without brain metastasis, without bone metastasis, with or without first-line immune maintenance therapy, with cross-line immune therapy, with or without chest radiotherapy, and without brain radiotherapy. In contrast, although survival benefits were observed in females, patients >65 years old, those with bone metastasis, and those who did not receive cross-line immunotherapy, these differences were not statistically significant. However, the HR suggested a reduced risk of death. Moreover, the wide confidence intervals (Cis) likely reflect the small sample size (25). The number of patients with liver metastasis and those who received brain radiotherapy was too small to be effectively analysis.

Further research is needed to explore the impact of different induction chemotherapy cycles in these populations.

As a retrospective study, selection bias was unavoidable. Additionally, the limited sample size restricted some subgroup analyses. However, the extended follow-up period provided robust data in this regard. This study identified that receiving ≥6 cycles of induction chemotherapy was a significant prognostic factor in first-line immunochemotherapy for ES-SCLC eventually. These findings may serve as a theoretical foundation for future prospective studies and contribute to improving the survival outcomes of ES-SCLC patients.

Conclusions

In first-line immunochemotherapy for ES-SCLC, patients who received ≥6 cycles of induction chemotherapy had longer PFS and OS than those who received fewer cycles. Moreover, this survival benefit was evident across most subgroups, highlighting the potential of extending induction chemotherapy as a clinical strategy for improving treatment outcomes in ES-SCLC.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-2025-207/rc

Data Sharing Statement: Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-2025-207/dss

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (No. 2025032116232902) and the requirement of informed consent for this retrospective study was waived. All participating hospitals/centers were informed and agreed with this study.

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