Application value and safety of trilaciclib in first-line chemotherapy combined with immunotherapy for extensive-stage small cell lung cancer: A real-world study

YANPING CUI[1], HONGJUAN ZHANG[1], LIZHI WANG[1] and XINGYI LOU[2]

[1]Department of Radiotherapy and Chemotherapy, Chengde Central Hospital, Chengde, Hebei 067000, P.R. China; [2]Endoscopy Center, The First People's Hospital of Yunnan Province, Kunming, Yunnan 650032, P.R. China

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Abstract. The present study is a single-center, retrospective real-world study that aimed to evaluate the myeloprotective effect, safety and impact on survival prognosis of trilaciclib in first-line chemotherapy combined with immunotherapy for patients with extensive-stage small cell lung cancer (ES-SCLC) in China. A total of 180 newly diagnosed patients with ES-SCLC who received first-line chemotherapy combined with immunotherapy at Chengde Central Hospital from January 2020 to January 2024 were included. Patients were divided into two groups based on whether they received trilaciclib: The trilaciclib group (n=90) and the control group (n=90). Baseline characteristics were matched between the two groups, and treatment regimens were identical, with only the trilaciclib group receiving trilaciclib before chemotherapy. Differences between the groups were compared in terms of myelosuppression-related adverse reactions, chemotherapy completion rates, efficacy [objective response rate (ORR), disease control rate] and survival outcomes [progression-free survival (PFS), overall survival (OS)]. Statistical Package for the Social Sciences 26.0 was used for statistical analysis. The trilaciclib group showed significant advantages over the control group in terms of myelosuppression, including a lower incidence of grade 3-4 neutropenia (17.7 vs. 65.6%; P<0.001), anemia (≥grade 3; 15.6 vs. 30.0%; P=0.021), and thrombocytopenia (≥grade 3; 11.1 vs. 25.6%; P=0.012). Furthermore, the usage rate of granulocyte colony-stimulating factor, the incidence of febrile neutropenia and hospitalization rates due to myelosuppression were significantly lower in the trilaciclib group compared with the control group (P<0.01). The rate of chemotherapy delay, dose adjustment, and interruption was significantly lower in the trilaciclib group compared with the control group, with a greater number of cycles completed on average in the trilaciclib group (5.3±0.7 vs. 4.1±1.9; P=0.037). In terms of efficacy, the ORR in the trilaciclib group was higher than the control group (86.7 vs. 75.6%), although the difference did not reach statistical significance (P=0.057). Survival analysis showed that the median PFS in the trilaciclib group was 6.7 months, significantly higher than the 5.3 months of the control group [hazard ratio (HR)=0.677; 95% confidence interval, 0.502-0.912; P=0.0075)]. The median OS was 15.1 months in the trilaciclib group and 12.8 months in the control group, with no statistically significant difference (P=0.0886). The 1-, 2- and 3-year OS rates for the trilaciclib group were 63.3, 42.2 and 17.8%, respectively, with a 1-year PFS rate of 28.9%, all higher than the control group. Multivariate analysis identified an Eastern Cooperative Oncology Group (ECOG) performance status of 1 (HR=1.837; P=0.004), >3 metastatic sites (HR=7.392; P<0.001) and the presence of baseline brain metastasis (HR=2.196; P<0.001) as independent adverse prognostic factors for OS. For PFS, both the number of metastatic sites and treatment modality were independent predictors, with patients in the control group having a significantly higher risk of progression compared with those receiving trilaciclib (HR=1.495; P=0.008). These findings indicated that trilaciclib significantly reduced myelosuppression-related adverse events in first-line chemotherapy combined with immunotherapy for ES-SCLC, improved chemotherapy adherence and prolonged progression-free survival (PFS). No statistically significant difference in OS was observed between the trilaciclib and control groups. The 3-year OS rates were 17.8% for the trilaciclib group and 11.1% for the control group, with a low absolute difference of 6.7%. The number of metastatic sites and treatment method were independent influencing factors for PFS, while ECOG score

Correspondence to: Professor Lizhi Wang, Department of Radiotherapy and Chemotherapy, Chengde Central Hospital, 11 Guangren Street, Shuangqiao, Chengde, Hebei 067000, P.R. China
E-mail: oncology_132@163.com

Abbreviations: ES-SCLC, extensive-stage small cell lung cancer; OS, overall survival; PFS, progression-free survival; ORR, objective response rate; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; G-CSF, granulocyte colony-stimulating factor; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; CI, confidence interval; CT, computed tomography; MRI, magnetic resonance imaging; EP, etoposide plus cisplatin; EC, etoposide plus carboplatin

Key words: extensive-stage small cell lung cancer, trilaciclib, chemotherapy, immunotherapy

and baseline brain metastasis were independent poor prognostic factors for OS. In summary, trilaciclib is a potentially promising myeloprotective agent that improves PFS without compromising overall survival in patients with ES-SCLC.

Introduction

Small cell lung cancer (SCLC) is an aggressive and highly malignant subtype of lung cancer, accounting for ~15% of all lung cancer cases (1,2). Its clinical features include rapid tumor growth and a high propensity for distant metastasis. The fact that most patients are diagnosed at the extensive stage [extensive-stage SCLC (ES-SCLC)] (3) means that the prognosis of ES-SCLC is poor, with the median overall survival (OS) typically <12 months, and survival time further shortens with the development of treatment resistance (4,5). Currently, platinum-based doublet chemotherapy [such as etoposide plus cisplatin (EP) or etoposide plus carboplatin (EC)] remains the first-line standard treatment for patients with ES-SCLC (6,7). Although these chemotherapy regimens show high efficacy in the early stages, patients often face a gradual decline in treatment effectiveness due to the rapid progression of the tumor and the development of resistance (8,9). Moreover, chemotherapy-induced myelosuppression, which often causes severe clinical adverse events such as anemia, neutropenia and thrombocytopenia, significantly impacts the quality of life (QoL) and survival prognosis of patients (10,11). This myelosuppression, while a predictable consequence of chemotherapy, poses a considerable challenge in maintaining adequate treatment regimens and leads to complications such as prolonged hospitalizations and additional supportive care needs. Furthermore, these adverse effects often result in dose reductions or interruptions, further reducing the overall efficacy of cancer treatment. Traditional methods to address myelosuppression mainly involve symptomatic supportive treatments, such as the use of granulocyte colony-stimulating factor (G-CSF) or blood transfusions (12,13). However, these methods are reactive rather than preventive, often being administered after the onset of myelosuppression. This delay in intervention fails to address the underlying issue in a timely manner and may still carry certain risks, such as infections from prolonged neutropenia or transfusion-related complications.

Therefore, the development of novel strategies to manage myelosuppression, especially preventive treatments, is of utmost importance to improve patient outcomes and treatment adherence. Trilaciclib, a short-acting and reversible cyclin-dependent kinase 4/6 inhibitor, has garnered considerable attention in clinical practice as a potential myeloprotective agent for patients undergoing chemotherapy (14-16). Trilaciclib functions by transiently blocking hematopoietic stem cells in the G_1 phase of the cell cycle, preventing chemotherapy drugs from damaging bone marrow cells, thereby effectively preventing chemotherapy-induced myelosuppression (17). Several clinical studies have demonstrated that trilaciclib has a significant myeloprotective effect in patients with ES-SCLC. It not only considerably reduces chemotherapy-related myelosuppression events but also decreases related hospitalization rates, blood transfusion needs and the use of supportive therapies, thereby improving the QoL of patients without diminishing the antitumor efficacy of chemotherapy (18-20). Given its promising efficacy, trilaciclib has the potential to improve the treatment landscape for ES-SCLC, particularly in managing the adverse effects of chemotherapy while maintaining treatment efficacy. Despite the promising results observed in these trials, there is a need for more research focusing on the real-world application and safety of trilaciclib in diverse patient populations, especially in China, where clinical practices and patient demographics may differ. Real-world data will offer more generalizable insights and potentially highlight challenges or benefits that controlled trials may not fully capture.

Although trilaciclib has shown positive results in several international clinical trials and has been applied in some countries and regions, research on the real-world application and safety of trilaciclib in Chinese patients with ES-SCLC remains relatively limited. In addition, cultural and healthcare system differences may affect the accessibility and outcomes of treatment, highlighting the importance of evaluating trilaciclib's role in different settings. Therefore, the present study aims to retrospectively assess the myeloprotective effect, safety and impact on survival outcomes of trilaciclib in first-line chemotherapy for patients with ES-SCLC in China. The findings from this study may help bridge the gap in understanding the clinical efficacy of trilaciclib in a Chinese population and contribute to evidence-based support for its use in the treatment of ES-SCLC. Moreover, the present study aims to offer stronger support for clinical decision-making by providing insights into its practical applications and potential benefits in improving the treatment outcomes and overall care of patients with ES-SCLC.

Materials and methods

General clinical information. The present study is a single-center, retrospective real-world research project conducted at Chengde Central Hospital. A total of 180 patients diagnosed with ES-SCLC between January 2020 and January 2024 were included based on the following inclusion criteria. The medical records of the patients were accessed specifically for the present study between January 2024 and February 2025, including all relevant treatment and follow-up data, with patient mortality or the end of follow-up as the endpoint. The inclusion criteria were as follows: i) Patients were histologically or cytologically confirmed to have SCLC; ii) patients were receiving platinum-based chemotherapy combined with immunotherapy; iii) patients were aged ≥18 years; iv) patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 (21); v) completion of at least two cycles of treatment with complete treatment data; vi) first-time diagnosis of ES-SCLC, or recurrent or metastatic disease meeting the criteria for extensive stage; and vii) patients had not received prior systemic therapy for SCLC. The exclusion criteria were as follows: i) Patients who had been diagnosed with other malignant tumors; ii) patients with severe heart, liver or kidney dysfunction, or other major complications; iii) patients with poor treatment compliance or incomplete clinical data; iv) patients with severe active infections or other major medical diseases; v) patients with missing data; and vi) patients who received other antitumor therapies or participated in other clinical trials during the study period. After excluding patients with missing data, the remaining 180 patients were included

for final analysis. All patients underwent a comprehensive evaluation before treatment, including physical examinations, blood tests, biochemical indicators (liver and kidney function, electrolytes, blood glucose levels, lipid profile, myocardial enzymes, amylase, alkaline phosphatase and lactate dehydrogenase), chest, abdominal and pelvic computed tomography (CT) or magnetic resonance imaging (MRI) scans, brain MRI or enhanced CT scans, and bone scans. Additionally, baseline clinical data were recorded, including age, sex, smoking history, ECOG performance status, programmed cell death 1 ligand 1 (PD-L1) expression status, tumor staging, number of metastatic sites and brain metastasis status. Patients were divided into two groups based on the treatment regimen: The trilaciclib group and the control group. The trilaciclib group and the control group each included 90 patients. The study was approved by the Ethics Committee of Chengde Central Hospital (Chengde, China; approval no. CDCHLL2023-407).

Treatment methods. Patients in the trilaciclib group received trilaciclib in combination with chemotherapy and immunotherapy. The chemotherapy regimen included EC (etoposide 100 mg/m^2 on days 1-3; carboplatin dosed according to an area under the curve of 5, corresponding to a dose of ~500 mg on day 1) or EP (etoposide 100 mg/m^2 on days 1-3; cisplatin 75 mg/m^2 on day 1). The immunotherapy regimen included the following drugs: 71 Patients received surufilumab, 8 received tislelizumab (4.5 mg/m^2 intravenously every 3 weeks), 6 received toripalimab (240 mg intravenously every 3 weeks), 3 received atezolizumab (1,200 mg intravenously every 3 weeks) and 2 received durvalumab (1,500 mg intravenously every 3 weeks). Each treatment cycle was 3 weeks, with a total of 4-6 cycles. After completing 4-6 cycles of chemotherapy, immunotherapy was continued as a monotherapy until disease progression or intolerable toxicity occurred. Trilaciclib was administered by intravenous infusion at a dose of 240 mg/m^2 on each day of chemotherapy (days 1-3 of the cycle), with administration completed 30 min prior to the start of chemotherapy. For patients experiencing treatment delays or dose adjustments, the dosage for subsequent chemotherapy cycles was appropriately adjusted based on specific circumstances. After disease progression, patients received second-line treatment, primarily with topotecan or irinotecan, and some patients received third-line treatment with paclitaxel or anlotinib.

Patients in the control group received the same chemotherapy regimen as the trilaciclib group combined with immunotherapy. The immunotherapy drugs included surufilumab (74 cases), tislelizumab (6 cases), toripalimab (6 cases), atezolizumab (3 cases) and durvalumab (1 case), but without trilaciclib. The second- and third-line treatment regimens after disease progression were the same as those for the trilaciclib group, primarily involving topotecan, irinotecan and in some cases, paclitaxel or anlotinib.

Observation indicators. Adverse events were graded according to the Common Terminology Criteria for Adverse Events version 5.0 by the National Cancer Institute (22,23). Treatment efficacy was evaluated using the Response Evaluation Criteria in Solid Tumors version 1.1 (24). The observation indicators included myelosuppression-related indicators, chemotherapy dose adjustment indicators, efficacy indicators, survival indicators and safety indicators. The myelosuppression-related indicators included: i) Incidence of grade 3 and 4 neutropenia (25); ii) duration of severe neutropenia during the first cycle; iii) number of patients using G-CSF and the average number of cycles of G-CSF use; iv) incidence of anemia (≥grade 3) (26) and the lowest hemoglobin level recorded for each patient during the study period; v) number of patients requiring red blood cell transfusions and the number of transfusion episodes; vi) incidence of thrombocytopenia (≥grade 3) (27) and the lowest platelet count recorded for each patient during the study period; vii) number of patients requiring platelet transfusions and the number of transfusion episodes; viii) incidence of febrile neutropenia and the number of related hospitalizations; and ix) number of patients hospitalized due to myelosuppression and the number of hospitalization days. Chemotherapy dose adjustment indicators included: i) Number of patients with chemotherapy cycle delays, dose reductions and cycle interruptions; ii) number of patients completing ≥4 chemotherapy cycles; and iii) the average number of completed cycles. Efficacy indicators were as follows: i) Objective response rate (ORR), including complete response (CR) and partial response (PR); and ii) disease control rate, including CR, PR and stable disease (SD). Survival indicators were progression-free survival (PFS) and overall survival (OS). OS is defined as the time from the initiation of treatment to death from any cause or the time of last follow-up. PFS is defined as the time from the initiation of treatment to disease progression or death from any cause. The Cox proportional hazards model was used to evaluate potential factors affecting PFS and OS, including age, sex, ECOG score, immunotherapy regimen, number of metastatic sites, baseline brain metastasis, brain radiotherapy, chest radiotherapy, chemotherapy regimen and PD-L1 expression status. Safety indicators consisted of the incidence of drug-related adverse events during treatment.

Follow-up. The follow-up methods in the present study included regular outpatient visits, telephone follow-up and review of medical records. The specific follow-up schedule was as follows: Year 1, follow-up every 2 months; years 2-3, follow-up every 3-4 months; years 4-5, follow-up every 6 months; and >5 years, annual follow-up. The follow-up content included medical history inquiry, physical examination, laboratory tests and imaging examinations (such as chest, abdominal and pelvic CT or MRI, brain MRI or CT) to assess disease progression, treatment efficacy and the occurrence of adverse events. During follow-up, the time of disease progression, mortality and cause of death were recorded in detail. The follow-up cut-off date was set as February 1, 2025, with patient mortality or the end of follow-up as the endpoint. Throughout the study, efforts were made to ensure the authenticity and accuracy of follow-up data, with timely updates to the follow-up database. Strict quality control and data verification procedures were implemented, including regular audits of patient data, cross-checking of medical records, validation of key clinical outcomes, and verification of follow-up dates to ensure consistency and accuracy.

Statistical analysis. Data analysis in the present study was performed using Statistical Package for the Social Sciences

27.0 statistical software (IBM Corp.). For normally distributed continuous data, values were expressed as mean ± standard deviation, and inter-group comparisons were performed using the unpaired independent sample t-test. For non-normally distributed continuous data, normality was assessed using the Shapiro-Wilk test, and values were expressed as median (interquartile range), with inter-group comparisons conducted using the Mann-Whitney U test. Categorical data were expressed as frequency (percentage), and inter-group comparisons were performed using the χ^2 test or Fisher's exact probability test. Survival data were analyzed using the Kaplan-Meier method to estimate PFS and OS, and the median survival time and its 95% confidence interval (CI) were calculated. The log-rank test was used to compare survival curves between groups, with a two-tailed P<0.05 considered statistically significant. Additionally, Cox proportional hazards models were used for multivariate analysis to identify factors influencing PFS and OS. Cox regression analysis was performed to evaluate the independent effects of clinical variables such as age, sex, ECOG performance status and immunotherapy regimen on survival outcomes. The corresponding hazard ratio (HR) and 95% CI were calculated. Variables were selected based on clinical significance and univariate analysis results. P<0.05 was considered to indicate a statistically significant difference. Propensity score matching (PSM) was used to match patients between the trilaciclib group and the control group based on clinical variables such as age, sex, ECOG performance status, PD-L1 expression and the number of metastatic sites. After matching, the balance between the two groups was assessed using standardized mean differences (SMD), with all variables having SMD values of <0.1, indicating adequate matching.

Results

Comparison of general clinical data. There were no statistically significant differences between the trilaciclib group and the control group in terms of age, sex, smoking history, ECOG performance status, PD-L1 expression status, number of metastatic sites, baseline brain metastasis and brain radiotherapy status (all P>0.05), indicating that the baseline characteristics of the two groups were well-matched and comparable, as shown in Table I. Brain metastasis is considered a key controlled variable in this study due to its potential impact on prognosis and treatment outcomes in patients with ES-SCLC. The brain is a common site for metastasis in ES-SCLC, and its presence may influence both the treatment approach and survival outcomes (28).

Comparison of myelosuppression. Compared with the control group, the trilaciclib group had a significantly lower incidence of grade 3 (14.4 vs. 45.6%) and grade 4 neutropenia (3.3 vs. 20.0%) (χ^2=42.263; P<0.001). The duration of severe neutropenia during the first cycle was significantly shorter in the trilaciclib group [0 (0-1) days vs. 4 (2-6) days; Z=-9.592; P<0.001]. The proportion of patients using G-CSF in the trilaciclib group was also significantly lower (18.9 vs. 51.1%; χ^2=20.537), as was the average number of cycles of G-CSF use (1.5±0.6 vs. 3.2±1.5; t=-10.681) (both P<0.001). In terms of anemia, the incidence of grade ≥3 anemia in the trilaciclib group was 15.6%, significantly lower than the control group at 30.0% (χ^2=5.338; P=0.021). The lowest hemoglobin value was higher in the trilaciclib group (94±9 vs. 76±11 g/l; t=7.862; P<0.001), and the number of patients requiring red blood cell transfusions (18.9 vs. 43.3%; χ^2=12.546; P=0.002) and the number of transfusion episodes (1.0±0.6 vs. 2.0±0.8; t=-7.697; P<0.001) were also significantly lower. For thrombocytopenia, the incidence of grade ≥3 thrombocytopenia in the trilaciclib group was 11.1%, significantly lower than the control group at 25.6% (χ^2=6.271; P=0.012). The lowest platelet count was higher in the trilaciclib group (84±16x10^9 vs. 61±13x10^9/l; t=8.109; P<0.001), and the number of patients requiring platelet transfusions (7.8 vs. 21.1%; χ^2=6.474; P=0.011) and the number of transfusion episodes (1.0±0.4 vs. 1.9±0.6; t=-7.682; P<0.001) were significantly reduced. Additionally, the incidence of febrile neutropenia in the trilaciclib group was significantly lower than in the control group (4.4 vs. 17.8%; χ^2=8.100; P=0.004), as was the number of hospitalizations due to febrile neutropenia (3.3 vs. 15.6%; χ^2=7.860; P=0.005). The number of hospitalizations related to myelosuppression (7.8 vs. 21.1%; χ^2=6.474; P=0.011) and the number of hospitalization days (4.2±0.9 vs. 8.2±2.7 days; t=-7.128; P<0.001) were also significantly lower in the trilaciclib group. Regarding chemotherapy dose adjustments, the trilaciclib group had significantly lower rates of chemotherapy cycle delays (12.2 vs. 41.1%; χ^2=19.205; P<0.001), dose reductions (15.6 vs. 37.8%; χ^2=11.364; P<0.001) and cycle interruptions (5.6 vs. 20.0%; χ^2=8.424; P=0.004) compared with the control group. The proportion of patients completing ≥4 chemotherapy cycles was higher in the trilaciclib group (91.1 vs. 75.6%; χ^2=7.840; P=0.005), and the average number of completed chemotherapy cycles was also higher (5.3±0.7 vs. 4.1±1.9; t=6.274; P=0.037). Detailed data are shown in Table II.

Survival analysis comparison. In the present study, the median OS for all patients was 13.9 months (Fig. 1), and the median PFS was 6.1 months (Fig. 2). Group analysis showed that the median OS for the trilaciclib group was 15.1 months, compared with 12.8 months for the control group. Although the median OS in the trilaciclib group was 15.1 months compared to 12.8 months in the control group, the difference was not statistically significant (P=0.0886). The 1-, 2- and 3-year OS rates for the trilaciclib group were 63.3, 42.2 and 17.8%, respectively, while the rates for the control group were 52.2, 35.6 and 11.1% (Fig. 3). For PFS, the median PFS for the trilaciclib group was 6.7 months, significantly longer than the 5.3 months of the control group (HR=0.677; 95% CI=0.502-0.912; P=0.0075). The 1-year PFS rate for the trilaciclib group was 28.9% compared with 21.1% for the control group (Fig. 4).

Subgroup analyses were performed to evaluate the impact of different immunotherapeutic agents and chemotherapy regimens on survival outcomes. Among patients receiving immunotherapy, those treated with Surufilumab had a median OS of 14.8 months, compared with 13.6 months in those receiving other programmed cell death protein 1 (PD-1)/PD-L1 inhibitors (P=0.4836; Fig. 5). The median PFS was 6.3 months in the Surufilumab group and 5.7 months in the PD-1/PD-L1 inhibitors group (P=0.2838; Fig. 6). Regarding chemotherapy regimens, the median OS for the EP group was 14.1 and 14.5 months for the EC group (P=0.9654; Fig. 7).

Table I. Comparison of general clinical data between the trilaciclib group and the control group.

Characteristic	Trilaciclib group, N (%)	Control group, N (%)	χ^2	P-value
Age, years				
Median	63.5	61.5		
<65	52 (57.8)	61 (67.8)		
≥65	38 (42.2)	29 (32.2)	1.926	0.165
Sex				
Female	43 (47.8)	34 (37.8)		
Male	47 (52.2)	56 (62.2)	1.838	0.175
ECOG performance status				
0	68 (75.6)	74 (82.2)		
1	22 (24.4)	16 (17.8)	1.201	0.273
Smoking history				
Never smoked	14 (15.6)	8 (8.9)		
Former smoker	72 (80.0)	75 (83.3)		
Current smoker	4 (4.4)	7 (7.8)	2.516	0.284
PD-L1 expression				
Negative	71 (78.9)	62 (68.9)		
Positive	19 (21.1)	28 (31.1)	2.332	0.127
Number of metastatic sites				
1	29 (32.2)	18 (20.0)		
2-3	40 (44.4)	53 (58.9)		
>3	21 (23.3)	19 (21.1)	0.639	0.726
Baseline brain metastasis				
No	74 (82.2)	77 (85.6)		
Yes	16 (17.8)	13 (14.4)	0.370	0.543
Brain radiotherapy				
No	75 (78.3)	79 (85.0)		
Yes	15 (21.7)	9 (15.0)	0.891	0.345
Chest radiotherapy				
No	63 (70.0)	71 (78.9)		
Yes	27 (30.0)	19 (21.1)	1.869	0.172
Chemotherapy regimen				
EP	47 (52.2)	52 (57.8)		
EC	43 (47.8)	38 (42.2)	0.561	0.454

ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed cell death 1 ligand 1; EP, etoposide plus cisplatin; EC, etoposide plus carboplatin.

The corresponding median PFS was 5.8 and 6.3 months, respectively (P=0.8694; Fig. 8).

PSM analysis. After performing PSM to balance key baseline characteristics between the trilaciclib and control groups, each group was reduced to 63 patients, resulting in 63 patients in the trilaciclib group and 63 patients in the control group. Table III presents the baseline clinical characteristics of the two groups after PSM, showing that the groups were well-matched in terms of key clinical variables such as age, ECOG performance status and number of metastatic sites. The results of the survival analysis after PSM showed that the median OS for the trilaciclib group was 15.3 months compared with 13.1 months for the control group, with no statistically significant difference (P=0.1592; Fig. 9). By contrast, the median PFS for the trilaciclib group was 7.7 months, significantly longer than the 5.0 months of the control group (P=0.0159), with a HR of 0.6558 (95% CI=0.4581-0.9388; Fig. 10).

Analysis of factors affecting OS and PFS. To further explore the independent predictive factors influencing survival outcomes, Cox proportional hazards model analyses were performed for both OS and PFS, with results presented in

Table II. Comparison of myelosuppression between the trilaciclib group and the control group.

Myelosuppression-related indicators	Trilaciclib group, N=90	Control group, N=90	χ^2/T/Z	P-value
Neutropenia, n (%)				
Grade 3	13 (14.4)	41 (45.6)		
Grade 4	3 (3.3)	18 (20.0)	42.263	<0.001
Duration of severe neutropenia, days (range)	0 (0-1)	4 (2-6)	-9.592	<0.001
G-CSF use				
Number of patients using G-CSF, n (%)	17 (18.9)	46 (51.1)	20.537	<0.001
Average number of cycles of G-CSF use	1.5±0.6	3.2±1.5	-10.681	<0.001
Anemia				
Grade ≥3, n (%)	14 (15.6)	27 (30.0)	5.338	0.021
Lowest hemoglobin value, g/l	94±9	76±11	7.862	<0.001
Number of patients requiring RBC transfusions, n (%)	17 (18.9)	39 (43.3)	12.546	0.002
Number of RBC transfusion episodes (per person)	1.0±0.6	2.0±0.8	-7.697	<0.001
Thrombocytopenia				
Grade ≥3, n (%)	10 (11.1)	23 (25.6)	6.271	0.012
Lowest platelet count, $x10^9$/l	84±16	61±13	8.109	<0.001
Number of patients requiring platelet transfusions, n (%)	7 (7.8)	19 (21.1)	6.474	0.011
Number of platelet transfusion episodes (per person)	1.0±0.4	1.9±0.6	-7.682	<0.001
FN				
Incidence of FN, n (%)	4 (4.4)	16 (17.8)	8.100	0.004
Number of hospitalizations due to FN, n (%)	3 (3.3)	14 (15.6)	7.860	0.005
Myelosuppression-related hospitalizations				
Number of hospitalizations, n (%)	7 (7.8)	19 (21.1)	6.474	0.011
Hospitalization days	4.2±0.9	8.2±2.7	-7.128	<0.001
Chemotherapy dose adjustments				
Number of patients with chemotherapy cycle delays, n (%)	11 (12.2)	37 (41.1)	19.205	<0.001
Number of patients with dose reductions, n (%)	14 (15.6)	34 (37.8)	11.364	<0.001
Number of patients with chemotherapy cycle interruptions, n (%)	5 (5.6)	18 (20.0)	8.424	0.004
Number of patients completing ≥4 chemotherapy cycles, n (%)	82 (91.1)	68 (75.6)	7.840	0.005
Average number of chemotherapy cycles completed (cycles)	5.3±0.7	4.1±1.9	6.274	0.037

Data presented as n (%) where indicated or mean ± standard deviation. G-CSF, granulocyte colony-stimulating factor; RBC, red blood cell; FN, Febrile neutropenia.

Tables IV and V. In the multivariate analysis for OS, the ECOG performance status, number of metastatic sites and baseline brain metastasis were identified as independent risk factors. Compared with patients with an ECOG score of 0, those with a score of 1 had a significantly increased risk of mortality (HR=1.876; 95% CI=1.231-2.858; P=0.003). Compared with patients with only one metastatic site, those with 2-3 metastatic sites had a significantly higher risk of mortality (HR=2.194; 95% CI=1.485-3.241; P<0.001), and the risk further increased for patients with >3 metastatic sites (HR=7.066; 95% CI=4.114-12.139; P<0.001). Patients with baseline brain metastasis also had a significantly

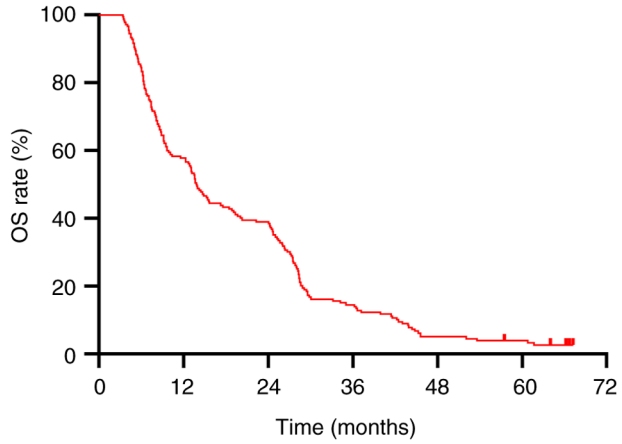

Figure 1. OS in the trilaciclib and control groups. OS, overall survival.

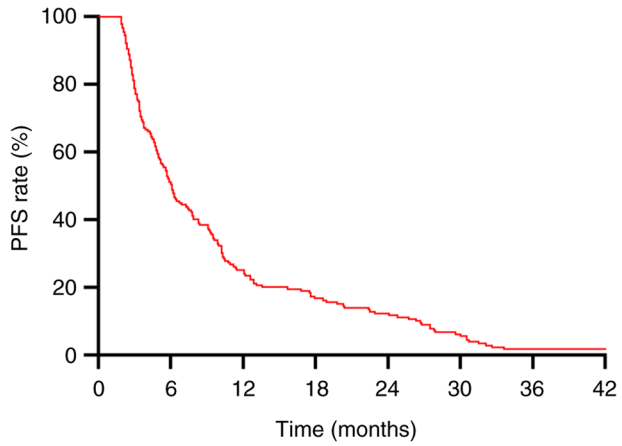

Figure 2. PFS in the trilaciclib and control groups. PFS, progression-free survival.

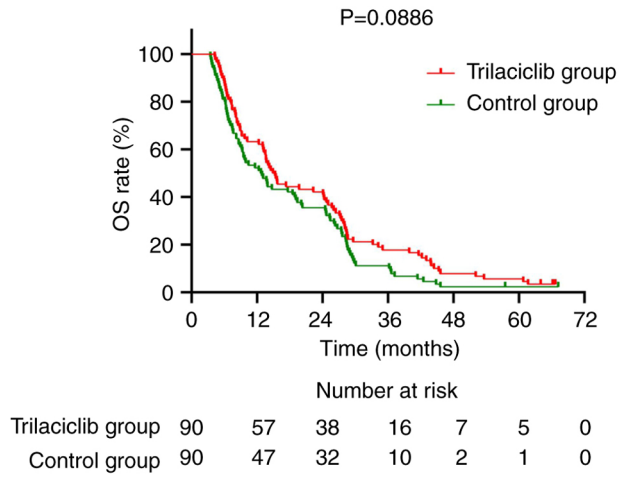

Figure 3. OS rates (1-, 2- and 3-year) in the trilaciclib and control groups. OS, overall survival.

higher risk of death compared with those without brain metastasis (HR=2.183; 95% CI=1.394-3.417; P<0.001). For overall survival (OS), no statistically significant difference was observed between the trilaciclib and control groups

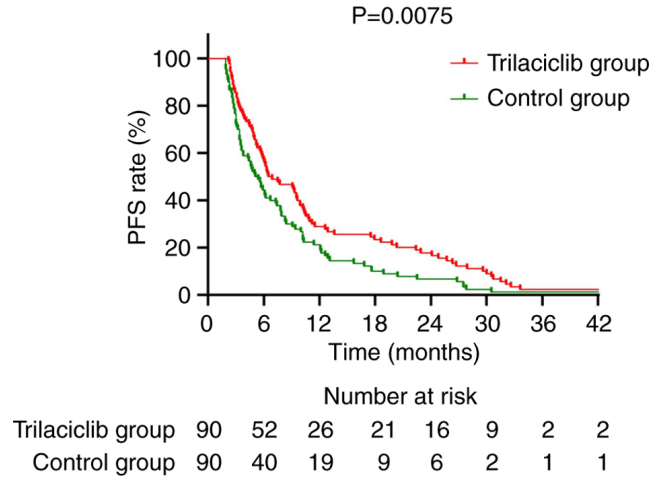

Figure 4. PFS rate (1-year) in the trilaciclib and control groups. PFS, progression-free survival.

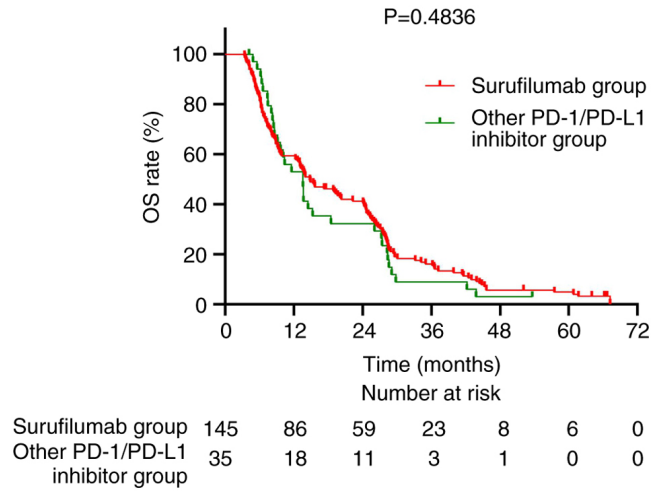

Figure 5. Kaplan-Meier curve comparing OS between surufilumab and other PD-1/PD-L1 inhibitors. OS, overall survival; PD-1, programmed death protein 1; PD-L1, programmed death-ligand 1.

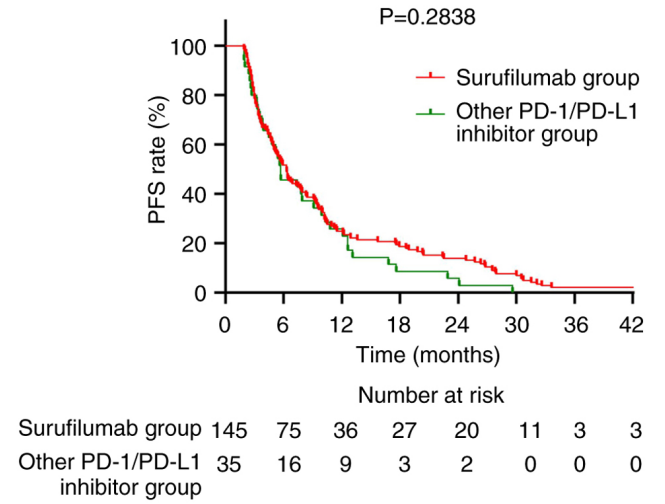

Figure 6. Kaplan-Meier curve comparing PFS between surufilumab and other PD-1/PD-L1 inhibitors. PFS, progression-free survival; PD-1, programmed death protein 1; PD-L1, programmed death-ligand 1.

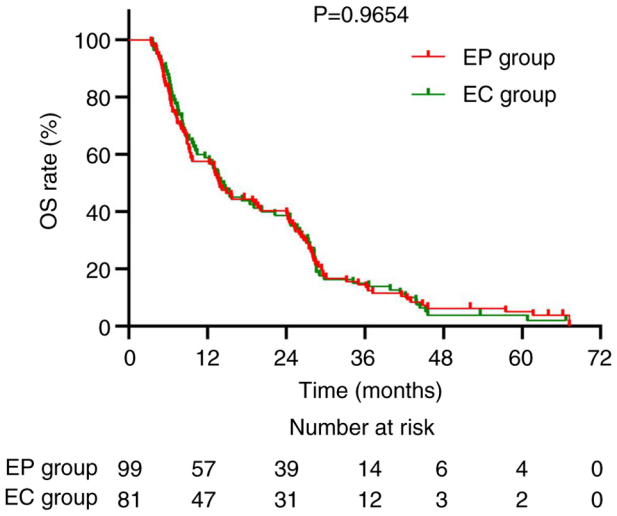

Figure 7. Kaplan-Meier curve comparing OS between EP and EC chemotherapy regimens. OS, overall survival; EP, etoposide plus cisplatin; EC, etoposide plus carboplatin.

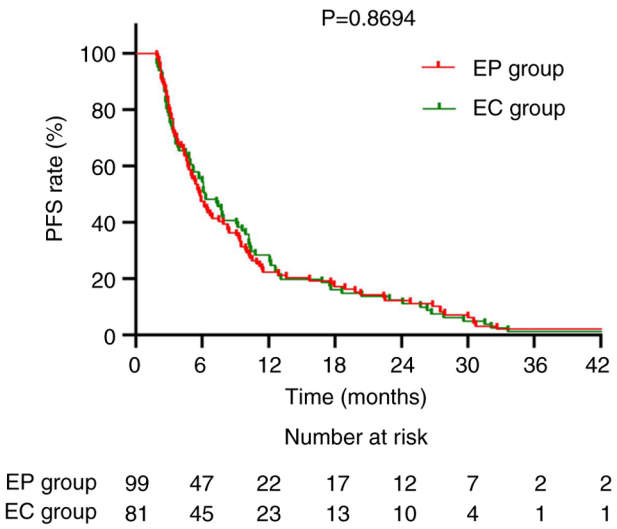

Figure 8. Kaplan-Meier curve comparing PFS between EP and EC chemotherapy regimens. PFS, progression-free survival; EP, etoposide plus cisplatin; EC, etoposide plus carboplatin.

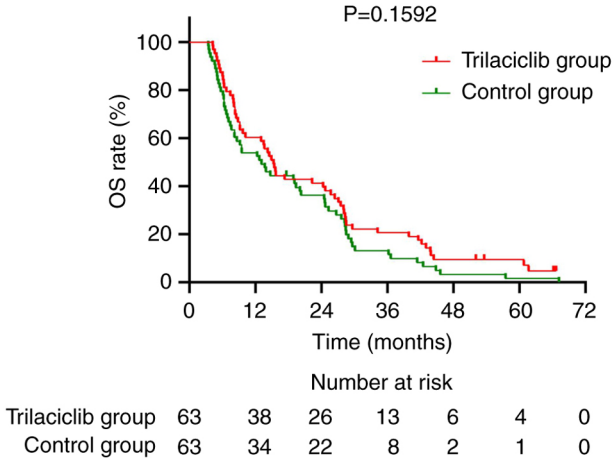

Figure 9. Kaplan-Meier curve comparing OS between the trilaciclib and control groups after PSM. OS, overall survival; PSM, propensity score matching.

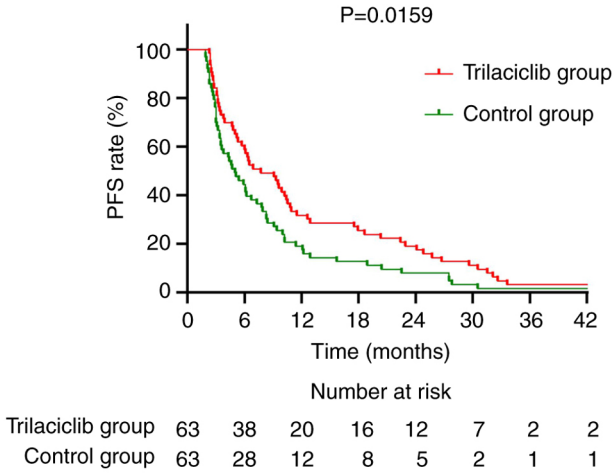

Figure 10. Kaplan-Meier curve comparing PFS between the trilaciclib and control groups after PSM. PFS, progression-free survival; PSM, propensity score matching.

(HR=1.306; 95% CI=0.965-1.766; P=0.083). Patients in the control group had a 30.6% higher risk of mortality compared with those receiving trilaciclib, based on the hazard ratio (HR=1.306). This calculation was derived from comparing the hazard ratio for OS between the two groups, but the difference did not reach statistical significance (P=0.083). Treatment modality (trilaciclib vs. control), type of immunotherapeutic agent (surufilumab vs. others) and chemotherapy regimen (EP vs. EC) were not independently associated with OS in the multivariate model (all P>0.05) (Table IV).

In the multivariate analysis for PFS, the treatment modality and number of metastatic sites were identified as independent factors affecting PFS. Compared with patients with only one metastatic site, those with 2-3 metastatic sites had a significantly increased risk of disease progression (HR=1.508; 95% CI=1.045-2.176; P=0.028), and the risk further increased for patients with >3 metastatic sites (HR=3.150; 95% CI=1.922-5.164; P<0.001). Compared with the trilaciclib group, patients in the control group had a significantly increased risk of disease progression (HR=1.495; 95% CI=1.109-2.014; P=0.008), indicating that trilaciclib independently reduced the risk of progression. Although ECOG performance status and baseline brain metastasis showed some trend of impact in the multivariate analysis for PFS, they did not reach statistical significance (Table V).

Efficacy comparison. The efficacy assessment results after treatment showed that in the trilaciclib group, the CR rate was 3.3%, the PR rate was 83.3%, the SD rate was 11.1% and the PD rate was 2.2%. In the control group, the CR rate was 2.2%, the PR rate was 73.3%, the SD rate was 18.9% and the PD rate was 5.6%. The differences between the two groups in terms of each efficacy category (CR, PR, SD and PD) did not reach statistical significance (all P>0.05; Table VI). In terms of ORR (CR + PR), the trilaciclib group had an ORR of 86.6%, higher than the 75.5% observed in the control group. However,

Table III. Baseline clinical characteristics of the trilaciclib and control groups after propensity score matching.

Characteristic	Trilaciclib group, n (%)	Control group, n (%)	χ^2	P-value
Age, years				
Median	63.2	63.0		
<65	36 (57.1)	35 (55.6)		
≥65	27 (42.9)	28 (44.4)	0.032	0.857
Sex				
Female	29 (46.1)	31 (49.2)		
Male	34 (53.9)	32 (50.8)	0.127	0.721
ECOG performance status				
0	48 (76.2)	47 (74.6)		
1	15 (23.8)	16 (25.4)	0.043	0.836
PD-L1 expression				
Negative	51 (81.0)	49 (77.8)		
Positive	12 (19.0)	14 (22.2)	0.194	0.660
Number of metastatic sites				
1	20 (31.7)	19 (30.2)		
2-3	28 (44.4)	27 (42.9)		
>3	15 (23.8)	17 (27.0)	0.169	0.919
Baseline brain metastasis				
No	54 (85.7)	52 (82.5)		
Yes	9 (14.3)	11 (17.5)	0.238	0.626

ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed cell death 1 ligand 1.

Table IV. Multivariate and univariate analysis of factors affecting overall survival.

	Univariate analysis			Multifactorial analysis		
Characteristics	HR	95% CI	P-value	HR	95% CI	P-value
Age, years						
<65	1.000					
≥65	1.090	0.800-1.486	0.584			
Sex						
Male	1.000					
Female	1.102	0.814-1.491	0.529			
ECOG performance status						
0	1.000			1.000		
1	2.751	1.892-4.000	<0.001	1.876	1.231-2.858	0.003
PD-L1 expression						
Negative	1.000					
Positive	1.061	0.755-1.491	0.733			
Number of metastatic sites						
1	1.000		<0.001	1.000		<0.001
2-3	2.473	1.689-3.620	<0.001	2.194	1.485-3.241	<0.001
>3	9.670	5.774-16.194	<0.001	7.066	4.114-12.139	<0.001
Baseline brain metastasis						
No	1.000			1.000		
Yes	2.629	1.728-3.999	<0.001	2.183	1.394-3.417	<0.001

Table IV. Continued.

	Univariate analysis			Multifactorial analysis		
Characteristics	HR	95% CI	P-value	HR	95% CI	P-value
Brain radiotherapy						
Yes	1.000			1.000		
No	1.696	1.110-2.590	0.015	1.173	0.902-2.148	0.129
Chest radiotherapy						
Yes	1.000					
No	1.267	0.898-1.788	0.177			
Chemotherapy regimen						
EC	1.000			1.000		
EP	1.047	0.774-1.416	0.765	1.101	0.809-1.500	0.540
Immunotherapy agent						
Surufilumab	1.000			1.000		
Others	1.165	0.823-1.534	0.498	1.141	0.837-1.598	0.452
Treatment modality						
Trilaciclib group	1.000			1.000		
Control group	1.306	0.965-1.766	0.083	1.168	0.853-1.600	0.333

HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed cell death 1 ligand 1; EP, etoposide plus cisplatin; EC, etoposide plus carboplatin.

Table V. Univariate and multivariate analysis of factors affecting progression-free survival.

	Univariate analysis			Multifactorial analysis		
Characteristics	HR	95% CI	P-value	HR	95% CI	P-value
Age, years						
<65	1.000					
≥65	1.197	0.882-1.624	0.248			
Sex						
Male	1.000					
Female	1.068	0.792-1.438	0.667			
ECOG performance status						
0	1.000			1.000		
1	2.025	1.402-2.925	<0.001	1.397	0.936-2.084	0.101
PD-L1 expression						
Negative	1.000					
Positive	1.038	0.741-1.455	0.828			
Number of metastatic sites						
1	1.000		<0.001	1.000		<0.001
2-3	1.633	1.140-2.339	0.007	1.508	1.045-2.176	0.028
>3	4.081	2.590-6.430	<0.001	3.150	1.922-5.164	<0.001
Baseline brain metastasis						
No	1.000			1.000		
Yes	1.748	1.163-2.626	0.007	1.484	0.983-2.242	0.061
Brain radiotherapy						
Yes	1.000					
No	1.404	0.924-2.134	0.112			

Table V. Continued.

Characteristics	Univariate analysis			Multifactorial analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Chest radiotherapy						
Yes	1.000					
No	1.267	0.901-1.781	0.173			
Chemotherapy regimen						
EC	1.000					
EP	1.085	0.807-1.458	0.589			
Treatment modality						
Trilaciclib group	1.000			1.000		
Control group	2.387	1.319-3.745	<0.001	1.495	1.109-2.014	0.008

HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed cell death 1 ligand 1; EP, etoposide plus cisplatin; EC, etoposide plus carboplatin.

Table VI. Comparison of efficacy between the trilaciclib group and the control group.

Efficacy	Trilaciclib group, N (%)	Control group, N (%)	χ^2	P-value
CR	3 (3.3)	2 (2.2)		
PR	75 (83.3)	66 (73.3)		
SD	10 (11.1)	17 (18.9)		
PD	2 (2.2)	5 (5.6)	3.875	0.275

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

the difference between the groups did not reach statistical significance (χ^2=3.626; P=0.057; data not shown).

Discussion

ES-SCLC is an aggressive subtype of lung cancer with an poor prognosis. At present, the standard of care primarily comprises platinum-based doublet chemotherapy in combination with immunotherapy (29). However, these regimens are frequently associated with severe myelosuppression, which significantly affects patients' treatment tolerance and QoL (30). As a novel myeloprotective agent, trilaciclib has shown promise in mitigating this issue in clinical practice (31). The present study is, to the best of our knowledge, the first real-world investigation conducted in a Chinese population to comprehensively assess the myeloprotective effects, safety profile and prognostic impact of trilaciclib in the first-line treatment of ES-SCLC, offering important clinical insights and application value.

The findings of the present study demonstrated that trilaciclib, when combined with chemotherapy and immunotherapy, significantly improved PFS, which aligns with previous clinical trials involving trilaciclib. Notably, in a phase II randomized trial conducted by Weiss *et al* (18), trilaciclib combined with EP (etoposide + carboplatin) achieved a median PFS of 6.2 months in ES-SCLC patients, consistent with the results of the present study and reinforcing the beneficial effect of trilaciclib on PFS. Another study confirmed that trilaciclib, in combination with chemotherapy and atezolizumab, significantly reduced the incidence of myelosuppression and improved QoL, with a notable improvement in PFS but no significant advantage in OS (32). These findings are consistent with the present study, in which PFS was significantly prolonged while OS did not reach statistical significance.

In terms of response, the ORR in the trilaciclib group was slightly higher than in the control group; however, differences in CR, PR, SD and PD rates between the groups were not statistically significant, in line with previous clinical studies (17,33). Weiss *et al* (18) also reported that although trilaciclib improved chemotherapy tolerability, it did not significantly increase ORRs. The present study also found clear myeloprotective effects of trilaciclib, including significant reductions in severe neutropenia, anemia, thrombocytopenia, G-CSF use and transfusion requirements. These findings are consistent with those reported by Daniel *et al* (32), who demonstrated that trilaciclib significantly reduced the incidence of chemotherapy-induced myelosuppression in clinical settings. By enabling patients to maintain scheduled chemotherapy doses and cycles, trilaciclib may further translate into improved treatment outcomes and QoL, which is one of its key clinical advantages.

Although the trilaciclib group showed a modest improvement in median OS compared with the control group, the difference was not statistically significant. This is similar to

the findings by Daniel *et al* (32), which showed that trilaciclib could mitigate myelosuppression and maintain antitumor efficacy without significantly prolonging OS. Possible reasons for this include limited follow-up duration, relatively small sample size and differences in post-progression treatment strategies. In fact, second- and third-line treatment choices can substantially influence overall survival outcomes. A recent study involving benmelstobart, anlotinib and chemotherapy further demonstrated that combining multi-targeted anti-angiogenic agents, such as anlotinib and bevacizumab, with immunotherapy significantly improved OS (up to 19.3 months), clearly outperforming the current standard chemoimmunotherapy alone (34). These findings suggest that trilaciclib could potentially be explored in combination with other antitumor agents to further enhance survival benefits. However, the potential influence of heterogeneity in immunotherapeutic agents and chemotherapy regimens on survival outcomes should be considered.

In the present subgroup analyses, surufilumab demonstrated longer OS and PFS compared with other PD-1/PD-L1 inhibitors, although the differences were not statistically significant. Similarly, no significant differences in OS or PFS were observed between patients receiving EP vs. EC regimens. These findings indicate that the observed clinical benefit of trilaciclib is unlikely to be confounded by the type of immunotherapy or chemotherapy regimen used, thereby supporting the robustness of the primary results. To elucidate the prognostic value of trilaciclib, multivariate Cox regression analysis was conducted. The results showed that, compared with patients treated with trilaciclib, those in the control group had a significantly increased risk of disease progression (HR=1.495; 95% CI=1.109-2.014; P=0.008), indicating an independent protective effect of trilaciclib on PFS. No statistically significant difference in OS was observed between the trilaciclib and control groups (HR=1.306; 95% CI=0.965-1.766; P=0.083). Further analysis showed that ECOG performance status, number of metastatic sites and baseline brain metastasis were independent poor prognostic factors for OS, which aligns with the results of other studies (35,36). This highlights the importance of considering these variables in treatment planning. The impact of immunotherapy type and chemotherapy regimen on survival did not show statistically significant differences in the present model, emphasizing the robust effect of trilaciclib. This suggests that even after controlling for confounding variables such as ECOG performance status, number of metastatic sites and presence of brain metastases, trilaciclib independently contributed to delayed disease progression. The novelty of the present study lies in its being, to the best of our knowledge, the first real-world clinical investigation of trilaciclib in a Chinese ES-SCLC population. It provides an objective and comprehensive evaluation of the myeloprotective efficacy, antitumor performance and safety profile of trilaciclib. Unlike prior randomized controlled trials, the present real-world study reflects the complexity of routine clinical practice, involves a broader patient population and yields findings that are more generalizable to actual treatment settings. The present results offer important evidence-based support for clinicians and demonstrate strong clinical applicability and value for broader implementation.

Nonetheless, the present study has several limitations. First, as a retrospective, non-randomized study, selection bias could not be fully eliminated. To mitigate this limitation, PSM was employed to match patients in the trilaciclib and control groups based on baseline characteristics such as age, ECOG performance status and number of metastatic sites. While PSM helped reduce baseline imbalances between the groups, it is important to note that residual confounding variables may still exist. Second, the relatively small sample size limited the statistical power for subgroup analyses, potentially affecting the robustness and generalizability of certain findings. Third, the follow-up duration was limited and long-term survival data for some patients are still being collected, which may underestimate or overestimate the true OS difference. Fourth, the lack of blinding in the study could have introduced subjectivity in efficacy and safety assessments. Future prospective, randomized, controlled trials are required to further validate the efficacy and safety of trilaciclib across different patient populations.

In summary, the present real-world study supported the myeloprotective role of trilaciclib in first-line treatment of ES-SCLC. Trilaciclib effectively reduced chemotherapy-induced myelosuppression, improved treatment compliance and prolonged PFS, thereby enhancing overall treatment safety without compromising antitumor efficacy. Although a statistically significant OS benefit was not demonstrated, trilaciclib exhibited promising clinical potential, particularly in preserving QoL by reducing chemotherapy-induced myelosuppression. The reduction in severe neutropenia, anemia and thrombocytopenia in the trilaciclib group not only improved treatment tolerance but also contributed to improved patient outcomes in terms of QoL. While OS did not show significant improvement, these myeloprotective effects are clinically meaningful, as they may lead to fewer treatment delays, reduced hospitalization and improved overall treatment compliance. Further large-scale, long-term prospective studies are warranted to clarify role of trilaciclib in SCLC management and identify the populations most likely to benefit.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YC performed the data analysis and wrote the paper. LW was responsible for the research design and guided the revision of the paper. HZ provided clinical cases, participated in data analysis and interpretation, and revised the manuscript

critically for important intellectual content. XL contributed to the research design, provided data collection support and assisted in drafting the manuscript. YC and LW confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The current study was performed in accordance with the Declaration of Helsinki and approved by the local Ethics Committee of Chengde Central Hospital (Chengde, P.R. China; approval no. CDCHLL2023-407). All patients and/or their families signed informed consent forms for study participation.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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