Benefits and risks of prophylactic glucocorticoids in platinum chemotherapy for extensive-stage small-cell lung cancer: A retrospective study

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Abstract. The objective of the present study was to analyze the effects of prophylactic glucocorticoid use on the efficacy and adverse reactions of platinum-based intravenous regimens in patients with extensive-stage small-cell lung cancer (ES-SCLC). The present study retrospectively analyzed 103 newly diagnosed patients with ES-SCLC treated with etoposide plus platinum at the First Affiliated Hospital of Anhui Medical University from August 2022 to December 2024. Patients were divided into glucocorticoid (63 cases) and control (40 cases) groups. Baseline characteristics, adverse reaction rates and treatment outcomes were compared between groups. The hormone group showed no significant differences in objective response rate (ORR) and disease control rate (DCR) but had lower incidences of nausea/vomiting (P=0.005), constipation (P=0.002) and leukopenia (P=0.009). In patients also receiving immune checkpoint inhibitors (ICIs), the hormone group had improved renal function protection (P=0.026). Although hypertension incidence was higher in the hormone group, the difference was not statistically significant (P>0.05). Hyperglycemia rates and median survival time were similar between groups. In conclusion, prophylactic glucocorticoids do not significantly affect ORR, DCR, or median survival in patients with ES-SCLC on etoposide plus platinum with or without ICIs but can reduce nausea/vomiting, constipation and leukopenia. They may protect kidney function when combined with ICIs. No major adverse events were linked to glucocorticoid use, so their prophylactic use is recommended in platinum-based ES-SCLC therapy.

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Abbreviations: LC, lung cancer; SCLC, small cell lung cancer; ES-SCLC, extensive-SCLC; ORR, objective response rate; DCR, disease control rate; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; CT, computed tomography; PRN, *pro re nata*; i.v., intravenous; p.o., *per os* (oral); AUC, area under the curve

Key words: ES-SCLC, glucocorticoid, chemotherapy, platinum

Introduction

Lung cancer (LC) remains the leading cause of cancer-related mortality worldwide (1). Small cell LC (SCLC), accounting for ~15% of all LCs (2), is classified into limited-stage and extensive-stage (ES-SCLC) according to the VALSG staging system. The five-year relative survival rate for SCLC is ~6.4% (3), most patients are diagnosed at the extensive stage (4). For over 30 years, platinum plus etoposide has been the standard first-line treatment (5). In the latest NCCN guidelines (6), atezolizumab and durvalumab, as immune checkpoint inhibitors (ICIs) combined with platinum-etoposide, have been officially established as the preferred first-line treatment options for ES-SCLC.

During chemotherapy for patients with LC, various adverse reactions often occur. Glucocorticoids, such as dexamethasone, have anti-inflammatory, immunosuppression and anti-allergic effects (7) and may help reduce chemotherapy-related adverse reactions, thus being widely used in chemotherapy regimens for patients with LC (8). Although dexamethasone is routinely used for antiemesis, the optimal timing-prophylactic versus symptom-triggered-remains undefined. In clinical practice, there are two main strategies: One is prophylactic use, where dexamethasone is routinely administered before the initiation of chemotherapy or prior to the onset of adverse reactions, with the expectation that early intervention will reduce the incidence and severity of adverse reactions; the other is episodic use, where symptomatic treatment is only provided after patients develop clear symptoms of adverse reactions (such as severe nausea and vomiting and drug allergic reactions). Each of these strategies has its own considerations: Prophylactic use may reduce the suffering caused by adverse reactions, but long-term or excessive use may increase the risk of infections, blood glucose fluctuations and other side effects; while episodic use can avoid unnecessary drug exposure, it may lead to the aggravation of adverse reactions due to delayed intervention, and even affect the progress of chemotherapy. It

is precisely due to the uncertainty in the timing of dexamethasone administration and the controversies surrounding the balance between efficacy and safety of different administration strategies (8,9) that the present study intended to adopt the prophylactic dexamethasone administration regimen. By systematically observing its efficacy in controlling adverse reactions, patient tolerance and related safety indicators during platinum-etoposide chemotherapy, the present study aimed to provide clinical evidence for clarifying the optimal timing of dexamethasone administration in LC chemotherapy.

Materials and methods

General data. The present study retrospectively collected data of 289 patients with SCLC admitted to the First Affiliated Hospital of Anhui Medical University (Hefei, China) from August 2022 to December 2024. After excluding 116 cases not meeting the inclusion criteria, 57 cases meeting the exclusion criteria and 13 cases lost to follow-up, 103 patients were finally included. Among them, 63 patients who received glucocorticoids during chemotherapy were assigned to the hormone group and 40 patients who did not receive glucocorticoids were assigned to the control group. The present study aimed to compare the differences in treatment outcomes, adverse reaction rates and quality of life between the two groups.

Inclusion criteria were as follows: i) Patients aged >18 years; ii) newly diagnosed ES-SCLC confirmed by histology or cytology; iii) Eastern Cooperative Oncology Group (ECOG) score ≤2; iv) expected survival >2 months; v) first-line treatment drugs containing etoposide plus platinum.

Exclusion criteria were as follows: i) Previous surgery or radiotherapy; ii) allergy to glucocorticoids or contraindications for glucocorticoid use; iii) concurrent other malignancies; iv) severe liver or kidney dysfunction; v) pregnant or breastfeeding women. To provide a comprehensive visual overview of the present study's design, a detailed technical road-map was constructed, which is presented in the graphical abstract (Fig. 1).

Treatment methods. All patients received etoposide plus platinum combination chemotherapy, repeated every 3 weeks. ICIs could be combined and all were administered one day before chemotherapy in the present study. Hormone group: Dexamethasone tablets 4.5 mg (Tianjin Xinyi Jinjin Pharmaceutical Co., Ltd., specification 0.75 mg, cat. no. H31020793) were orally administered 30 min before intravenous (i.v.) etoposide daily, once a day. Control Group: No routine prophylactic oral administration of dexamethasone acetate tablets was given before or during chemotherapy. If patients developed definite chemotherapy-related adverse reactions (such as grade II or higher nausea/vomiting, drug allergic reactions and infusion-related reactions), symptomatic treatment was provided according to clinical guidelines, including i.v. or oral glucocorticoid therapy with dexamethasone when necessary. *Pro re nata* (PRN) dexamethasone was administered immediately upon meeting any of the following per-specified criteria: i) Breakthrough CINV (≥ grade 2 despite prophylaxis): 8-12 mg i.v./*per os* (p.o.), repeatable once per 24 h; discontinued when symptoms ≤ grade 1, no taper. ii) Acute infusion/hypersensitivity reaction: 10 mg i.v. bolus, chemotherapy paused; infusion resumed at 50% rate after complete resolution. No further dose administered in absence of recurrence within 1 h. iii) Other transient toxicities (fatigue, anorexia, mild transaminitis) requiring rapid symptom relief: iv) 4 mg p.o. each morning for ≤5 days; withheld if glucose >13.9 mmol/l or active infection. Stop without tapering once symptoms improve (9). Among the 40 control patients, 11 received PRN dexamethasone after breakthrough nausea/vomiting or hypersensitivity reactions.

Etoposide injection (Qilu Pharmaceutical Co., Ltd.; specification 5 ml: 0.1 g, cat. no. H20143143), 100 mg/m^2, i.v. infusion, days 1-3; Cisplatin injection (Jiangsu Hosen Pharmaceutical Co., Ltd.; specification 30 mg: 6 ml, cat. no. H20040813), 25 mg/m^2, i.v. infusion, days 1-3; Carboplatin injection (Qilu Pharmaceutical Co., Ltd., specification 50 mg: 10 ml, cat. no. H20020181), AUC=5, i.v. infusion, day 1; Lobaplatin for injection (Hainan Chang'an International Pharmaceutical Co., Ltd.; specification 50 mg, cat. no. H20050308), 30 mg/m^2, i.v. infusion, day 1. ICIs included: Atezolizumab 1,200 mg per dose, Durvalumab 1,500 mg per dose, Adebrelimab 20 mg/kg per dose and Serplulimab 4.5 mg/kg per dose. Symptomatic treatments such as antiemetic and gastric protection were provided during chemotherapy.

Study endpoints. Primary endpoint: Incidence of nausea or vomiting during the first chemotherapy cycle (cycle 1).

Secondary endpoints: Incidence of other adverse events (constipation, leukopenia, anemia, thrombocytopenia and renal dysfunction), objective response rate (ORR), disease control rate (DCR) and median overall survival (OS).

Observation indicators. Adverse reactions were assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 (10). Various adverse reactions during chemotherapy, such as hypertension, hyperglycemia, nausea/vomiting, constipation, leukopenia, anemia, hypoalbuminemia, ALT elevation, AST elevation, renal dysfunction, hypokalemia, hyponatremia and hypocalcemia, were observed and recorded, with their incidence and severity graded as I, II, III and IV. Renal dysfunction was defined as eGFR <60 ml/min/1.73 m^2 (corresponding to CTCAE v5.0 grade ≥2: 30-<60 ml/min/1.73 m^2 for grade 2, 15-<30 for grade 3, and <15 for grade 4).

Clinical efficacy was evaluated based on the Response Evaluation Criteria in Solid Tumors version 1.1 (11). Contrast-enhanced computed tomography or magnetic resonance imaging was repeated 2-4 weeks after every two cycles of chemotherapy, with positron emission tomography reserved for inconclusive cases and baseline imaging was performed within 14 days before treatment initiation. Complete response (CR) was defined as the disappearance of all target lesions; partial response (PR) as ≥30% reduction in the sum of target lesion diameters; stable disease (SD) as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease and progressive disease (PD) as ≥20% increase in the sum of target lesion diameters or the appearance of new lesions. ORR and DCR were calculated as follows: ORR=(CR+PR)/total number of cases x100%, DCR=(CR + PR + SD)/total number of cases x100%.

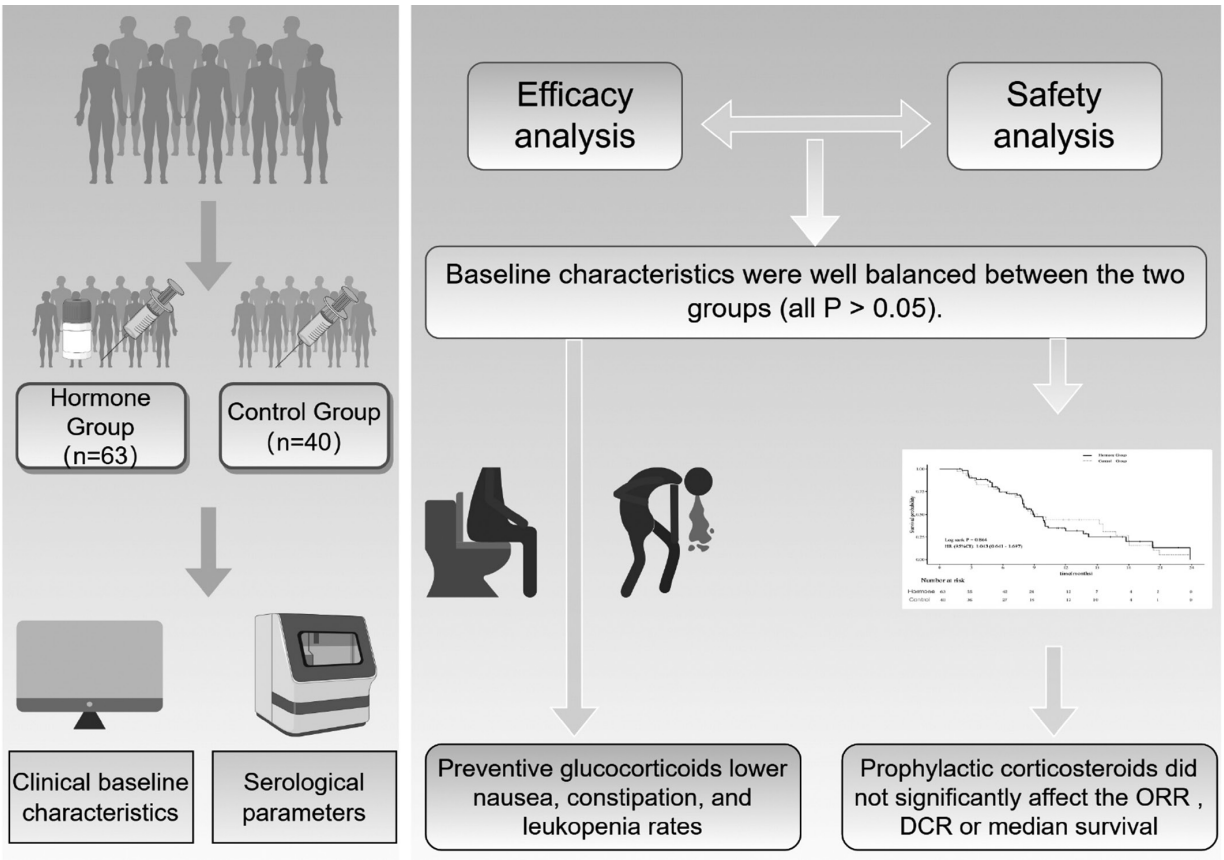

Figure 1. Graphical abstract. ORR, objective response rate; DCR, disease control rate.

Statistical methods. SPSS 27.0 (IBM Corp.) software was used to process the collected case data. Chi-square tests were conducted for statistical analysis. For every 2x2 comparison of categorical outcomes, the expected cell frequency (E) was evaluated first. If all E≥5, the standard Pearson χ^2 test was applied. Whenever any E fell below 5, the analysis was switched to two-tailed Fisher's exact test. Group comparisons were made with the two-sample t-test. Kaplan-Meier survival curves were used to assess the cumulative risk of endpoint events; the 95% confidence interval for each median survival time was calculated with the log-log (Greenwood) method with Log-rank tests to examine intergroup differences. A significance level of P<0.05 was set for all observed indicators. For numerical variables [for example, age, body mass index (BMI) and laboratory indices] missing values (range 0.5-9.2% per variable) were imputed once using mean imputation.

Results

Baseline differences. A total of 103 subjects were finally included and divided into the hormone group (n=63) and the control group (n=40). Baseline data were analyzed for differences. Statistical analysis showed no significant differences between the two groups in sex, age, smoking history, ECOG performance status, or BMI (P>0.05), indicating favorable comparability (Table I).

Clinical efficacy. As shown in Table II, the hormone group had 37 cases (58.73%) of PR, 10 cases (15.87%) of SD and 16 cases (25.40%) of PD. The control group had 19 cases (47.50%) of PR, 10 cases (25.00%) of SD, and 11 cases (27.50%) of PD. The ORR and DCR were similar between the two groups (ORR: 58.73 vs. 47.50%, P=0.265; DCR: 74.60 vs. 72.50%, P=0.813). Further analysis showed no statistical significance in ORR and DCR between the glucocorticoid and control groups, whether in patients treated with etoposide plus platinum alone or in combination with ICIs (P>0.05, data not shown).

Adverse reactions. As shown in Table III, compared with the control group, the hormone group had lower incidences of grade II-IV nausea/vomiting (19.05 vs. 45.00%, χ^2=7.98, P=0.005), constipation (3.17 vs. 25.00%, χ^2=9.3, P=0.002) and leukopenia (20.63 vs. 45.00%, χ^2=6.9, P=0.009). These results indicate that glucocorticoids can effectively alleviate chemotherapy-induced nausea/vomiting, constipation and leukopenia. However, there were no significant differences between the two groups in the incidence of grade II-IV anemia, thrombocytopenia, hypoalbuminemia, ALT elevation, AST elevation, renal dysfunction, hypokalemia, hyponatremia, hypocalcemia, or thyroid dysfunction, suggesting that glucocorticoids have no significant effect on improving these conditions.

In patients treated with etoposide plus platinum, the hormone group had significantly lower incidences of grade I-III nausea/vomiting (54.84 vs. 87.50%, χ^2=5.01, P=0.025) and constipation (9.68 vs. 43.75%, χ^2=5.42, P=0.02) compared with the control group (Table IV). However, there were no significant differences between the two groups in the

Table I. Clinical characteristics of patients in two groups.

	Total (n=103)	Hormone group (n=63)	Control group (n=40)	x^2	P-value
Sex				2.06	0.151
Male	94 (91.26)	60 (95.24)	34 (85.00)		
Female	9 (8.74)	3 (4.76)	6 (15.00)		
Age				1.90	0.168
≥60 years	34 (33.01)	24 (38.10)	10 (25.00)		
<60 years	69 (66.99)	39 (61.90)	30 (75.00)		
Smoking history				1.91	0.167
Yes	50 (48.54)	34 (53.97)	16 (40.00)		
No	53 (51.46)	29 (46.03)	24 (60.00)		
Eastern Cooperative Oncology Group					0.215
0	6 (5.83)	3 (4.76)	3 (7.50)		
1	74 (71.84)	49 (77.78)	25 (62.50)		
2	23 (22.33)	11 (17.46)	12 (30.00)		
Body mass index					0.482
<18.5	7 (6.80)	5 (7.94)	2 (5.00)		
18.5-24	67 (65.05)	43 (68.25)	24 (60.00)		
>24	29 (28.16)	15 (23.81)	14 (35.00)		
eGFR	69.46	69.45 (±16.36)	69.42 (±15.14)		0.993

Fisher's exact test was used when any cell count <5.

Table II. Clinical efficacy of all patients.

	Total (n=103)	Hormone group (n=63)	Control group (n=40)	x^2	P-value
Complete response	0	0	0		
Partial response	56 (54.37)	37 (58.73)	19 (47.50)		
Stable disease	20 (19.42)	10 (15.87)	10 (25.00)		
Progressive disease	27 (26.21)	16 (25.40)	11 (27.50)		
Objective response rate	54.37%	58.73%	47.50%	1.24	0.265
Disease control rate	73.79%	74.60%	72.50%	0.06	0.813

Fisher's exact test was used when any cell count <5.

incidence of grade I-III leukopenia, anemia, thrombocytopenia, hypoalbuminemia, ALT elevation, AST elevation, renal dysfunction, hypokalemia, hyponatremia, hypocalcemia, or thyroid dysfunction.

In patients treated with etoposide plus platinum combined with ICIs, the hormone group had significantly lower incidences of grade II-IV nausea/vomiting (9.38 vs. 37.50%, χ^2=6.44, P=0.011) and leukopenia (18.75 vs. 54.17%, χ^2=7.67, P=0.006) compared with the control group (Table V). Notably, grade ≥2 renal dysfunction occurred in 0% of the hormone group versus 20.83% of controls (P=0.026); this difference was not observed in the overall cohort or the chemotherapy-alone subgroup. No significant differences were observed between the two groups in the incidence of grade II-IV constipation, anemia, thrombocytopenia, hypoalbuminemia, ALT elevation, AST elevation, hypokalemia, hyponatremia, hypocalcemia, or thyroid dysfunction.

Survival analysis. Kaplan-Meier analysis (Fig. 2) showed that the median survival time was 8.9 months [95% confidence interval (CI): 8.00-12.03] in the hormone group and 9.3 months (95% CI: 7.97-16.80) in the control group, with no significant difference between the two groups (Log-rank P=0.864, hazard ratio=1.043, 95% CI: 0.641-1.697). Further analysis showed no significant differences in median survival time between the glucocorticoid and control groups, whether in patients treated with etoposide plus platinum alone or in combination with ICIs (P>0.05, data not shown).

Discussion

Glucocorticoids can alleviate chemotherapy-induced adverse reactions through various mechanisms (12). Their anti-inflammatory effects can inhibit the release of inflammatory mediators, reducing tissue inflammation and relieving symptoms such as

Table III. Incidence of grade II-IV adverse reactions in all patients.

	Hormone group (n=63)	Control group (n=40)	x^2	P-value
Nausea and vomiting	12 (19.05)	18 (45.00)	7.98	0.005
Constipation	2(3.17)	10 (25.00)	9.30	0.002
Hypertension	28 (44.44)	13 (32.50)	1.46	0.227
Hyperglycemia	9 (14.29)	5 (12.50)	0.07	0.797
Leukopenia	13 (20.63)	18 (45.00)	6.90	0.009
Anemia	8 (12.70)	10 (25.00)	2.57	0.109
Thrombocytopenia	2 (3.17)	1 (2.50)	<0.001	0.999
Hypoproteinemia	3 (4.76)	2 (5.00)	<0.001	0.999
ALT elevation	2 (3.17)	1 (2.50)	<0.001	0.999
AST elevation	1 (1.59)	2 (5.00)	0.16	0.687
Renal dysfunction	2 (3.17)	6 (15.00)	3.27	0.071
Hypokalemia	0 (0.00)	3 (7.50)		0.999
Hyponatremia	6(9.52)	3 (7.50)	<0.001	0.999
Hypocalcemia	7 (11.11)	3 (7.50)	0.07	0.793
Hypothyroidism	1 (1.59)	4 (10.00)	2.15	0.143

Fisher's exact test was used when any cell count <5.

Table IV. Incidence of grade I-III adverse reactions in etoposide plus platinum.

	Hormone group (n=31)	Control group (n=16)	x^2	P-value
Nausea and vomiting	17 (54.84)	14 (87.50)	5.01	0.025
Constipation	3 (9.68)	7 (43.75)	5.42	0.020
Hypertension	20 (64.52)	7 (43.75)	1.86	0.172
Hyperglycemia	10 (32.26)	5 (31.25)	0.001	0.999
Leukopenia	18 (58.06)	11 (68.75)	0.51	0.475
Anemia	24 (77.42)	12 (75.00)	0.001	0.999
Thrombocytopenia	3 (9.68)	0		0.512
Hypoproteinemia	6(19.35)	5 (31.25)	0.30	0.583
ALT elevation	10 (32.26)	4 (25.00)	0.03	0.858
AST elevation	5 (16.13)	1 (6.25)	0.25	0.617
Renal dysfunction	12 (38.71)	4 (25.00)	0.88	0.347
Hypokalemia	3 (9.68)	1 (6.25)	<0.001	0.999
Hyponatremia	9 (29.03)	4 (25.00)	<0.001	0.999
Hypocalcemia	13 (41.94)	5 (31.25)	0.51	0.475

Fisher's exact test was used when any cell count <5.

vomiting and constipation (13). Additionally, they can stabilize mast cell and lysosomal membranes, reducing the occurrence of allergic and toxic reactions (14), which may have a positive impact on preventing severe adverse reactions. However, long-term use of glucocorticoids may lead to a series of side effects, such as metabolic disorders (15). This dilemma places clinicians in the challenging position of continuously weighing therapeutic benefit against potential harm. In the context of LC chemotherapy, a pivotal and still unresolved question is whether dexamethasone should be administered only after adverse events have manifested, or whether prophylactic use is more likely to maximize net clinical benefit. Consequently, optimizing the strategic deployment of dexamethasone remains an urgent unmet need.

To address this central controversy, the present study specifically interrogates the prophylactic dexamethasone paradigm. The results showed that compared with the control group, the hormone group had a significantly lower incidence of nausea/vomiting, confirming the effectiveness of prophylactic glucocorticoid use in reducing chemotherapy-related nausea/vomiting and after adjusting for age, sex and ECOG performance status in a multivariable logistic regression model, the incidence of vomiting remained significantly lower in the prophylactic dexamethasone group than in the non-prophylactic

Table V. Incidence of Grade II-IV adverse reactions in etoposide plus platinum combine with immune checkpoint inhibitors.

	Hormone group (n=32)	Control group (n=24)	x^2	P-value
Nausea and vomiting	3 (9.38)	9 (37.50)	6.44	0.011
Constipation	1 (3.12)	5 (20.83)	2.83	0.092
Hypertension	14 (43.75)	8 (33.33)	0.62	0.430
Hyperglycemia	3 (9.38)	3 (12.50)	<0.001	0.999
Leukopenia	6 (18.75)	13 (54.17)	7.67	0.006
Anemia	2 (6.25)	7 (29.17)	3.78	0.052
Thrombocytopenia	0	1 (4.17)		0.429
Hypoproteinemia	3 (9.38)	1 (4.17)	0.05	0.822
ALT elevation	1 (3.12)	1 (4.17)		0.999
AST elevation	0	1 (4.17)		0.429
Renal dysfunction	0	5 (20.83)		0.026
Hypokalemia	0	2 (8.33)		0.179
Hyponatremia	4 (12.50)	1 (4.17)	0.37	0.543
Hypocalcemia	3 (9.38)	1 (4.17)	0.05	0.822
Hypothyroidism	1 (3.12)	4 (16.67)	1.65	0.199

Fisher's exact test was used when any cell count <5.

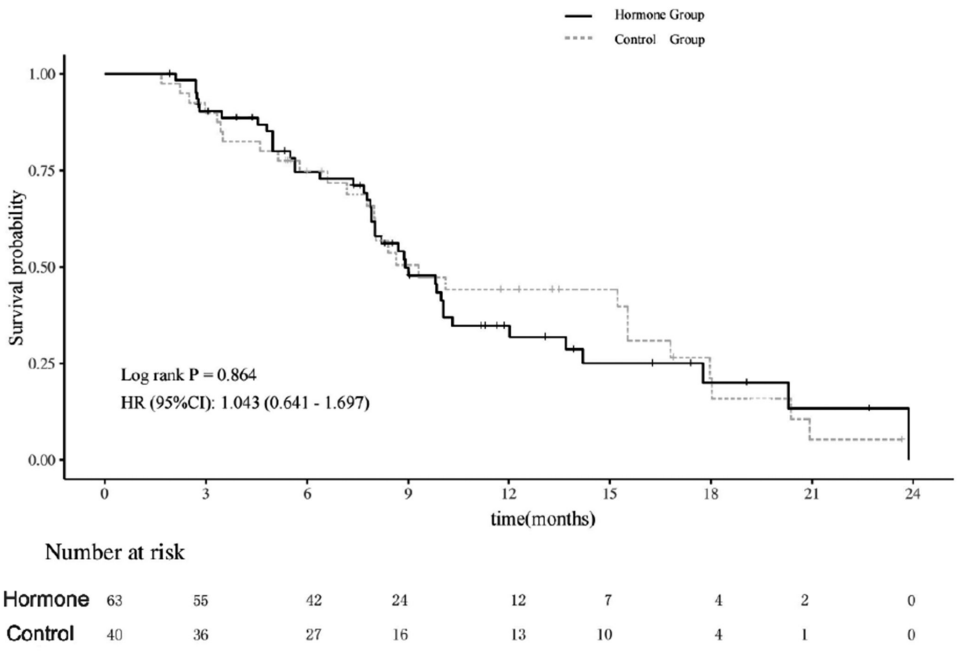

Figure 2. Survival analysis curve for all patients. CI, confidence interval; HR, hazard ratio.

group (Table SII), consistent with the pharmacological actions of glucocorticoids (7). Nausea/vomiting is a common adverse reaction to chemotherapy and glucocorticoids can alleviate vomiting symptoms by inhibiting neurotransmitter release and regulating gastrointestinal function (16). In patients treated with etoposide plus platinum and all patients, the hormone group had a significantly lower incidence of constipation. Glucocorticoids can improve intestinal motility, promote water absorption in the intestines and make stools softer and easier to pass (17). In patients treated with etoposide plus platinum combined with ICIs and all patients, the hormone group had a significantly lower incidence of leukopenia. Glucocorticoids may regulate the immune system and hematopoietic function of the body, reducing the inhibitory effects of chemotherapy drugs on bone marrow hematopoietic cells and thereby lowering the risk of leukopenia (18). Moreover, in patients receiving etoposide plus platinum combined with ICIs, the hormone group had significantly less renal dysfunction, suggesting a potential kidney-protective effect of prophylactic dexamethasone in this chemo-immunotherapy subset (19).

Glucocorticoids can reduce renal tubular injury, inflammation and improve renal microcirculation caused by chemotherapy drugs, thus reducing the risk of renal dysfunction (20), which is of significant clinical importance for patients with ES-SCLC receiving chemotherapy. Renal dysfunction not only affects the quality of life of patients but may also limit the dosage and course of subsequent chemotherapy drugs (21). Although this renal benefit is intriguing, it was observed exclusively in the chemo-immunotherapy subgroup and needs prospective validation. Notably, all analyses adhered to the intention-to-treat principle, rescue dexamethasone was administered only after documented nausea/vomiting or other breakthrough toxicities and therefore could not bias the primary endpoint assessment (incidence of nausea/vomiting). Nevertheless, such rescue therapy constitutes a potential confounder in survival analyses. To address this, both univariate and multivariate Cox regression analyses were performed after excluding patients who received any systemic glucocorticoid. The results remained consistent, showing that prophylactic versus no prophylactic dexamethasone did not significantly affect overall survival either before or after this exclusion (Table SI).

Concerns have been raised that sustained systemic glucocorticoids (≥10 mg prednisone-equivalent daily) can attenuate the efficacy of immune-checkpoint inhibitors (22). In the present cohort study, however, short-term chemotherapy-linked dexamethasone (4.5 mg orally for 3 days) did not adversely affect ORR, DCR or OS in patients receiving ICIs. These findings align with prospective data showing that brief steroid pulses for anti-emesis do not significantly diminish efficacy of ICIs (23). Until further randomized evidence is available, the lowest effective dose and shortest feasible duration of dexamethasone should be preferred.

However, in terms of hypertension, the hormone group showed a higher incidence compared with the control group, although the difference was not statistically significant. This trend suggests that prophylactic glucocorticoid use may increase the risk of hypertension, possibly related to the physiological effects of glucocorticoids in promoting sodium and water retention (24). However, due to limitations such as sample size, no significant difference was observed. For patients with a history of hypertension or other cardiovascular risk factors, it is recommended to closely monitor blood pressure changes during treatment and take appropriate measures to avoid potential adverse effects, such as administering antihypertensive therapy if necessary. Additionally, glucocorticoids can lead to increased blood glucose levels by promoting gluconeogenesis and reducing peripheral tissue glucose uptake (25). Although there was no direct data supporting this in the present study, based on previous research (26,27), long-term or high-dose use of glucocorticoids may increase the risk of hyperglycemia. In the present study, glucocorticoids were used prophylactically for a short term, therefore no hyperglycemia events were observed. However, based on previous research results, patients with diabetes or abnormal glucose regulation should have their blood glucose monitored during treatment, and any abnormalities should be promptly addressed. Regarding other adverse reactions, such as anemia, thrombocytopenia, hypoalbuminemia, AST elevation, ALT elevation and electrolyte disturbances, no significant differences were observed between the two groups. It should be noted that, although subgroup analyzes were attempted, the limited sample size rendered most of these subgroups underpowered. Residual confounding cannot be fully excluded and needs to be validated in larger-scale or pooled datasets. In conclusion, prophylactic glucocorticoid use has certain benefits for patients with ES-SCLC on platinum-based doublet therapy. It can alleviate nausea and vomiting, reduce the risk of leukopenia, and decrease the incidence of constipation, thereby improving patients' treatment experience and boosting adherence. The present study found no significant adverse events linked to prophylactic glucocorticoid use. Additionally, no significant differences in ORR, DCR, or median survival were observed between the two groups, indicating that prophylactic glucocorticoid use does not affect treatment efficacy. In clinical practice, recognizing the dual-edged nature of glucocorticoids and using them appropriately can optimize treatment and enhance patients' quality of life.

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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

WQ and YX designed the study. WQ, WD and ZY were responsible for data collection and statistical analysis. WQ wrote and plotted the manuscript. YX reviewed and revised the manuscript and provided funding support. WQ and YX 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 present study was approved (approval no. PJ 2025-04-98) by the Ethics Committee of the First Affiliated Hospital of Anhui Medical University. As a retrospective study with no additional risks to patients' treatment or personal information, it was granted an informed consent exemption.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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