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Sustained myeloprotection and economic impact of trilaciclib during first-line chemotherapy for extensive-stage small-cell lung cancer: a propensity score-matched real-world cohort study

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Research Article

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Abstract

Background

Chemotherapy-induced hematologic toxicity remains a challenge in extensive-stage small-cell lung cancer (ES-SCLC). We evaluated associations between trilaciclib use, hematologic toxicity, cumulative toxicity burden, and supportive care drug-cost offsets.

Methods

This retrospective study compared first-line platinum–etoposide chemotherapy with or without trilaciclib. Propensity score matching targeted a 1:2 ratio. Matched-set regression, generalized estimating equations, and count and recurrence models assessed patient-level, longitudinal, and cumulative outcomes. Sensitivity analyses assessed residual confounding. Growth factor drug-cost offsets were explored.

Results

Among 461 screened patients, 135 matched patients (49 trilaciclib, 86 controls) were included. Trilaciclib use was associated with lower grade 3–4 hematologic toxicity (16.3% vs 52.3%; OR, 0.20; P < 0.001), neutropenia (16.3% vs 48.8%; OR, 0.23; P < 0.001), and granulocyte colony-stimulating factor utilization (55.1% vs 82.6%; OR, 0.32; P = 0.003). Cycle-adjusted analyses supported these associations; no significant treatment-by-cycle interactions were detected. Cumulative toxicity burden was lower with trilaciclib (median affected cycles per patient, 0 vs 1; P = 0.003), with fewer recurrent grade 3–4 toxicity events (4.1% vs 20.9%; P = 0.029). Under a four-cycle daily whole-vial costing scenario, estimated trilaciclib costs were RMB 11,184 per patient, with growth factor drug-cost offsets of RMB 380 (95% bootstrap CI, − 147 to 911). Sensitivity analyses yielded directionally consistent estimates.

Conclusions

Trilaciclib use was associated with lower severe hematologic toxicity, cumulative toxicity burden, and supportive care requirements. Estimated growth factor drug-cost offsets covered only a small proportion of acquisition costs. Comprehensive economic evaluations incorporating broader clinical benefits are warranted.

Introduction

Extensive-stage small-cell lung cancer (ES-SCLC) is an aggressive malignancy characterized by rapid progression, early metastatic dissemination, and poor long-term survival. Small-cell lung cancer accounts for approximately 13%–15% of lung cancers, and the majority of patients present with

extensive-stage disease at diagnosis(Rudinet al. 2021). Despite recent advances with immune checkpoint inhibitors (ICIs) combined with platinum–etoposide chemotherapy, outcomes remain unsatisfactory, and cytotoxic chemotherapy continues to represent a fundamental component of first-line treatment(Hornet al. 2018,Paz-Areset al. 2022). Chemotherapy-induced myelosuppression (CIM), including severe neutropenia, anemia, and thrombocytopenia, remains a clinically important toxicity that may increase infection risk, require supportive interventions, and result in chemotherapy delays or dose modifications(Adamoet al. 2022,Kudereret al. 2022). Therefore, strategies that preserve hematopoietic function while maintaining chemotherapy intensity are clinically meaningful.

Trilaciclib is a first-in-class intravenous cyclin-dependent kinase 4/6 inhibitor developed to prevent CIM(Dhillon 2021,Heet al. 2017). By inducing transient and reversible G1-phase arrest in hematopoietic stem and progenitor cells, trilaciclib protects bone marrow progenitors from chemotherapy-induced injury(Dhillon 2021,Heet al. 2017). Randomized clinical trials have demonstrated that administration of trilaciclib before chemotherapy reduces severe neutropenia and improves multiple hematologic outcomes in patients with ES-SCLC(Chenget al. 2024,Weisset al. 2019). Pooled analyses of randomized studies further supported its multilineage myeloprotective effects involving neutrophils, erythroid cells, and lymphocytes(Liuet al. 2024).

However, evidence generated from randomized trials may not fully represent routine clinical practice, where patients are more heterogeneous and treatment patterns may differ from clinical trial settings. Real-world studies evaluating trilaciclib in ES-SCLC have emerged; however, available studies have primarily focused on short-term hematologic outcomes and safety. A Chinese real-world study reported reduced CIM among patients receiving trilaciclib, but its single-arm design and limited sample size restricted comparative assessment(Chenet al. 2024). Another retrospective study suggested potential benefits of trilaciclib in patients receiving first-line chemoimmunotherapy, including reduced hematologic toxicity and supportive care requirements(Goldschmidtet al. 2023); however, comprehensive evaluation of longitudinal protection patterns and cumulative toxicity burden remains limited.

Although reduced myelosuppression may decrease supportive care use, the extent to which growth factor drug-cost reductions offset trilaciclib acquisition costs in routine practice is uncertain(Fanget al. 2025). Particularly in healthcare systems where drug acquisition costs and supportive care expenditures must be balanced, whether reductions in supportive care utilization can meaningfully offset trilaciclib-associated costs remains an important clinical and health economic question.

We therefore evaluated (1) severe hematologic toxicity and supportive care utilization, (2) longitudinal and cumulative toxicity burden during evaluable chemotherapy cycles, and (3) exploratory, scenario-based growth factor–related drug-cost offsets among patients with ES-SCLC receiving first-line platinum–etoposide chemotherapy.

Methods

Study design and patient selection

This retrospective real-world cohort study included consecutive patients with ES-SCLC who received first-line platinum–etoposide chemotherapy at Chongqing University Cancer Hospital between January 2023 and June 2026. The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Chongqing University Cancer Hospital (CZLS2026083-A). The requirement for informed consent was waived because of the retrospective design and the use of de-identified clinical data.

Eligible patients were required to have histologically confirmed ES-SCLC, receive platinum–etoposide as first-line systemic treatment, and complete at least three evaluable chemotherapy cycles. Patients were excluded if they received radiotherapy or surgery during the evaluated period, received prophylactic hematopoietic growth factor support before documented chemotherapy-induced hematologic toxicity in the first cycle, had incomplete baseline clinical or laboratory data, or had incomplete trilaciclib exposure. Patients were classified into the trilaciclib group if trilaciclib was administered before chemotherapy in all evaluable cycles; those without trilaciclib exposure were assigned to the control group. Cycle-specific denominators and recorded cycle counts are provided in Supplementary Tables S1–S2 and Supplementary Figure S1.

Data collection

Baseline demographic, clinical, disease-related, treatment-related, and laboratory characteristics were retrospectively collected. Demographic variables included age, sex, smoking history, and body mass index. Clinical characteristics included Eastern Cooperative Oncology Group performance status (ECOG PS) and modified Charlson Comorbidity Index (CCI). Disease-related characteristics included metastatic sites: brain, liver, bone, lung, distant lymph nodes and pleural effusion. Treatment-related variables included platinum regimen (carboplatin or cisplatin) and concomitant immunotherapy. Baseline laboratory parameters obtained before the first cycle included white blood cell count, absolute neutrophil count (ANC), hemoglobin, platelet count, and serum albumin. Patients with missing key data required for primary analyses were excluded; no imputation was performed, and all analyses were based on complete-case data.

Propensity score matching

To reduce confounding from non-randomized treatment assignment, propensity score matching (PSM) was performed using logistic regression including prespecified baseline variables: age, sex, ECOG PS, modified CCI, baseline ANC, hemoglobin, albumin, and platinum regimen. Nearest-neighbor matching without replacement targeted up to two control patients per trilaciclib-treated patient, with a caliper width of 0.2; consequently, not every treated patient necessarily had two matched controls. Balance of propensity-score model covariates was assessed using absolute standardized mean differences

(SMDs), with values < 0.1 considered indicative of adequate balance. Patient-level binary outcomes were compared using conditional logistic regression stratified by matched set.

Assessment of hematologic toxicity and supportive care

Hematologic toxicities were graded according to CTCAE version 5.0. The primary endpoint was the patient-level occurrence of at least one grade 3–4 hematologic toxicity during evaluable chemotherapy cycles. Secondary endpoints included grade 3–4 neutropenia, thrombocytopenia, anemia, febrile neutropenia, and use of myelosuppression-related supportive care (short-acting G-CSF, PEG-G-CSF, erythropoiesis-stimulating agents, thrombopoietin or thrombopoietin receptor agonists, and blood transfusions). Cycle-level toxicity and G-CSF use were recorded separately for each evaluable chemotherapy cycle. Cumulative toxicity burden was summarized as the number of cycles with grade 3–4 hematologic toxicity per patient; recurrent toxicity was defined as toxicity in at least two evaluable cycles, and toxicity-free cycles as evaluable cycles without grade 3–4 hematologic toxicity. Rare outcomes were summarized descriptively when matched-set effect estimates were not reliably estimable (Supplementary Table S3). Cycle-specific descriptive counts are provided in Supplementary Table S4.

Partial cost-offset analysis

An exploratory partial drug-cost offset analysis compared between-group mean cumulative short-acting G-CSF injection counts and PEG-G-CSF–flagged chemotherapy cycles per patient in the matched cohort. Each PEG-G-CSF–flagged cycle was assumed to correspond to one administration. Institutional unit prices were RMB 273.83 per short-acting G-CSF injection and RMB 1,255 per PEG-G-CSF administration. Assumptions and unit prices are documented in Supplementary Table S6.

Trilaciclib acquisition cost was estimated for an assumed representative body surface area of 1.65 m^2 at 240 mg/m^2/day on three consecutive days per cycle. At 396 mg/day, assuming independently prepared daily doses, whole-vial charging without reuse across days, 300-mg vials, and RMB 466 per vial, two vials per day (six per cycle) were required, corresponding to RMB 11,184 over four cycles. Cost-offset sensitivity analyses considered patients with four evaluable cycles, complete four-cycle matched sets, and per-cycle standardization (Supplementary Table S5). Uncertainty was assessed using 5,000 matched-set bootstrap resamples with random seed 20261011 (Supplementary Table S6 and Supplementary Figure S2).

Statistical analysis

Continuous variables were summarized as medians (interquartile ranges), and categorical variables as frequencies (percentages). Patient-level binary outcomes in the PSM cohort were analyzed using conditional logistic regression stratified by matched set, with odds ratios (ORs), 95% confidence intervals

(CIs), and two-sided *P* values reported. For sparse or zero-event outcomes, non-estimable (NE) effect estimates were not interpreted as evidence of equivalent event risks; corresponding event counts are provided in Supplementary Table S3.

Longitudinal grade 3–4 hematologic toxicity, grade 3–4 neutropenia, and G-CSF utilization were analyzed using logistic generalized estimating equations (GEE), with chemotherapy cycle as a categorical covariate, patient-level clustering, an exchangeable working correlation structure, and robust standard errors. Treatment-by-cycle interactions were assessed in separate models, and sensitivity analyses were restricted to the first three cycles. Additional matched-set conditional logistic models adjusted for immunotherapy use to assess residual confounding. Evaluable denominators were reported separately for each cycle (Supplementary Table S1). Nonsignificant treatment-by-cycle interactions were not interpreted as proof of equal treatment effects across cycles.

Cumulative grade 3–4 hematologic toxicity events across evaluable cycles were analyzed using negative binomial regression with an offset for the number of evaluable cycles and cluster-robust standard errors at the matched-set level. Recurrent severe hematologic toxicity, defined as grade 3–4 toxicity occurring in at least two cycles, was assessed using matched-set conditional logistic regression. Toxicity-free cycle proportions were summarized descriptively and evaluated using cycle-adjusted logistic GEE models.

Secondary analyses were exploratory without adjustment for multiple comparisons. Cost uncertainty was quantified using matched-set bootstrap resampling; cost comparisons were descriptive and scenario-based. All tests were two-sided, with $P < 0.05$ considered statistically significant. Analyses were performed using R version 4.4.1 and Python.

Results

Study cohort and baseline characteristics

A total of 461 patients with ES-SCLC who received first-line platinum–etoposide chemotherapy were screened. After applying the predefined eligibility criteria, 169 patients were included in the analysis cohort, comprising 52 patients in the trilaciclib group and 117 patients in the control group (Fig. 1). Following PSM, 49 patients in the trilaciclib group and 86 patients in the control group were included in the final comparative cohort. The distribution of propensity scores demonstrated substantial overlap between groups after matching, and the propensity-score model covariates showed improved balance after matching, with absolute SMDs below 0.1 (Fig. 2). Baseline characteristics of the matched cohort are presented in Table 1. Most baseline characteristics were generally comparable between groups, although immunotherapy use remained more frequent in the trilaciclib group than in the control group (79.6% vs. 60.5%). This residual imbalance was addressed in subsequent sensitivity analyses. The numbers of evaluable patients were 49 versus 86 in cycles 1–3 and 44 versus 86 in cycle 4 (trilaciclib

versus control), contributing 191 and 344 evaluable patient-cycles, respectively (Supplementary Table S1; Supplementary Figure S1).

Table 1
Baseline characteristics after PSM.

Characteristic	Trilaciclib (n = 49)	Control (n = 86)
Demographic characteristics		
Age, years	65.0 (58.0–71.0)	66.0 (59.2–71.8)
Age ≥ 65 years, n (%)	25 (51.0)	47 (54.7)
Male sex, n (%)	41 (83.7)	73 (84.9)
Smoking history, n (%)	47 (95.9)	85 (98.8)
Body mass index, kg/m²	22.5 (20.8–24.3)	23.1 (21.5–25.5)
Clinical characteristics		
ECOG performance status, n (%)		
0	7 (14.3)	8 (9.3)
1	38 (77.6)	72 (83.7)
2	4 (8.2)	6 (7.0)
Modified Charlson Comorbidity Index, score	1.0 (0.0–1.0)	1.0 (0.0–1.0)
Treatment characteristics		
Platinum regimen, n (%)		
Carboplatin	25 (51.0)	40 (46.5)
Cisplatin	24 (49.0)	46 (53.5)
Immunotherapy use, n (%)	39 (79.6)	52 (60.5)
Baseline laboratory parameters		
Absolute neutrophil count, ×10⁹/L	4.6 (3.3–5.8)	4.5 (3.5–5.8)
Hemoglobin, g/L	130.0 (123.0–144.0)	134.0 (124.2–142.8)
Platelet count, ×10⁹/L	259.0 (201.0–336.0)	241.5 (201.0–302.0)
Albumin, g/L	42.3 (39.2–43.9)	41.0 (38.8–44.9)
Disease characteristics		
Brain metastasis, n (%)	12 (24.5)	13 (15.1)
Liver metastasis, n (%)	14 (28.6)	19 (22.1)

Data are presented as median (interquartile range) for continuous variables and number (%) for categorical variables. ECOG, Eastern Cooperative Oncology Group.

Characteristic	Trilaciclib (n = 49)	Control (n = 86)
Bone metastasis, n (%)	12 (24.5)	21 (24.4)
Lung metastasis, n (%)	22 (44.9%)	27 (31.4%)
Lymph node metastasis, n (%)	45 (91.8%)	71 (82.6%)
Pleural effusion, n (%)	9 (18.4%)	13 (15.1%)

Data are presented as median (interquartile range) for continuous variables and number (%) for categorical variables. ECOG, Eastern Cooperative Oncology Group.

Trilaciclib reduced chemotherapy-induced hematologic toxicity and G-CSF utilization

After PSM, grade 3–4 hematologic toxicity occurred in 16.3% (8/49) of patients in the trilaciclib group compared with 52.3% (45/86) in the control group. Trilaciclib treatment was associated with significantly lower odds of grade 3–4 hematologic toxicity (OR, 0.20; 95% CI, 0.079–0.484; $P < 0.001$) (Table 2; Fig. 3). Among specific hematologic toxicities, grade 3–4 neutropenia showed a similar pattern, occurring in 16.3% of patients receiving trilaciclib compared with 48.8% of controls (OR, 0.23; 95% CI, 0.100–0.553; $P < 0.001$). Grade 3–4 thrombocytopenia, anemia, and febrile neutropenia were uncommon in both groups, with insufficient events to support reliable matched effect estimation for some endpoints (Supplementary Table S3).

Table 2
Hematologic toxicity, supportive care utilization, and treatment modifications in the matched cohort.

Outcome	Control	Trilaciclib	OR	CI95%	P value
Any grade 3–4 hematologic toxicity	45/86 (52.3%)	8/49 (16.3%)	0.20	0.079–0.484	0.0004
Grade 3–4 neutropenia	42/86 (48.8%)	8/49 (16.3%)	0.23	0.100-0.553	0.0009
Grade 3–4 thrombocytopenia	8/86 (9.3%)	3/49 (6.1%)	0.68	0.170–2.712	0.746
Grade 3–4 anemia	1/86 (1.2%)	0/49 (0%)	NE	NE	NE
Febrile neutropenia	4/86 (4.7%)	0/49 (0%)	NE	NE	NE
G-CSF use	71/86 (82.6%)	27/49 (55.1%)	0.32	0.148–0.683	0.0033
PEG-G-CSF secondary prophylaxis	23/86 (26.7%)	9/49 (18.4%)	0.61	0.269–1.386	0.3
Anemia-related supportive treatment	21/86 (24.4%)	12/49 (24.5%)	1.01	0.402–2.426	1
Thrombocytopenia-related supportive treatment	14/86 (16.3%)	9/49 (18.4%)	1.16	0.403–3.171	0.814
Dose reduction	17/86 (19.8%)	11/49 (22.4%)	1.17	0.503–2.739	0.8257
Chemotherapy delay	5/86 (5.8%)	7/49 (14.3%)	3.53	0.876–14.091	0.1199
Myelosuppression-related hospitalization	4/86 (4.7%)	1/49 (2%)	0.37	0.039–3.352	0.653

Data are presented as number (%). ORs were estimated for trilaciclib versus control using conditional logistic regression accounting for matched sets. G-CSF, granulocyte colony-stimulating factor; PEG-G-CSF, pegylated granulocyte colony-stimulating factor. Anemia-related supportive treatment included erythropoiesis-stimulating agents and red blood cell transfusion. Thrombocytopenia-related supportive treatment included thrombopoietin, thrombopoietin receptor agonists, and platelet transfusion. NE denotes not reliably estimable because of sparse or zero events; no finite OR or Wald interval is presented for these endpoints.

Trilaciclib use was also associated with reduced G-CSF utilization. The proportion of patients requiring G-CSF support was significantly lower in the trilaciclib group than in the control group (55.1% vs 82.6%; OR, 0.32; 95% CI, 0.148–0.683; $P = 0.0033$). PEG-G-CSF secondary prophylaxis was numerically less frequent in the trilaciclib group (18.4% vs 26.7%), although the difference did not reach statistical significance (OR, 0.61; 95% CI, 0.269–1.386; $P = 0.300$). No significant differences were observed between groups in anemia-related supportive treatment, Thrombocytopenia-related supportive treatment, chemotherapy dose reduction, chemotherapy delay, or myelosuppression-related hospitalization (Table 2).

Sustained hematologic protection across chemotherapy cycles

Cycle-specific analyses included 49 trilaciclib-treated patients and 86 controls in each of cycles 1–3, and 44 and 86, respectively, in cycle 4 (Supplementary Table S1; Supplementary Figure S1). In cycle-adjusted GEE models, trilaciclib was associated with lower grade 3–4 hematologic toxicity (OR, 0.207; 95% CI, 0.094–0.455; *P* < 0.001), grade 3–4 neutropenia (OR, 0.194; 95% CI, 0.093–0.404; P < 0.001), and G-CSF utilization (OR, 0.434; 95% CI, 0.257–0.733; *P* = 0.002). No statistically significant treatment-by-cycle interactions were detected (*P* = 0.294, 0.349, and 0.622, respectively. Descriptive cycle-specific outcomes are presented in Supplementary Table S4.

To assess the potential influence of reduced patient numbers in cycle 4, sensitivity analyses restricted to cycles 1–3 yielded consistent results for grade 3–4 hematologic toxicity (OR, 0.178; 95% CI, 0.079–0.399), grade 3–4 neutropenia (OR, 0.214; 95% CI, 0.096–0.481), and G-CSF use (OR, 0.439; 95% CI, 0.252–0.765). Sensitivity analyses addressing residual confounding showed consistent results after adjustment for immunotherapy use: grade 3–4 hematologic toxicity (adjusted OR, 0.198; 95% CI, 0.079–0.492; *P* < 0.001), grade 3–4 neutropenia (adjusted OR, 0.223; 95% CI, 0.092–0.543; *P* < 0.001), and G-CSF use (adjusted OR, 0.311; 95% CI, 0.141–0.686; *P* = 0.0038).

Reduction of cumulative hematologic toxicity burden across chemotherapy cycles

Across evaluable cycles, the median number of grade 3–4 hematologic toxicity events per patient was 0 (IQR, 0–0) with trilaciclib versus 1 (IQR, 0–1) in controls (Fig. 5A). In a negative binomial model accounting for evaluable cycles and matched-set clustering, the incidence rate ratio was 0.291 (95% CI, 0.130–0.652; *P* = 0.003). Recurrent grade 3–4 hematologic toxicity in at least two cycles occurred in 4.1% versus 20.9% of patients (matched-set conditional logistic regression OR, 0.192; 95% CI, 0.044–0.845; *P* = 0.029; Fig. 5B). In addition, trilaciclib-treated patients had a higher proportion of toxicity-free chemotherapy cycles compared with controls (94.8% vs 79.9%; (cycle-adjusted GEE, *P* < 0.001) (Fig. 5C).

Partial cost-offset analysis of trilaciclib-associated G-CSF utilization reduction

Following PSM, mean cumulative short-acting G-CSF injections were 1.94 with trilaciclib versus 2.83 in controls (Fig. 6A). PEG-G-CSF secondary prophylaxis was recorded for 9/49 (18.4%) versus 23/86 (26.7%) patients (Fig. 6B); cost estimation instead used mean cumulative PEG-G-CSF–flagged cycles per patient (0.367 versus 0.477).

Using institutional unit prices and the assumption of one PEG-G-CSF administration per flagged cycle, estimated short-acting G-CSF and PEG-G-CSF drug-cost offsets were approximately RMB 243 and RMB 137 per patient, respectively, totaling RMB 380.13. The 95% matched-set bootstrap CI was − 146.89 to 910.70 RMB. Estimates were RMB 317.20 among patients with four evaluable cycles and RMB 301.54 in

complete four-cycle matched sets; the estimated per-cycle difference was RMB 88.54 (Supplementary Table S5; Supplementary Figure S2).

Under the assumed four-cycle daily whole-vial charging scenario, estimated trilaciclib acquisition cost was RMB 11,184 per patient. Growth factor–related offsets represented approximately 3.4% of this amount, corresponding to a scenario-based net incremental drug cost of approximately RMB 10,804 per patient (Fig. 6C; Supplementary Table S6).

Discussion

In this retrospective real-world cohort study of patients with ES-SCLC receiving first-line platinum–etoposide chemotherapy, trilaciclib was associated with a substantial reduction in grade 3–4 hematologic toxicity after PSM, primarily driven by reduced severe neutropenia. Importantly, longitudinal analyses demonstrated that this protective effect was maintained across the first four chemotherapy cycles, with a lower cumulative hematologic toxicity burden. However, reductions in growth factor-related supportive care costs offset only a small proportion of trilaciclib acquisition costs, highlighting the need to further define its clinical and economic value in different healthcare settings.

The reduction in severe neutropenia observed in our study is consistent with randomized trials demonstrating the myeloprotective effects of trilaciclib in ES-SCLC(Chenget al. 2024,Weisset al. 2019). Trilaciclib protects hematopoietic stem and progenitor cells through transient and reversible G1-phase arrest, reducing chemotherapy-induced bone marrow injury(Dhillon 2021,Heet al. 2017). In our cohort, the most pronounced benefit was observed in the neutrophil lineage, whereas significant differences were not observed for anemia or thrombocytopenia. This pattern is consistent with previous evidence that neutropenia represents the predominant clinically relevant manifestation of CIM during platinum–etoposide treatment(Chenget al. 2024,Weisset al. 2019). The lack of significant differences in erythroid and platelet outcomes may be explained by the low incidence of grade 3–4 events, limited statistical power, different recovery kinetics among hematopoietic lineages, and the relatively short observation period.

Although trilaciclib reduced severe hematologic toxicity and G-CSF utilization, no significant differences were observed in febrile neutropenia, myelosuppression-related hospitalization, chemotherapy dose reduction, or treatment delay. These findings may differ from some randomized studies(Dinget al. 2025,Weisset al. 2021) because downstream complications were relatively uncommon in our cohort and may have been mitigated by contemporary supportive care practices. Routine blood count monitoring, timely initiation of G-CSF, and prompt management of hematologic abnormalities may reduce the incremental benefit of additional myeloprotection on severe clinical consequences. Therefore, in healthcare settings with established supportive care pathways, the primary value of trilaciclib may be reflected in reducing the occurrence and cumulative burden of hematologic toxicity rather than preventing all downstream complications.

Beyond conventional toxicity endpoints, our study provides additional insight into the temporal pattern of trilaciclib-associated myeloprotection. While previous studies mainly evaluated toxicity incidence within predefined treatment periods(Dinget al. 2025), our cycle-level analysis assessed whether the protective effect persisted during repeated chemotherapy exposure. No statistically significant treatment-by-cycle interactions were detected, although these tests do not establish identical effects across cycles. Furthermore, cumulative toxicity burden and recurrent toxicity analyses capture the overall hematologic impact of repeated chemotherapy exposure rather than isolated events, supporting the potential role of trilaciclib as a strategy for sustained myeloprotection during frontline treatment.

The interpretation of these findings should consider the evolving treatment landscape of ES-SCLC. During the study period, ICIs became incorporated into first-line therapy, and concomitant immunotherapy was more common among patients receiving trilaciclib. Although this reflects contemporary treatment evolution and represents a potential source of residual confounding, ICIs are not considered major contributors to acute CIM compared with platinum–etoposide chemotherapy(Yinet al. 2023). PSM was performed to balance major baseline characteristics; however, residual confounding cannot be completely excluded. Sensitivity analyses adjusting for immunotherapy use yielded effect estimates consistent with the primary matched analyses, although residual confounding cannot be excluded.

Previous economic evaluations have suggested that trilaciclib may provide favorable economic value by reducing the clinical and financial burden associated with CIM(Abrahamet al. 2022,Fanget al. 2025). However, these model-based analyses relied largely on clinical trial data and assumptions regarding healthcare utilization(Abrahamet al. 2022,Fanget al. 2025). In our real-world cohort, trilaciclib was associated with reduced G-CSF utilization, while assumption-based growth factor cost offsets represented a small proportion of estimated trilaciclib acquisition costs. In China, recent reductions in G-CSF acquisition prices may further reduce the potential cost offsets achievable through decreased growth factor utilization. These findings suggest that the value of trilaciclib may extend beyond direct supportive care savings and should be evaluated within a broader framework incorporating prevention of severe complications, quality of life, patient burden, preservation of chemotherapy intensity, and healthcare resource utilization. Importantly, trilaciclib should not be considered a substitute for routine hematologic monitoring or supportive care, as patients may still require surveillance and management of residual myelosuppression.

Several limitations should be acknowledged. First, the retrospective single-center design introduces potential selection bias and residual confounding despite PSM. Second, some outpatient laboratory results and supportive care interventions after discharge were unavailable; however, hematologic assessments and documented management strategies surrounding chemotherapy administration were consistently captured for both groups, allowing comparable evaluation of toxicity patterns. Third, differences related to treatment era and immunotherapy exposure could not be completely eliminated. Finally, this study focused on the first four chemotherapy cycles and was not designed to evaluate survival outcomes. Prospective multicenter studies with longer follow-up, comprehensive healthcare

utilization data, and formal cost-effectiveness analyses are needed to further clarify the clinical and economic role of trilaciclib in ES-SCLC. The partial economic analysis was restricted to growth factor–related drug costs and relied on institutional prices and original vial-use and PEG-G-CSF costing assumptions rather than complete patient-level dispensing and billing records; accordingly, the net incremental cost should not be interpreted as a comprehensive cost-effectiveness estimate.

Conclusions

In this PSM real-world cohort study, trilaciclib use was associated with lower severe hematologic toxicity and G-CSF utilization across evaluable cycles of first-line chemotherapy for ES-SCLC. Under the original costing assumptions, estimated growth factor–related offsets covered only a small fraction of estimated trilaciclib acquisition costs. Further research with comprehensive patient-level resource and billing data is required to determine its overall economic value.

Declarations

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Author contributions

Wen Chen, Yubingxue Liu, and Li Li contributed to material preparation, data collection, and analysis. Wen Chen, Yubingxue Liu, Li Li, and Tingxiu Xiang contributed to drafting the manuscript. Wen Chen prepared the figures. All authors commented on previous versions of the manuscript and read and approved the final manuscript.

Competing interest

The authors declare no competing interests.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Chongqing University Cancer Hospital (CZLS2026083-A). The requirement for informed consent was waived because of the retrospective design and the use of de-identified clinical data.

Data availability

Aggregate results supporting the analyses are reported in this article and Supplementary Tables S1–S6 and Supplementary Figures S1–S2. Individual-level clinical data are not publicly provided because of patient confidentiality and institutional governance. Requests for de-identified data may be considered by the corresponding author subject to applicable ethics, institutional approvals, and data-protection requirements.

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Figures

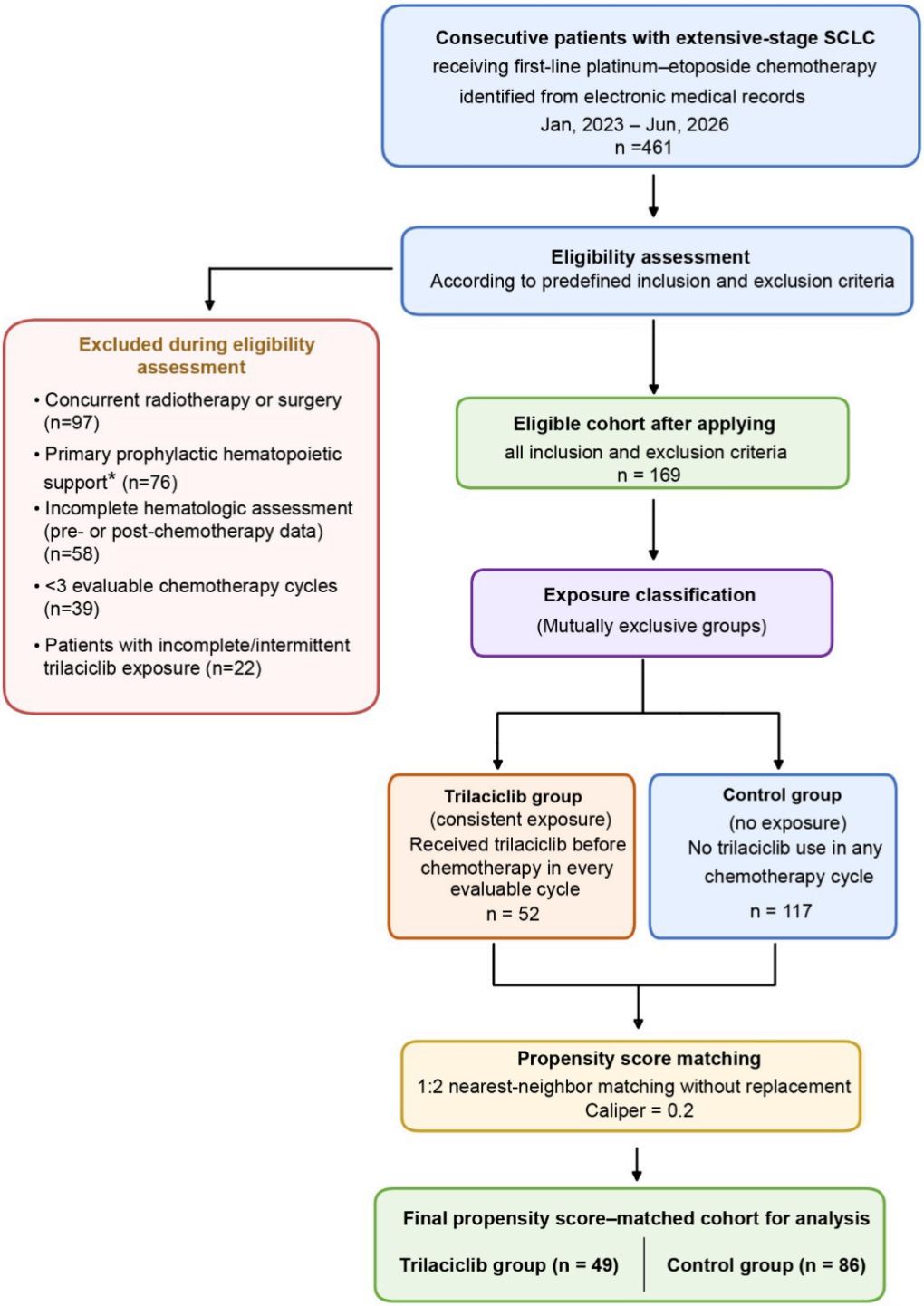


Figure 1

Study flow diagram of patient selection and PSM. *Primary prophylactic hematopoietic support was defined as hematopoietic growth factor administration before chemotherapy-induced hematologic toxicity during cycle 1.

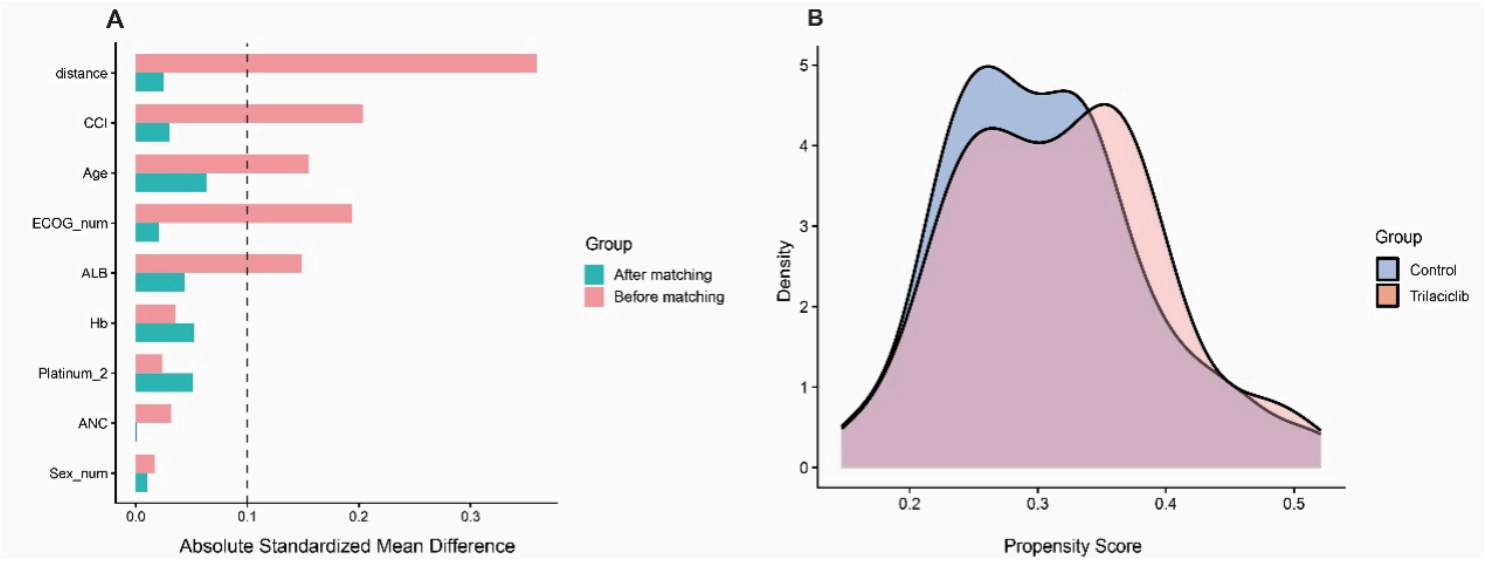


Figure 2

Assessment of covariate balance and propensity score distribution after PSM. (A) Absolute SMDs for covariates included in the propensity score model before and after matching. The dashed vertical line indicates the predefined threshold of SMD <0.1, suggesting adequate covariate balance. (B) Distribution of propensity scores in the trilaciclib and control groups after matching, demonstrating substantial overlap between groups.

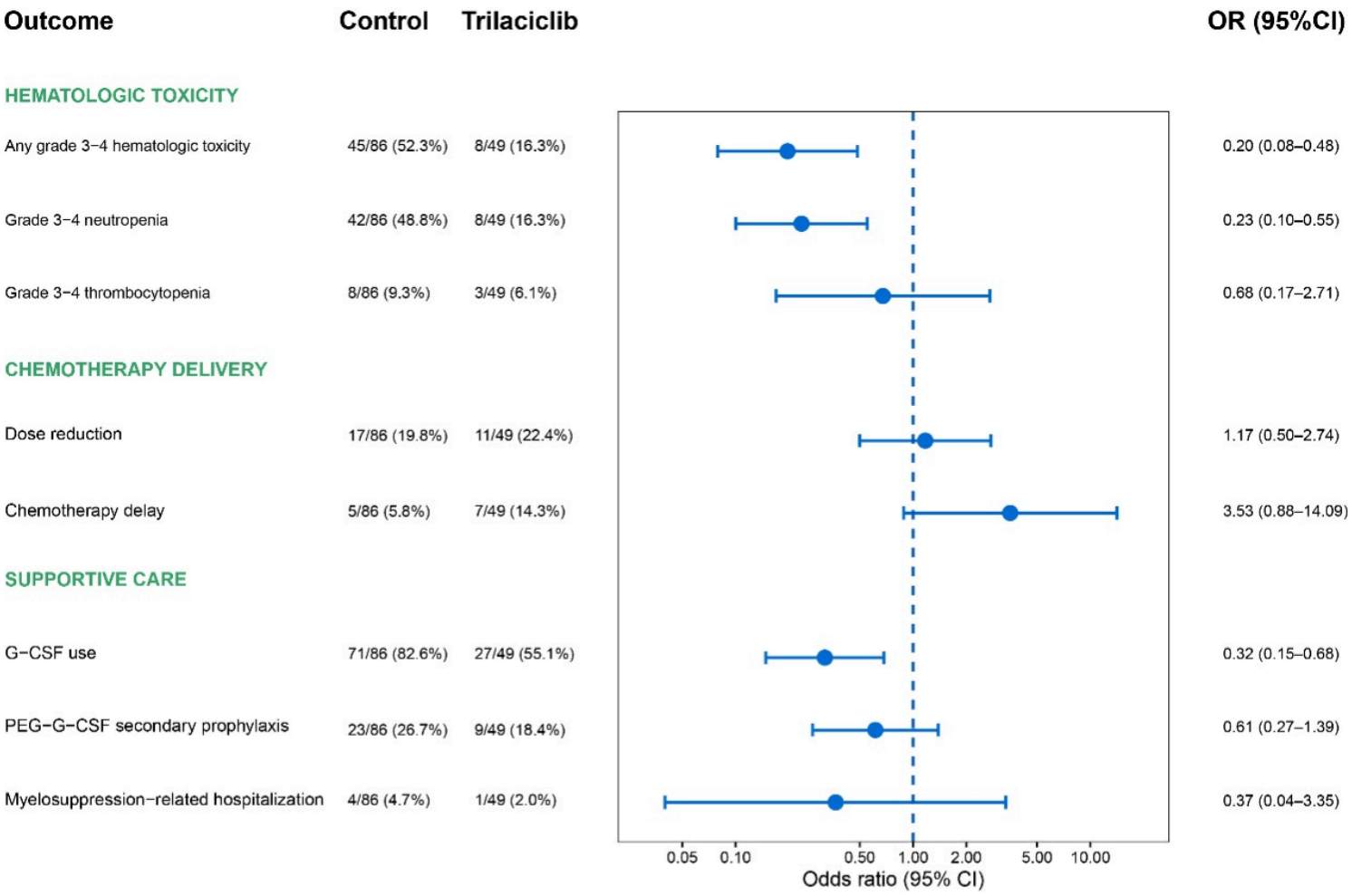


Figure 3

Forest plot of clinical outcomes associated with trilaciclib use after PSM. ORs and 95% CIs were estimated using conditional logistic regression accounting for matched sets. ORs <1 indicate lower odds of events in the trilaciclib group compared with controls.

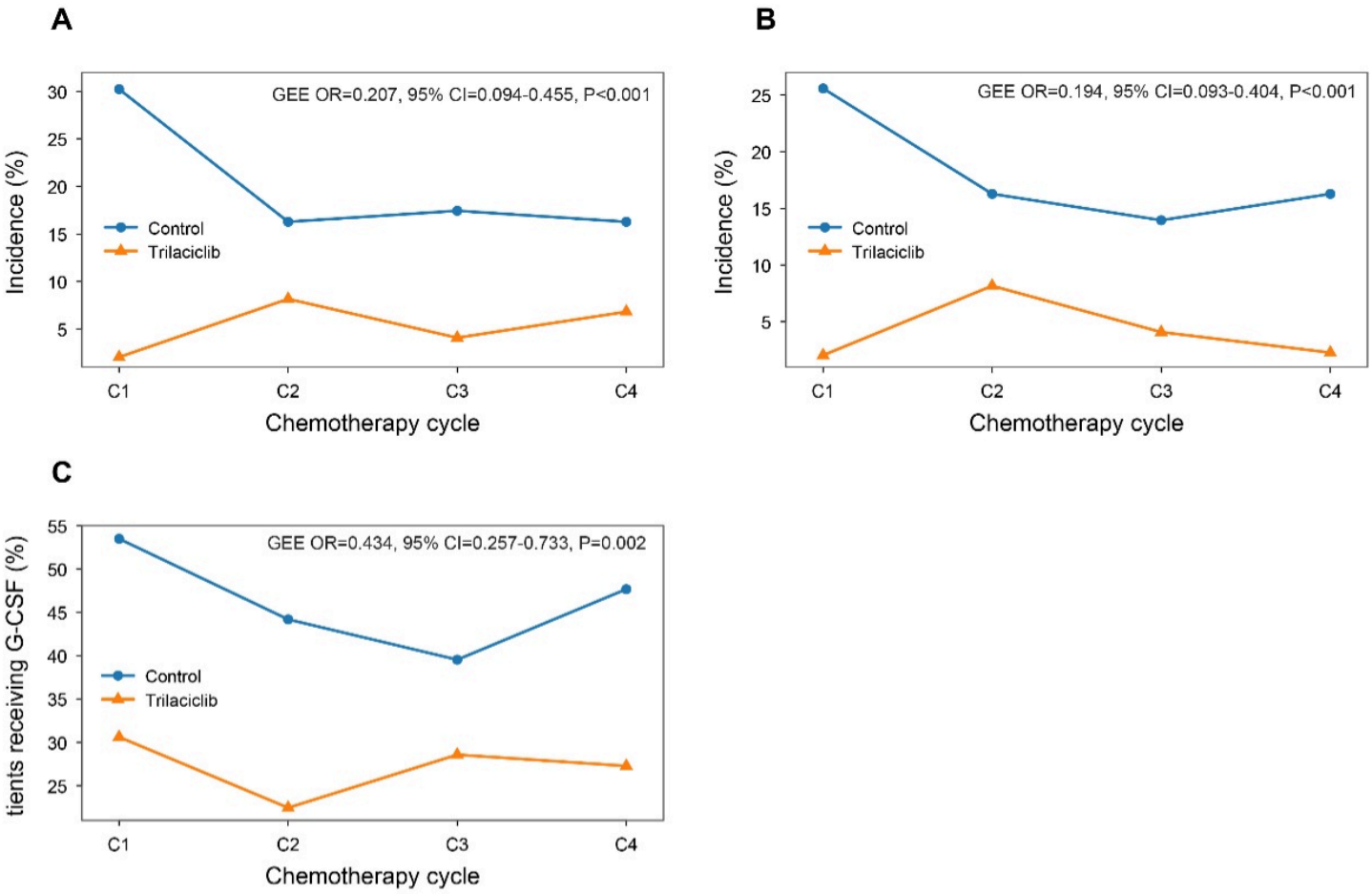


Figure 4

Longitudinal patterns of hematologic toxicity and supportive care utilization across chemotherapy cycles. (A) Grade 3–4 hematologic toxicity. (B) Grade 3–4 neutropenia. (C) G-CSF utilization. Reported ORs and 95% CIs are from cycle-adjusted logistic GEE main models with patient-level clustering and exchangeable working correlation; treatment-by-cycle interactions were evaluated separately.

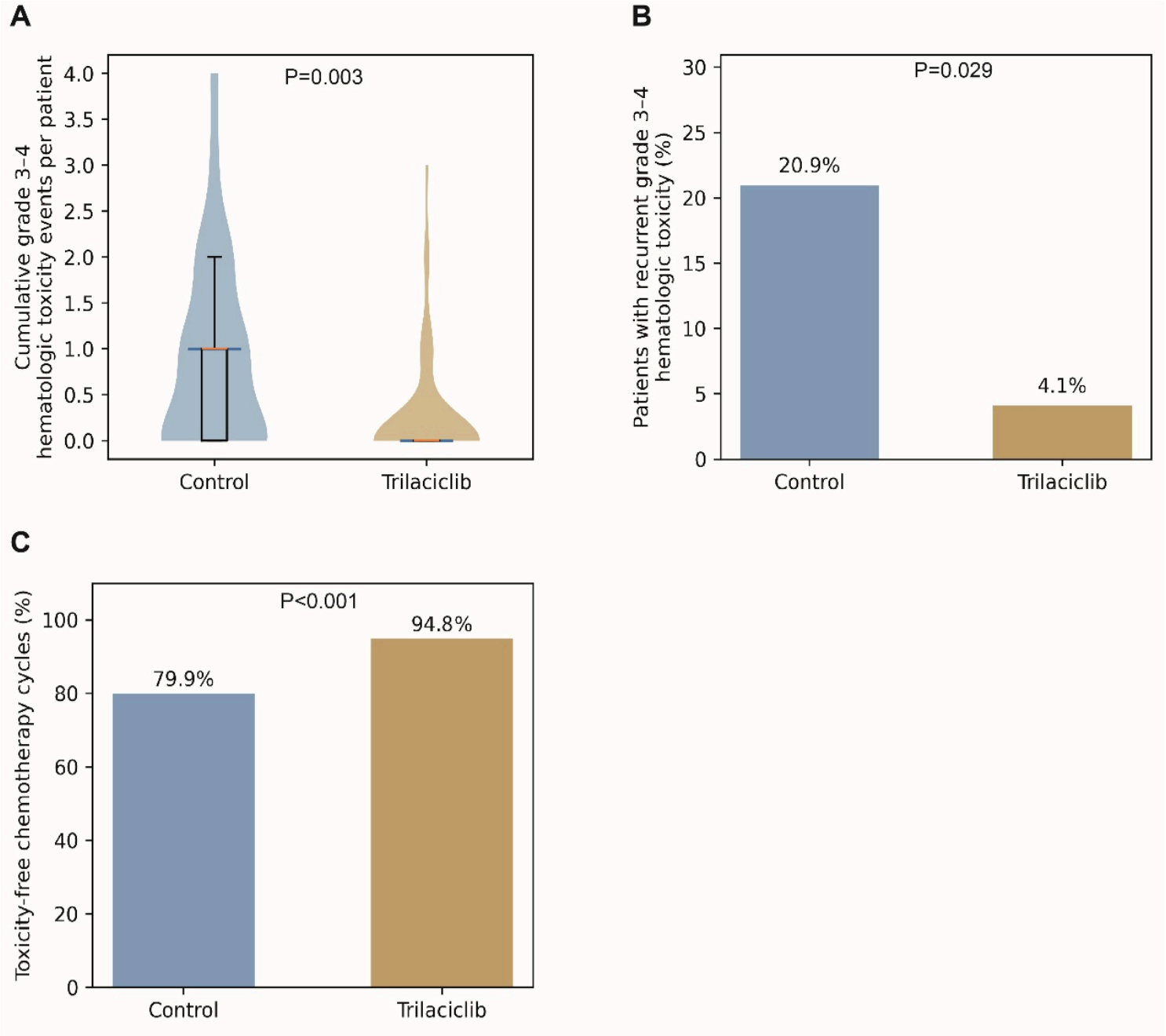


Figure 5

Cumulative hematologic toxicity burden during first-line chemotherapy. (A) Cumulative grade 3–4 hematologic toxicity events per patient; P value from negative binomial regression adjusted for evaluable cycles with matched-set cluster-robust standard errors. (B) Patients experiencing grade 3–4 hematologic toxicity in at least two cycles; *P*value from matched-set conditional logistic regression. (C) Proportion of evaluable chemotherapy cycles without grade 3–4 hematologic toxicity (trilaciclib, 181/191; control, 275/344); P value from cycle-adjusted logistic GEE.

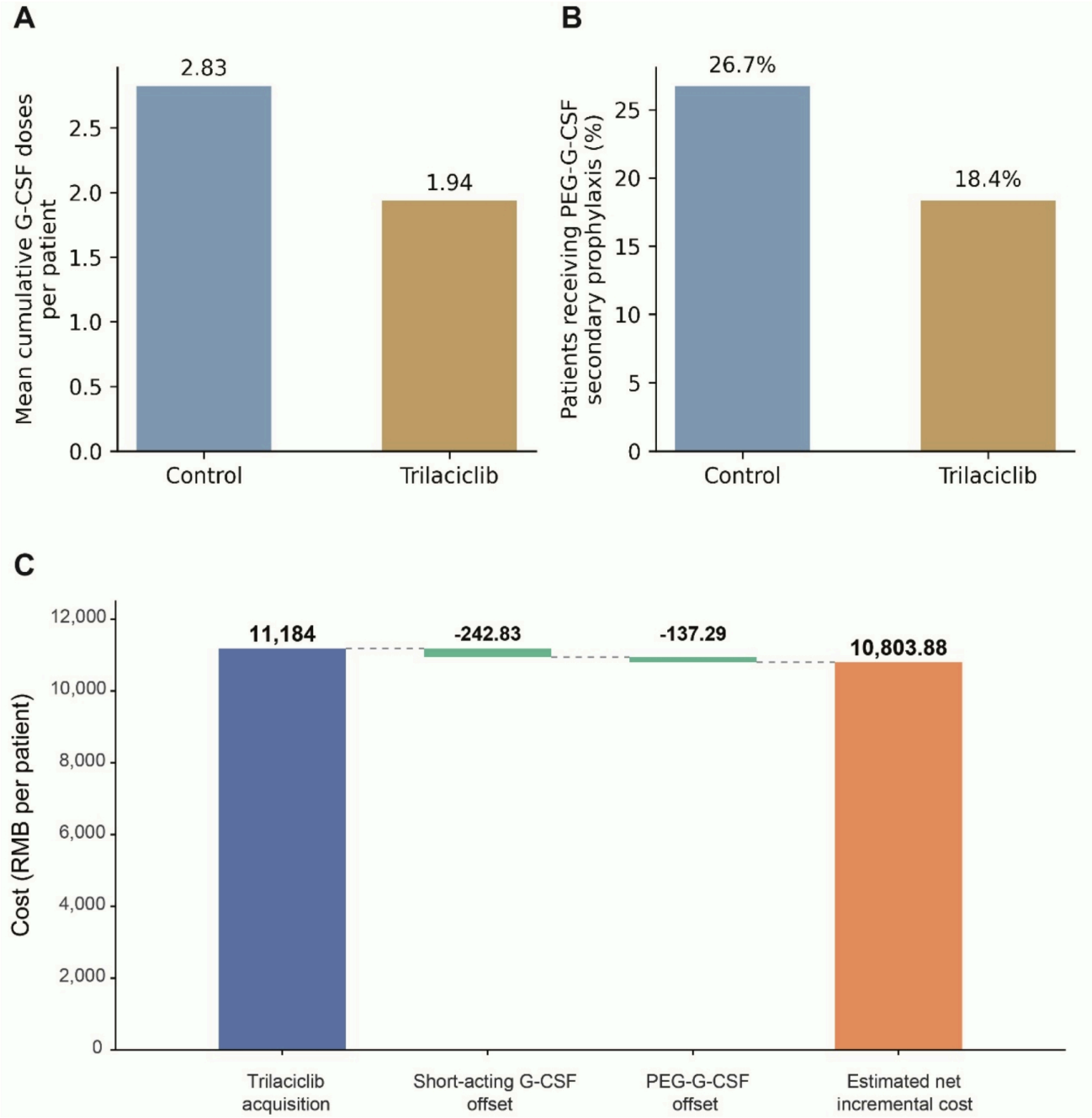


Figure 6

Growth factor utilization and scenario-based partial drug-cost estimates. (A) Mean cumulative short-acting G-CSF injections per patient. (B) Percentage of patients with recorded PEG-G-CSF secondary prophylaxis. (C) Assumed four-cycle trilaciclib acquisition cost, estimated G-CSF offsets, and scenario-based net incremental drug cost.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TableS6Costassumptionsanduncertainty.xlsx
- TableS2Cyclesandrecordedstopreasons.xlsx
- TableS3Rareeventsdescriptive.xlsx
- TableS5Costoffsetsensitivity.xlsx
- TableS4Cyclespecificoutcomes.xlsx
- TableS1Cycledenominators.xlsx