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Research Article

Retrospective evaluation of the efficacy and safety of granulocyte colony-stimulating factor use in extensive-stage small cell lung cancer

Granülosit koloni stimülan faktörün yaygın evre küçük hücreli akciğer kanserinde etkinlik ve güvenilirliğinin retrospektif analizi

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Abstract

Aim: Extensive-stage small cell lung cancer (ES-SCLC) is associated with a poor prognosis, with platinum-based chemotherapy being the mainstay of treatment. Chemotherapy-induced neutropenia can lead to treatment delays and hospitalizations due to febrile neutropenia. The use of granulocyte colony-stimulating factor (G-CSF) reduces the incidence of chemotherapy-induced neutropenia and febrile neutropenia. This study aims to evaluate the impact of G-CSF use on prognosis and its safety in extensive-stage SCLC.

Material and Methods: This single-center retrospective study included 80 patients. Patients were categorized based on G-CSF use, and overall survival (OS) and progression-free survival (PFS) were compared between groups. Univariate and multivariate analyses were performed using the Cox regression model to identify prognostic factors. The safety of G-CSF use was also evaluated.

Results: The median OS was 11.0 months in the G-CSF group and 8.6 months in the non-G-CSF group (p = 0.026). The median PFS was 8.0 months in the G-CSF group and 7.0 months in the non-G-CSF group (p = 0.044). The median OS was 15.1 months in the primary prophylaxis group and 10.2 months in the secondary prophylaxis group (p = 0.099). The median PFS was 10.0 months in the primary prophylaxis group and 7.4 months in the secondary prophylaxis group (p = 0.014). In the multivariate analysis, G-CSF use was identified as an independent prognostic factor for longer overall survival (OS) (HR: 0.51; 95% CI: 0.28–0.90, p = 0.021) and progression-free survival (PFS) (HR:0.57, 95% CI: 0.34-0.95, p = 0.031). No adverse events related to G-CSF use were observed in 69 patients (86.3%). Severe adverse event (grade 3) (thrombocytopenia) was observed in only 1 patient (1.3%).

Conclusion: In the current study, the use of G-CSF was found to improve overall survival in patients with extensive-stage small cell lung cancer (ES-SCLC). Further large-scale prospective studies are needed to support these findings.

Keywords: small cell lung cancer, G-CSF, chemotherapy, prognostic, febrile neutropenia

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Öz

Amaç: Yaygın evre küçük hücreli akciğer kanseri (ES-SCLC), kötü prognozlu olup tedavisinde platin bazlı kemoterapi temel yaklaşımdır. Kemoterapinin yol açtığı nötropeni, febril nötropeni nedeniyle tedavi gecikmelerine ve hastaneye yatışlara neden olabilir. Granülosit koloni uyarıcı faktör (G-CSF) kullanımı, kemoterapiye bağlı nötropeni ve febril nötropeni insidansını azaltmaktadır. Bu çalışmanın amacı, ES-SCLC'de G-CSF kullanımının prognoz üzerindeki etkisini ve güvenilirliğini değerlendirmektir.

Gereç ve Yöntemler: Bu tek merkezli, retrospektif çalışmaya 80 hasta dahil edilmiştir. Hastalar G-CSF kullanımına göre sınıflandırılmış ve genel sağkalım (OS) ile progresyonsuz sağkalım (PFS) gruplar arasında karşılaştırılmıştır. Prognoza etki eden faktörleri belirlemek amacıyla Cox regresyon modeli kullanılarak tek değişkenli ve çok değişkenli analizler yapılmıştır. G-CSF kullanımının güvenilirliği de değerlendirilmiştir.

Bulgular: G-CSF grubunda medyan genel sağkalım (OS) 11,0 ay, G-CSF kullanılmayan grupta 8,6 aydı (p = 0,026). Medyan progresyonsuz sağkalım (PFS) G-CSF grubunda 8,0 ay, G-CSF kullanılmayan grupta 7,0 aydı (p = 0,044). Primer profilaksi grubunda medyan OS 15,1 ay, sekonder profilaksi grubunda ise 10,2 aydı (p = 0,099). Medyan PFS primer profilaksi grubunda 10,0 ay, sekonder profilaksi grubunda 7,4 aydı (p = 0,014). Multivariate analizde G-CSF kullanımı, daha uzun genel sağkalım (OS) (HR: 0,51; %95 CI: 0,28–0,90, p = 0,021) ve progresyonsuz sağkalım (PFS) (HR:0,57, %95 CI: 0,34-0,95, p = 0,031) için bağımsız bir prognostik faktör olarak tanımlandı. G-CSF kullanımına bağlı olarak 69 hastada (%86.3) herhangi bir advers olay gözlenmeyip, sadece 1 hastada (%1,3) ciddi (Grade 3) advers olay (trombositopeni) saptandı.

Sonuç: Bu çalışmada, yaygın evre küçük hücreli akciğer kanseri (ES-SCLC) hastalarında G-CSF kullanımının genel sağkalımı iyileştirdiği bulunmuştur. Bu bulguları desteklemek için daha geniş ölçekli prospektif çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: küçük hücreli akciğer kanseri, G-CSF, kemoterapi, prognostik, febril nötropeni

Introduction

Small cell lung cancer (SCLC) accounts for approximately 15% of all lung cancers [1]. At the time of diagnosis, 70% of patients present with extensive-stage disease, which is associated with a poor prognosis [2]. In this stage, the 5-year survival rate is less than 2%, with the majority of deaths occurring within the first two years. Platinum-based (carboplatin, cisplatin) myelosuppressive chemotherapies form the cornerstone of treatment in SCLC. Neutropenia is a dose-limiting toxicity of myelosuppressive chemotherapy and one of the main adverse effects leading to treatment delays or discontinuation. Such modifications in treatment can negatively impact therapeutic response and survival outcomes [3].

Febrile neutropenia (FN) is a significant cause of morbidity and mortality in patients receiving chemotherapy. The use of recombinant granulocyte colony-stimulating factor (G-CSF) reduces the incidence and severity of chemotherapy-induced neutropenia, thereby lowering the risk of FN [4]. Multiple guidelines recommend primary prophylactic use of G-CSF in treatment regimens with an FN risk >20%. For intermediate-risk regimens (10–20%), prophylactic G-CSF use is advised based on individual risk factors [5–8]. According to the National Comprehensive Cancer Network (NCCN) guidelines, patients receiving cisplatin/carboplatin and etoposide are classified as being at intermediate risk for FN, and routine primary prophylaxis with G-CSF is not recommended for these patients [9].

Filgrastim is among the most widely used recombinant G-CSFs. It stimulates the production, differentiation, and release of neutrophils from the bone marrow, increasing circulating leukocyte fractions within 24 hours of administration [10]. Despite its high cost and widespread use, the optimal timing and duration of filgrastim for primary prophylaxis of FN remain unclear [4,10–13].

In addition to its prophylactic use for neutropenia and FN, there is evidence suggesting G-CSF may also be produced by tumors and exert potential effects on immune cells. G-CSF is expressed in several cancer types [14,15]. The presence of G-CSF in the tumor microenvironment has been shown to promote tumor progression and metastasis, contributing to poor prognosis [16]. The therapeutic role of immunotherapy in SCLC highlights the importance of the tumor microenvironment in this disease. Nevertheless, the evidence regarding the potential benefits of G-CSF use for neutropenia and FN, as well as its possible detrimental effects

within the tumor microenvironment, remains inconclusive [17]. While previous studies in SCLC have primarily focused on patients receiving chemoradiotherapy in limited-stage disease or chemotherapy plus immunotherapy in extensive-stage disease, data on the clinical impact of G-CSF use in metastatic SCLC patients treated with chemotherapy alone remain limited [18–21]. This retrospective study aimed to investigate the efficacy and safety of G-CSF use in patients with metastatic SCLC.

Material and Methods

This study was designed as a single-center retrospective study. Patients who were diagnosed with extensive-stage small cell lung cancer (SCLC) at the time of diagnosis and presented to the Medical Oncology Department of Etlik City Hospital between October 2022 and October 2024 were included in the study. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Scientific Research Evaluation and Ethics Committee of Etlik City Hospital (Decision No: 1251, Date: 18.12.2024). All patients participating in the study have signed the informed consent form.

Inclusion criteria were as follows: age ≥18 years; not pregnant or breastfeeding; a diagnosis of extensive-stage small cell lung cancer (SCLC) confirmed both histopathologically and radiologically; receipt of at least three cycles of chemotherapy administered every 21 days, consisting of either carboplatin (AUC 5, Day 1) plus etoposide (80–100 mg/m^2, Days 1–3) or cisplatin (75 mg/m^2, Day 1) plus etoposide (80–100 mg/m^2, Days 1–3); no receipt of immunotherapy during the treatment period; administration of filgrastim (5 mcg/kg subcutaneously once daily) as the granulocyte colony-stimulating factor (G-CSF); regular clinical follow-up; and availability of complete clinical data.

Exclusion criteria included: incomplete data regarding chemotherapy and G-CSF administration; use of pegfilgrastim or other G-CSF formulations; presence of non-metastatic disease at diagnosis; or patients initially diagnosed with limited-stage SCLC who progressed to extensive-stage during follow-up. Hospital records, clinical assessments, and laboratory data of 132 patients were retrospectively reviewed. Of these, 80 patients who fulfilled the eligibility criteria were included in the study. The collected data comprised age, sex, Eastern Cooperative Oncology Group (ECOG) performance status, metastatic sites, chemotherapy regimen, and treatment response as assessed by the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, including objective response rate (ORR) and disease control rate (DCR). The objective response rate (ORR) was defined as the proportion of patients achieving a complete response (CR) or partial response (PR) to the treatment relative to the total number of patients. The disease control rate (DCR) was defined as the proportion of patients who achieved a complete response, partial response, or stable disease (SD) with treatment relative to the total patient population. Baseline laboratory parameters were recorded, including hemoglobin, neutrophil, lymphocyte, eosinophil counts, C-reactive protein (CRP), carcinoembryonic antigen (CEA), and albumin levels. Data regarding G-CSF administration during treatment were also collected, including the number of G-CSF doses administered per cycle in users, the indication for G-CSF use (primary vs. secondary prophylaxis for severe or febrile neutropenia), and G-CSF-related adverse events (AEs).

Statistical Analysis

In this study, G-CSF use was defined as primary prophylaxis if initiated from the first chemotherapy cycle. Secondary prophylaxis was defined as G-CSF use in patients with a history of severe neutropenia or febrile neutropenia in previous cycles. Severe neutropenia was defined as an absolute neutrophil count (ANC) below 500/μL. Febrile neutropenia (FN) was defined as a single oral temperature measurement >38.3°C or a temperature ≥38.0°C sustained for over an hour, in combination with an ANC <500 cells/μL, or an expected decline to <500 cells/μL within the following 48 hours.

Progression-free survival (PFS) was defined as the time from initiation of first-line chemotherapy to disease progression or death. Overall survival (OS) was defined as the time from initiation of treatment to death. The primary endpoint of the study was OS. Secondary endpoints included PFS and toxicity. Additional analyses were conducted to assess clinicopathological features associated with prognosis.

Patients were categorized into two groups based on G-CSF use. Patients who received G-CSF for at least three cycles, with a minimum of three doses per cycle, were included in the G-CSF group. Patients who received any dose of G-CSF during any cycle of treatment were not included in the non–G-CSF group. Descriptive statistics were presented as mean ± standart deviation (SD), median (interquartile range(IQR)), and frequency (%). Categorical variables were compared using the Fisher's exact test or Chi-square test. Continuous variables were assessed for normality using the Shapiro-Wilk test. Variables with a normal distribution were analyzed using

the independent samples t-test, whereas those deviating from normality were evaluated with the Mann-Whitney U test. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan–Meier method. Survival curves were compared using the log-rank test. Survival analyses were performed using R software (version 4.5.0, accessed 31.07.2025). Kaplan–Meier estimates and survival curves were generated using the 'survival' and 'survminer' packages. Survival durations were reported as median months with 95% confidence intervals (CIs). Power analysis was conducted using the 'powerCT' function from the 'powerSurvEpi' R package. Based on the sample size (n=80), hazard ratio (HR=0.51), and group allocation (49/80 in the experimental group), the estimated statistical power was approximately 84% at α=0.05.

A Cox regression model was used to identify independent prognostic factors associated with survival. Variables with p<0.05 in the univariate analysis were included in the multivariate analysis. All descriptive statistics and Cox regression analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA).

Results

The clinicopathological characteristics of the patients are presented in Tables 1 and 2.

Table 1. Characteristics of patients.

		G-CSF using (n%)	Non-G-CSF using (n%)	p
Age	Mean±SD	64.6±8.8	63.8±9.0	0.667
Sex	Female	6 (12.2%)	3 (9.7%)	1.000
	Male	43 (87.8%)	28 (90.3%)	
ECOG PS	0-1	43 (87.8%)	27 (87.1%)	1.000
	2-3	6 (12.2%)	4 (12.9%)	
ORR(%)	No	14 (28.6%)	13 (41.9%)	0.218
	Yes	35 (71.4%)	18 (58.1%)	
DCR(%)	No	13 (26.5%)	13 (41.9%)	0.152
	Yes	36 (73.5%)	18 (58.1%)	
Brain metastasis	No	39 (79.6%)	25 (80.6%)	0.909
	Yes	10 (20.4%)	6 (19.4%)	
Liver metastasis	No	33 (67.3%)	19 (61.3%)	0.958
	Yes	16 (32.7%)	12 (38.7%)	
Bone metastasis	No	22 (44.9%)	10 (32.3%)	0.261
	Yes	27 (55.1%)	21 (67.7%)	
	Total	49 (61%)	31 (39%)	

Abbrev.: ECOG PS: Eastern Cooperative Oncology Group Perfomance Status, ORR: Objective Response Rate, DCR: Disease Control Rate

Table 2. Laboratory findings of patients by G-CSF group.

	G-CSF using	Mean ± SD	p
Hemoglobin (g/dL)	No	14.1 ± 2.0	0.036
	Yes	12.7 ± 2.1	
Neutrophil (103/µl)	No	6.910 ± 1.482	0.262
	Yes	6.159 ± 2.428	
Lymphocyte (103/µl)	No	2.251 ± 0.656	0.433
	Yes	1.607 ± 0.967	
		Median (IQR)	
Eosinophil (103/µl)	No	0.155 (0.313)	0.638
	Yes	0.060 (0.095)	
CEA (µg/L)	No	8.1 (12.7)	0.388
	Yes	4.2 (16.0)	
CRP (mg/L)	No	11 (14)	0.102
	Yes	27 (56)	
Albumin (g/L)	No	39 (15)	1.000
	Yes	41 (13)	

Abbrev.: CEA: Carcinoembryogenic antigen, CRP: C-reactive protein

The median overall survival (OS) was 11.0 months (95% CI, 9.8–15.7) in the G-CSF group and 8.6 months (95% CI, 7.0–12.8) in the non-G-CSF group (Log-rank p = 0.026) (Table 3, Figure 1). The median OS was 15.1 months (95% CI, 10.7–NA) in the primary prophylaxis group and 10.2 months (95% CI, 8.5–15.7) in the secondary prophylaxis group (Log-rank p = 0.099) (Table 3, Figure3).

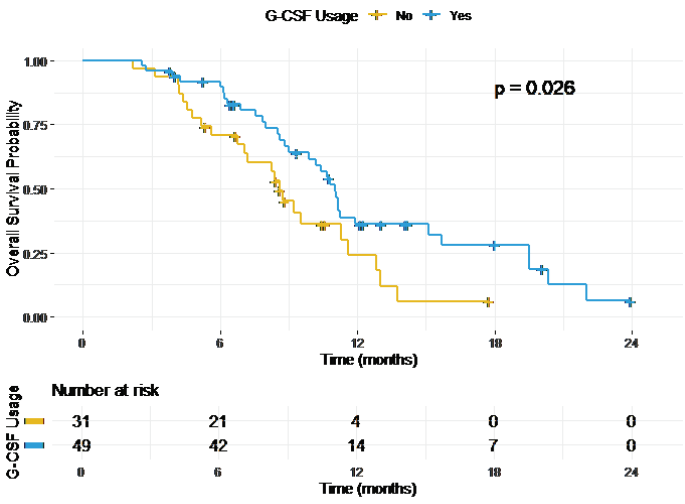

Figure 1. Overall Survival Curve Based on G-CSF Usage.

Table 3. mPFS and mOS Values Based on Overall G-CSF Use, Primary/Secondary Prophylaxis.							
		mOS (months)	CI (95%)	Log rank p	mPFS (months)	CI (95%)	Log rank p
G-CSF using	Yes (n=49)	11.0	9.8-15.7	**0.026**	8.0	7.3-10.0	**0.044**
	No (n=31)	8.6	7.0-12.8		7.0	6.0-8.5	
	Overall (n=80)	10.4	8.5-12.2		7.8	7.1-8.4	
Primary/ Secondary	Primary (n=19)	15.1	10.7-NA	**0.099**	10.0	8.1-20.8	**0.014**
	Secondary (n=28)	10.2	8.5-15.7		7.4	6.1-9.2	
	Overall (n=47)	11	10.1-11.9		8.0	7.2-8.7	
Abbrev.: mOS: median overall survival, mPFS: median progression-free survival, CI: Confidence interval							

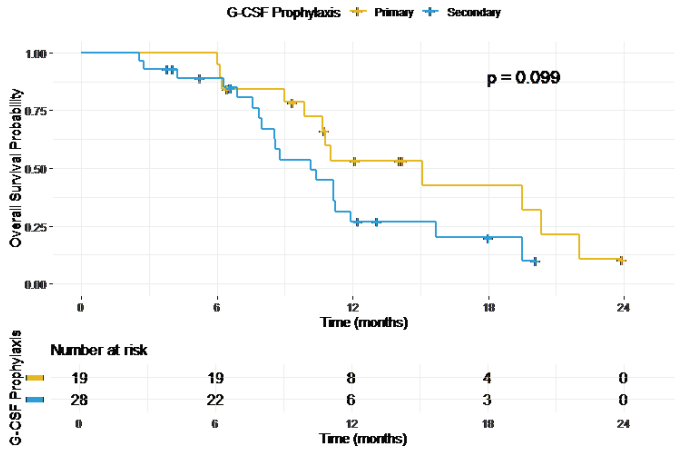

Figure 3. Overall Survival Curve Based on Primary/Secondary Prophylactic Use of G-CSF.

The median overall survival (OS) was 11.0 months (95% CI, 9.8–15.7) in the G-CSF group and 8.6 months (95% CI, 7.0–12.8) in the non-G-CSF group (Log-rank p = 0.026) (Table 3, Figure 1). The median OS was 15.1 months (95% CI, 10.7–NA) in the primary prophylaxis group and 10.2 months (95% CI, 8.5–15.7) in the secondary prophylaxis group (Log-rank p = 0.099)(Table 3, Figure3).

The median progression-free survival (PFS) was 8.0 months (95% CI, 7.3–10.0) in the G-CSF group and 7.0 months (95% CI, 6.0–8.5) in the non-G-CSF group (Log-rank p = 0.044) (Table 3, Figure 2). The median PFS was 10.0 months (95% CI, 8.1–20.8) in the primary prophylaxis group compared to 7.4 months (95% CI, 6.1–9.2) in the secondary prophylaxis group (Log-rank p = 0.014) (Table 3, Figure 4).

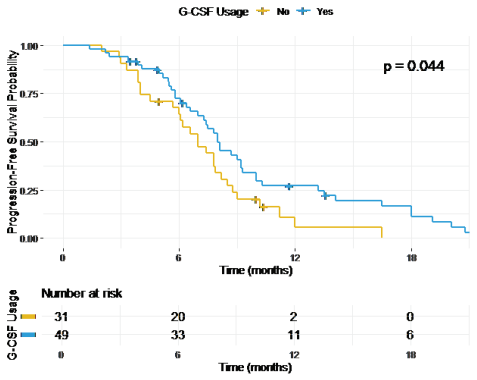

Figure 2. Progression-free Survival Curve Based on G-CSF Usage.

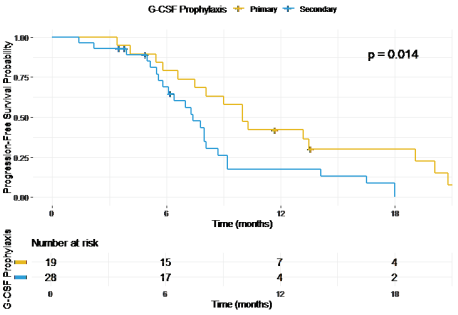

Figure 4. Progression-free Survival Curve Based on Primary/ Secondary Prophylactic Use of G-CSF

Univariate and multivariate analyses for PFS and OS are presented in detail in Table 4. In the multivariate model for PFS, patients with ECOG performance status (PS) 0–1 had a longer median PFS compared to those with ECOG PS 2–3 (7.8 vs. 5.0 months; HR: 2.64, 95% CI, 1.30-5.36; p = 0.007). The group that received G-CSF had a longer PFS (8.0 vs.7.0 months; HR:0.57, 95% CI: 0.34-0.95; p = 0.031).

In the multivariate model for overall survival (OS), patients with an ECOG performance status (PS) of 0–1 had a longer median OS compared to those with poorer ECOG PS (10.8 vs.

Table 4. Univariate and multivariate analyses for progression-free survival and overall survival.

		Median PFS (month)	Univariate analysis for PFS HR (95% CI) p	Multivariate analysis for PFS HR (95 % CI) p	Median OS (month)	Univariate analysis for OS HR (95% CI) p	Multivariate analysis for OS HR (95% CI) p
ECOG	**0-1**	7.8	**2.47**	**2.64**	10.8	**2.26**	**3.40**
	2-3	5.0	**1.22-4.99**	**1.30-5.36**	8.5	**1.09-4.70**	**1.56-7.44**
			0.012	**0.007**		**0.028**	**0.002**
G-CSF Using	**Yes**	8.0	**0.60**	**0.57**	11.0	**0.53**	**0.51**
	No	7.0	**0.36-0.99**	**0.34-0.95**	8.6	**0.30-0.93**	**0.28-0.90**
			0.048	**0.031**		**0.028**	**0.021**
Brain metastasis	**Yes**	8.1	0.73		11.1	0.70	
	No	7.4	0.40-1.32		9.2	0.36-1.37	
			0.302			0.28	
Liver metastasis	**Yes**	6.6	0.70,		7.9	**1.75**	**2.00**
	No	8.0	0.43-1.15		11.0	**1.02-3.02**	**1.12-3.54**
			0.165			**0.041**	**0.018**
Bone metastasis	**Yes**	7.5	1.04		11.0	0.81	
	No	8.1	0.64-1.68		9.5	0.47-1.38	
			0.869			0.443	
Albumin			0.99			0.97	
			0.96-1.02			0.94-1.01	
			0.707			0.281	
Hemoglobin			1.08			1.03	
			0.95-1.22			0.90-1.17	
			0.209			0.639	

Abbrev.: ECOG PS: Eastern Cooperative Oncology Group Perfomance Status, HR: Hazard Ratio, CI: Confidence interval, OS: overall survival, PFS:progression-free survival

8.5 months; HR: 3.40, 95% CI: 1.56–7.44, p = 0.002). Median OS was also longer in patients who received G-CSF (11.0 vs. 8.6 months; HR: 0.51, 95% CI: 0.28–0.90, p = 0.021). Conversely, patients with liver metastases had a shorter median OS (7.9 vs. 11.0 months; HR: 2.00, 95% CI: 1.12–3.54, p = 0.018).

Adverse events related to G-CSF use were not observed in 86.3% (n=69) of patients. The most common G-CSF-related adverse event was grade 1 fatigue, observed in 8.8% (n=7) of patients. A grade 3 adverse event (trombositopenia) was observed in only one patient (1.3%). Among those receiving G-CSF for secondary prophylaxis, 85% (n=16) received it due to severe neutropenia, while 15% (n=3) received it due to febrile neutropenia.

Discussion

In this retrospective study, we demonstrated that the use of granulocyte colony-stimulating factor (G-CSF) significantly prolonged overall survival (OS) in patients with extensive-stage small cell lung cancer (ES-SCLC) who were treated with platinum-based chemotherapy. However, no statistically significant differences were observed in objective response rate (ORR), or disease control rate (DCR) between the G-CSF and non-G-CSF groups.

The positive impact of G-CSF on survival can be explained by several biological and clinical mechanisms. G-CSF promotes neutrophil production through the activation of hematopoietic progenitor cells and reduces chemotherapy-induced immunosuppression, thereby significantly decreasing the risk of infection [22,23]. A comprehensive review and meta-analysis has demonstrated that G-CSF use in patients with solid tumors and lymphoma is associated with reduced infection-related mortality and early death [24]. A large-scale study in SCLC patients receiving cyclophosphamide, doxorubicin, and etoposide (CDE) chemotherapy showed that G-CSF reduced the severity, duration, and incidence

of neutropenia as well as the number of hospital admission days [25]. Similarly, Gatzemeier et al. reported that the use of lenograstim in SCLC patients treated with CDE did not significantly affect objective response or overall survival [26]. Another study involving patients with lung, breast, and colorectal cancers found that filgrastim prophylaxis was associated with a longer OS compared to placebo, although the difference did not reach statistical significance [27]. In our study, the longer OS observed in the G-CSF group (11.0 months vs. 8.6 months) suggests that G-CSF prophylaxis may contribute meaningfully to survival in ES-SCLC patients, who typically have a short survival expectancy.

Beyond enhancing neutrophil production, G-CSF also exerts various effects on the immune system. Preclinical data indicate that G-CSF can augment innate immune responses by activating macrophages, enhancing antigen presentation, and modulating the inflammatory microenvironment, potentially supporting antitumor macrophage activity and suppressing tumor progression [28]. In the current study, the very limited impact on PFS is consistent with previous reports suggesting that G-CSF does not directly inhibit tumor progression, but rather prolongs the period during which patients can receive continuous treatment [3,29]. Its also observed that although G-CSF may improve survival, its direct effect on tumor growth is limited [29]. Furthermore, we found that the primary prophylactic use of G-CSF resulted in longer PFS compared to secondary prophylaxis, a finding that remained significant in multivariate analysis. This suggests that initiating G-CSF early may be more effective in maintaining treatment continuity and ensuring that chemotherapy cycles are administered at full dose and on schedule. Prior studies have similarly reported that primary prophylaxis with G-CSF reduces episodes of febrile neutropenia, thereby improving chemotherapy adherence and delaying disease progression [30,31].

Filgrastim, a commonly used recombinant G-CSF, is generally associated with mild and transient side effects, most of which are also linked to chemotherapy itself. Severe adverse events are rare. Consistent with prior reviews, G-CSF-related side effects most commonly consist of chemotherapy-associated fever, bone pain, headache, and fatigue, and are usually mild. [32]. Its noted that filgrastim is generally well tolerated, with side effects occurring in 10–20% of patients. They also concluded that filgrastim is safe in the long term when used alongside chemotherapy, aside from infrequent events such as neutropenic fever, sepsis, and severe bone pain [33]. Serious adverse events attributed to G-CSF are uncommon. In this study, most patients did not experience any G-CSF-related adverse events, and those that did were primarily grade 1 in severity, supporting the notion that G-CSF is a well-tolerated supportive therapy. However, some studies have reported rare but serious complications associated with long-term G-CSF use, such as splenomegaly and splenic rupture [34]. Short-term and low-dose G-CSF use is generally associated with minimal adverse effects, with symptoms resolving quickly after discontinuation. Nonetheless, prolonged and high-dose use may rarely lead to more severe hematologic or immunologic reactions. Lapidari et al., in a systematic review, highlighted that these adverse effects were more frequently reported among patients previously exposed to immunosuppressive therapies. [35]. In conclusion, filgrastim is generally well tolerated in SCLC patients, and serious adverse effects are rare. However, cautious monitoring is advised for long-term or high-dose use, and a patient-specific approach is recommended when determining the appropriate G-CSF dosage.

Although there is currently insufficient evidence to definitively conclude that G-CSF use improves survival in extensive-stage small cell lung cancer, the survival benefit observed in our study may be explained by several mechanisms. The use of G-CSF may have contributed to improved survival by reducing the risk of febrile neutropenia, enabling the maintenance of chemotherapy dose intensity, and decreasing infection-related hospitalizations. In addition, patient-related factors such as comorbidities and the inclusion of individuals aged over 65 years who represent a population at higher risk for febrile neutropenia and for whom G-CSF use is particularly relevant may also account for the survival difference observed in our cohort.

Limitations of the study

The present study has several limitations. It is retrospective in nature, was conducted at a single center, and included a relatively small patient population. Furthermore, only data from first-line chemotherapy were included; thus, the effects of subsequent lines of treatment may have influenced overall outcomes. Additionally, the study population consisted exclusively of patients receiving chemotherapy alone, without immune checkpoint inhibitors, which are now part of standard treatment protocols for ES-SCLC (e.g., atezolizumab). The effects of G-CSF may differ in the context of chemoimmunotherapy. Therefore, the findings of our study should be interpreted with caution and considered applicable only to patients receiving chemotherapy without immunotherapy.

In conclusion, this study demonstrated that the use of G-CSF significantly increased overall survival and progression-free survival in patients with extensive-stage small cell lung cancer. Primary prophylactic use of G-CSF was found to have a positive impact on PFS. Our findings highlight the role of G-CSF in maintaining treatment continuity, its efficacy in reducing infection risk, and its immune system-supporting effects. The use of G-CSF was shown to be well-tolerated and a reliable treatment option in terms of adverse events. Prospective studies, with better standardization of G-CSF use and including immunotherapy regimens, are needed to validate our results.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Etlik City Hospital Scientific Research Evaluation and Ethics Committee (Decision No: 1251, Date: 18.12.2024).

Authors' contribution

Concept: GA, OS; Design: GA, GCU, OS; Data Collection and Processing: GA, GCU, KB; Analysis and Interpretation: GA, KB, OS; Literature Search: GCU, KB; Writing: GA, GCU; Critical Review: KB, OS.

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