DOI:10.31557/RRO.2024.10.2.173

REVIEW

Colony-Stimulating Factors During Radiotherapy and Chemoradiotherapy: Are Historical Concerns Still Justified?

Shayan Sheikhmiri[1], Seyed Alireza Javadinia[2], Amirhosein Rayegani[3]

[1]Shahid Beheshti University of Medical Sciences, Cancer Research Center, Tehran, Iran. [2] Non-Communicable Diseases Research Center, Sabzevar University of Medical Sciences, Sabzevar, Iran. [3]Department of Radiation Oncology, Omid Medical and Research Centre, Urmia University of Medical Sciences, Urmia, Iran.

Abstract

The use of colony-stimulating factors (CSFs) during radiotherapy (RT), particularly concurrent chemoradiotherapy (CRT), has historically been approached with caution because of toxicity concerns reported in earlier studies. However, much of the evidence underlying this caution predates contemporary radiation techniques and does not consistently distinguish granulocyte colony-stimulating factor (G-CSF) from granulocyte-macrophage colony-stimulating factor (GM-CSF). This brief review examines contemporary evidence regarding the safety and potential clinical utility of CSFs administered during RT and CRT. Available data suggest that G-CSF and pegylated G-CSF may reduce severe neutropenia and treatment interruptions in selected clinical settings, including craniospinal irradiation, pelvic CRT, and head and neck cancer, without consistently increasing clinically significant radiation-related toxicity. However, thoracic CRT, particularly when substantial mediastinal marrow is irradiated, remains a setting in which hematologic toxicity, including thrombocytopenia and transfusion requirements, warrants particular attention. Overall, current evidence does not support a uniform prohibition of CSF administration during RT or CRT, but neither does it establish routine prophylactic use for all patients. Decisions should be individualized according to treatment regimen, irradiated marrow volume, prior and concurrent chemotherapy, baseline hematologic risk, treatment intent, and the clinical consequences of treatment interruption. Further prospective comparative studies employing contemporary RT techniques are needed to firmly establish safety across diverse clinical settings.

Keywords: Colony-stimulating factors; G-CSF; Chemoradiotherapy; Radiotherapy; Neutropenia.

Rep Radiother Oncol, **10 (2)**, 173-180

Submission Date: 08/13/2024 Acceptance Date: 09/27/2024

Introduction

The use of colony-stimulating factors (CSFs) during radiotherapy (RT), particularly concurrent chemoradiotherapy (CRT), has traditionally been approached with caution. This practice is largely rooted in toxicity concerns reported in earlier clinical studies, including the Southwest Oncology Group (SWOG) experience [1], conducted in an era when radiation fields were generally less conformal and marrow-sparing techniques were not routinely available. These historical findings contributed to recommendations discouraging the routine use of CSFs during concurrent RT or CRT [2]. However, the applicability of these findings to contemporary treatment settings warrants reassessment.

An important consideration in interpreting the historical literature is the distinction between granulocyte colony-stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF). Although both agents stimulate hematopoietic recovery, their biological effects and clinical applications differ [3]. Consequently, safety or efficacy findings obtained with GM-CSF should not necessarily be extrapolated to G-CSF or pegylated G-CSF (PEG-G-CSF). This distinction is particularly relevant because much of the early evidence was generated before the widespread use of three-dimensional conformal RT (3DCRT), intensity-modulated RT (IMRT), volumetric-modulated

Corresponding Author:
Dr. Shayan Sheikhmiri
Shahid Beheshti University of Medical Sciences, Cancer Research Center, Tehran, Iran.
Email: Sheikhmiri.Shayan@gmail.com

arc therapy (VMAT), image-guided RT, and contemporary systemic treatment regimens.

Changes in radiation technology and treatment planning have also altered the extent and distribution of normal-tissue and bone-marrow irradiation. Consequently, the risk profile associated with combining CSFs and RT may differ from that observed in earlier treatment eras. At the same time, concerns regarding hematologic toxicity cannot be dismissed, particularly in treatment settings involving substantial marrow irradiation or intensive concurrent chemotherapy. The clinical relevance of these risks may also vary according to disease site, treatment intent, baseline hematologic status, and the potential consequences of treatment interruption.

The persistence of historical caution despite changes in treatment technology illustrates the importance of periodically reassessing established clinical practices against contemporary evidence. Rather than assuming that earlier safety concerns remain universally applicable or, conversely, that newer data have eliminated those concerns, the evidence should be evaluated according to the specific CSF agent, treatment setting, radiation technique, and expected hematologic risk. Building on our previous discussion of the relationship between historical clinical beliefs and supporting evidence [4], this review summarizes the available evidence on the concurrent use of CSFs during RT and CRT and considers whether historical restrictions remain justified in contemporary practice.

Craniospinal Irradiation (CSI) as a Marrow-Intensive Setting for CSF Support

The clinical utility of CSFs during RT appears to depend on treatment site, marrow exposure, and cumulative toxicity from RT and chemotherapy. Craniospinal irradiation (CSI) is a particularly marrow-intensive setting in which neutropenia and treatment interruptions may compromise treatment delivery. A pilot randomized study in patients with central nervous system tumors found that weekly prophylactic G-CSF increased white blood cell counts and reduced the need for therapeutic rescue G-CSF, with a numerically lower rate of treatment interruption in the G-CSF group [5]. Although the study was small and the difference in treatment interruption was not statistically significant, the findings suggest a potential benefit, particularly in patients with previous chemotherapy exposure and consequently reduced marrow reserve.

Further evidence from a prospective study of pediatric patients with medulloblastoma highlights the limitations of CSF support during CSI [6]. Despite prophylactic G-CSF administration, a substantial proportion of patients experienced treatment interruptions because of hematologic toxicity. These findings indicate that G-CSF may improve neutrophil recovery but cannot completely offset the hematologic burden of CSI. Younger age was also associated with greater hematologic toxicity, suggesting that patient-related factors may be as important as treatment characteristics in determining risk. Thus, although CSI represents a setting in which selective CSF support may be clinically useful, current evidence remains insufficient to support routine prophylactic use in all patients [7- 9].

Evidence from Gynecological Indications

Evidence from abdominopelvic RT similarly suggests that the benefits of CSF support may be context-dependent. An early study of patients with ovarian cancer undergoing extended-field RT found that filgrastim reduced treatment interruptions related to neutropenia; however, thrombocytopenia remained a dose-limiting toxicity and prevented treatment completion in some patients [10]. These findings illustrate an important limitation of G-CSF: correction of neutropenia does not necessarily prevent treatment interruption when other hematologic toxicities, particularly thrombocytopenia, become limiting.

More recent evidence in cervical cancer supports a potential role for pegylated G-CSF during concurrent CRT. In a 2021 clinical study, prophylactic PEG-rhG-CSF substantially reduced grade 3–4 neutropenia (77.78% vs. 10.0%) and eliminated febrile neutropenia in the intervention group, while also reducing chemotherapy delays [11]. However, RT completion time did not differ significantly between groups, and the study was limited by its small sample size.

A larger contemporary study of patients with cervical cancer receiving concurrent CRT further supported the potential benefit of PEG-rhG-CSF [12]. Growth factor support was associated with lower rates of grade 3–4 neutropenia, RT delays, and platinum dose adjustments, without significant differences in febrile neutropenia, grade 3–4 thrombocytopenia, anemia, or serious treatment-related adverse events. Because treatment interruptions and chemotherapy dose reductions may compromise adherence to definitive CRT, these findings support selective use of PEG-rhG-CSF in patients at substantial risk of treatment-related neutropenia. Overall, the available evidence suggests that CSF support may be beneficial in pelvic CRT, particularly when myelosuppression threatens timely chemotherapy delivery.

Evidence from Head and Neck Chemoradiotherapy

Recent evidence from nasopharyngeal carcinoma supports a potential role for PEG-rhG-CSF during contemporary head-and-neck CRT. A 2025 study reported fewer chemotherapy delays and RT interruptions among patients receiving PEG-rhG-CSF, together with higher white blood cell and absolute neutrophil counts and predominantly mild toxicity [13]. These findings are clinically relevant in intensive CRT, where hematologic toxicity may compromise treatment delivery. However, earlier studies have produced mixed results and generally support selective rather than routine use.

In patients with poor-prognosis head-and-neck cancer receiving intensified CRT, filgrastim facilitated escalation of hydroxyurea and reduced acute myelosuppression, although substantial cumulative myelosuppression and mucositis remained [14]. A small nonrandomized study in laryngeal cancer similarly suggested that

G-CSF-supported treatment was feasible and might reduce mucositis; however, the authors emphasized the need for further confirmation [15]. In a randomized postoperative RT trial that was discontinued prematurely, the administration of G-CSF was correlated with a reduction in grade 3 mucositis, fewer interventions for mucositis management, and a decreased duration of RT; however, it did not significantly improve the primary endpoint of percutaneous endoscopic gastrostomy requirement, and patient accrual fell considerably below the targeted enrollment [16]. Overall, these findings suggest that CSFs can be considered in selected high-risk head-and-neck CRT settings, particularly when hematologic toxicity threatens treatment continuity, but current evidence does not support routine use in all patients.

The Case of Thoracic Chemoradiotherapy

Thoracic CRT remains the setting in which historical concerns regarding CSF use require the greatest caution. In a secondary analysis of the CONVERT trial in limited-stage small-cell lung cancer (SCLC), prophylactic G-CSF was not associated with poorer survival, increased severe esophagitis or pneumonitis, or higher treatment-related mortality [17]. These findings challenge the historical concern that G-CSF necessarily increases radiation-related thoracic toxicity. However, G-CSF recipients had higher rates of severe thrombocytopenia and blood transfusion, although interpretation is limited by the nonrandomized design and potential confounding by indication. Notably, within-patient cycle-based comparisons showed lower rates of febrile neutropenia during G-CSF-supported cycles. These findings support a risk-adapted approach rather than routine prophylaxis, particularly when maintaining chemotherapy dose intensity is clinically important.

Earlier thoracic studies provide additional context. In the SWOG phase III trial of GM-CSF in limited-stage SCLC, GM-CSF reduced grade ≥3 leukopenia but did not significantly reduce severe neutropenia, provided no survival benefit, and was associated with concerns regarding infectious and cumulative hematologic toxicity [1]. In concurrent CRT for locally advanced esophageal cancer, prophylactic filgrastim reduced severe leukopenia but did not improve dose intensity, response, or survival, while treatment interruptions remained common [18]. The CALGB 39808 trial demonstrated the feasibility of concurrent CRT with G-CSF support in SCLC but was not designed to determine the efficacy of G-CSF [19]. Similarly, a phase II study reported no increase in pulmonary toxicity with G-CSF during thoracic CRT, although thrombocytopenia, anemia, and platelet transfusion remained frequent [20].

More recent observational studies provide somewhat more favorable findings but remain limited by their retrospective designs. A mixed esophageal and lung cancer series reported lower rates of febrile neutropenia, hospitalization, and intravenous antibiotic use with prophylactic PEG-rhG-CSF [21]. A retrospective propensity-matched SCLC study found that pegfilgrastim was associated with reductions in severe leukopenia, neutropenia, and treatment interruptions without an apparent increase in esophagitis or pulmonary toxicity, although no survival benefit was demonstrated [22]. Another retrospective lung cancer study suggested a survival association with therapeutic rather than prophylactic G-CSF; however, this association was not observed in the CRT subgroup [23]. Overall, contemporary evidence does not support a blanket prohibition of G-CSF during thoracic CRT, but the potential for thrombocytopenia and transfusion requirements reinforces the need for individualized risk assessment and close hematologic monitoring.

A 2024 systematic review and meta-analysis provides the most comprehensive pooled assessment of CSF use during concurrent thoracic CRT, although the report was not available in full text [24]. Across the included studies, prophylactic G-CSF reduced neutropenia, particularly in patients with SCLC, but did not consistently reduce febrile neutropenia, anemia, or thrombocytopenia or increase RT-related toxicity. Overall, the available thoracic evidence supports a targeted, risk-adapted, or protocol-based approach rather than universal prophylaxis. Persistent concerns regarding thrombocytopenia, cumulative marrow toxicity, and the absence of demonstrated survival benefit further support individualized use.

Evidence from Other Settings

Earlier studies of RT alone provide evidence that G-CSF can improve radiation-associated neutropenia or leukopenia during fractionated RT, including CSI. Studies in patients with Hodgkin lymphoma similarly reported increases in white blood cell and absolute neutrophil counts with filgrastim, while comparative studies of G-CSF-based strategies found similar leukocyte recovery without clear differences in treatment interruption or RT delivery [25, 26]. These findings demonstrate the hematologic activity of G-CSF during RT but do not establish a consistent benefit in clinically relevant treatment outcomes.

The effects of G-CSF may also depend on prior treatment exposure and the volume of irradiated bone marrow. A phase I study of large-field RT and a subsequent randomized pilot study raised concerns that recovery of peripheral blood counts may not fully reflect the effect of treatment on marrow reserve [27, 28]. The randomized study also suggested reduced recovery of CD34+ progenitor cells with concurrent G-CSF during large-field RT. Although these studies were small, they indicate that caution may be warranted when substantial volumes of bone marrow are irradiated.

The distinction between therapeutic and prophylactic CSF use is also important. Much of the earlier RT literature evaluated G-CSF for established or treatment-related neutropenia rather than routine primary prophylaxis. Accordingly, these data provide stronger support for selective therapeutic use when neutropenia threatens treatment delivery than for universal prophylactic administration.

The GM-CSF literature should be considered

separately from the G-CSF evidence. Studies of sargramostim have primarily examined immune modulation, treatment feasibility, and potential interactions with radiation-induced antitumor responses rather than conventional neutropenia prophylaxis [3]. A study in glioblastoma similarly focused on feasibility and immune activation during CRT rather than routine hematologic prophylaxis [29]. These findings suggest that concurrent GM-CSF and RT-based treatment can be feasible, but they should not be directly extrapolated to the routine use of G-CSF for neutropenia prevention.

Recommendations from the ASCO and NCCN Guidelines

The available evidence should be interpreted in the context of current clinical guidelines. Updated ASCO guidance conditionally recommends against routine CSF administration during concurrent chemotherapy and RT, particularly when the mediastinum is included in the radiation field, while acknowledging the low quality of supporting evidence and limited data for RT alone [30]. This recommendation represents a precaution rather than an absolute contraindication and should be distinguished from ASCO's broader risk-adapted recommendation for primary CSF prophylaxis when the anticipated risk of chemotherapy-induced febrile neutropenia is approximately 20% or higher.

The NCCN (V3.2026) similarly advises caution with prophylactic G-CSF during concurrent chemotherapy and RT rather than categorically prohibiting its use. This position is partly based on historical concerns, including earlier randomized studies involving GM-CSF [1]. However, the applicability of these findings to contemporary G-CSF formulations, modern RT techniques, and current CRT regimens remains uncertain. As discussed above, contemporary studies have not consistently demonstrated increased RT-related toxicity with prophylactic G-CSF, although the evidence remains limited and predominantly nonrandomized.

Accordingly, current guidelines are best interpreted as reflecting both historical safety concerns and continuing uncertainty rather than establishing an absolute contraindication. Decisions regarding CSF use should therefore be individualized according to the risk of febrile neutropenia, radiation field and mediastinal exposure, irradiated marrow volume, baseline marrow reserve, treatment technique, concurrent chemotherapy, and the potential clinical consequences of treatment interruption.

Figure 1. Clinical role of colony-stimulating factors during radiotherapy and concurrent chemoradiotherapy across different disease settings.

Summary and Recommendations

Summary

The available evidence indicates that G-CSF is effective in reducing treatment-related leukopenia and neutropenia during or after RT, supporting its role as a therapeutic intervention when clinically indicated. However, evidence remains insufficient to support its routine use as primary prophylaxis during RT or CRT, for preservation of long-term bone marrow function, or for improvement of survival outcomes.

Evidence for prophylactic G-CSF during concurrent CRT is heterogeneous and varies by disease site and treatment characteristics. In contemporary thoracic CRT, particularly for limited-stage small-cell lung cancer, G-CSF has generally been associated with lower rates of neutropenia and, in some studies, fewer treatment interruptions and hospitalizations. However, no consistent survival benefit has been demonstrated, and some studies have reported increased thrombocytopenia and transfusion requirements.

Historical concerns regarding CSF use during thoracic RT largely derive from the randomized SWOG trial of GM-CSF, which reported increased toxicity and treatment-related mortality [1]. More recent studies, including the CONVERT secondary analysis, have not reproduced these findings; however, much of the contemporary evidence is observational and remains susceptible to confounding by indication. Furthermore, findings involving GM-CSF should not be directly extrapolated to G-CSF.

Studies in head and neck, cervical, esophageal, and other malignancies demonstrate variable hematologic benefits, with more consistent reductions in neutropenia than improvements in dose intensity, treatment completion, or survival. Investigational uses of GM-CSF for mucosal protection or immune modulation should likewise be distinguished from routine G-CSF prophylaxis.

Evidence from large-field RT also suggests that recovery of peripheral neutrophil counts may not fully reflect effects on bone marrow reserve, including CD34+ progenitor-cell recovery and platelet production. Overall, current evidence supports selective therapeutic use of G-CSF for clinically significant or treatment-limiting neutropenia, while routine prophylactic administration during concurrent CRT remains insufficiently supported. Decisions should therefore be individualized according to treatment setting, irradiated marrow volume, chemotherapy intensity, baseline marrow reserve, and the clinical consequences of treatment interruption.

Table 1 summarizes the arguments for and against the use of CSFs during RT/CRT.

Recommendations

1. Avoid routine prophylactic G-CSF during concurrent chemoradiotherapy. In accordance with updated ASCO guidance, CSFs should generally not be administered routinely during concurrent chemotherapy and RT, particularly when the mediastinum is included in the radiation field. This recommendation reflects limited and mixed evidence rather than an absolute contraindication.

2. Distinguish therapeutic use from primary prophylaxis. G-CSF may be appropriate for clinically significant or persistent treatment-related neutropenia when it threatens continuation of potentially curative therapy, increases infection risk, or causes clinically important treatment delays. Therapeutic use should not be equated with routine prophylaxis at the initiation of CRT.

3. Consider prophylaxis selectively in high-risk

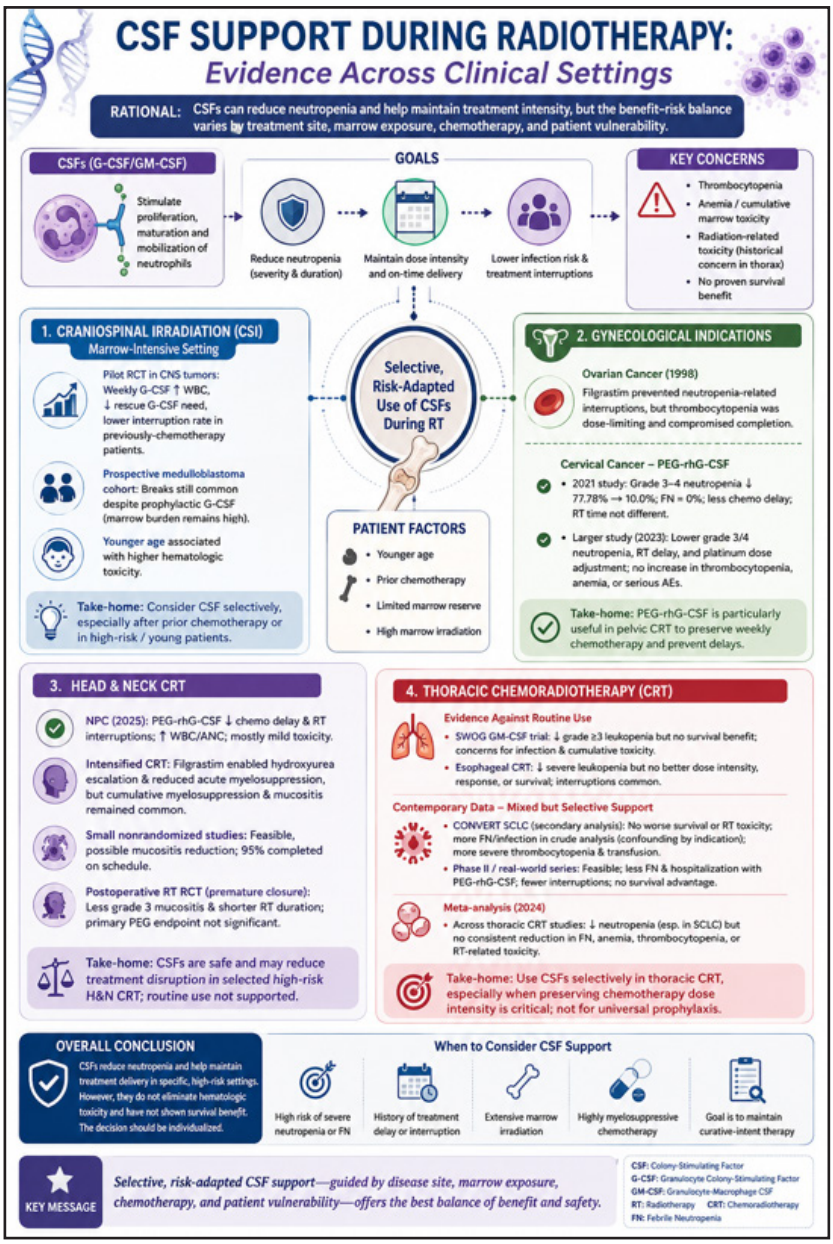


Figure 1. Schematic Overview of the Current Evidence Supporting Selective, Risk-adapted Use of Granulocyte Colony-stimulating Factors (G-CSFs) During Radiotherapy (RT) and Concurrent Chemoradiotherapy (CRT). The potential benefit of CSFs varies according to irradiated bone marrow volume, chemotherapy intensity, prior treatment, and individual marrow reserve. In craniospinal irradiation (CSI), G-CSFs may improve neutrophil recovery and reduce treatment interruptions in selected patients but do not completely prevent hematologic toxicity associated with extensive marrow irradiation. In gynecologic malignancies, particularly cervical cancer, pegylated G-CSF has been associated with reduced severe neutropenia and chemotherapy delays, although thrombocytopenia may remain dose-limiting. In head and neck CRT, contemporary evidence suggests improved treatment adherence in selected high-risk patients, whereas earlier studies provide mixed results and do not support routine prophylaxis. In thoracic CRT, contemporary evidence has not confirmed the historical concern of increased pulmonary toxicity; however, risks of thrombocytopenia and cumulative hematologic toxicity, together with the absence of a demonstrated survival benefit, support individualized rather than universal prophylactic use.

patients. The NCCN Guidelines for Hematopoietic Growth Factors (Version 3.2026) recommend caution when considering prophylactic G-CSF during concurrent chemotherapy and RT. Selective use may be considered when the risk of febrile neutropenia is substantial and treatment interruption could have important clinical consequences, provided that expected benefits outweigh potential risks.

4. Perform a treatment-specific risk–benefit assessment. Decisions should consider chemotherapy intensity, previous cytopenias and treatment exposure, baseline marrow reserve, age and comorbidities, radiation field and technique, mediastinal exposure, irradiated marrow volume, treatment intent, and available alternatives such as chemotherapy dose modification or treatment delay.

5. Exercise particular caution during thoracic and marrow-intensive RT. Mediastinal irradiation and extensive-field RT should not be considered

Table 1. Arguments For and Against G-CSF Use During RT/CRT.

Issue	Supporting argument	Opposing argument
Neutropenia control	Prophylactic G-CSF can reduce neutropenia during concurrent CRT and may help maintain planned treatment schedules [24].	Reduced neutropenia has not consistently translated into improved survival or locoregional control, and evidence varies across tumor types and regimens [24].
Treatment continuity	By reducing neutropenia-related delays and interruptions, G-CSF may facilitate completion of curative-intent CRT, particularly when overall treatment time is clinically important [12, 13, 22, 31].	Routine use may expose patients to additional treatment without proven oncologic benefit when treatment can be safely delivered through appropriate dose adjustment and marrow-sparing strategies [12, 13].
Hematologic safety	Contemporary studies in selected settings, including cervical cancer and SCLC, suggest acceptable safety and reductions in severe neutropenia and chemotherapy delays with pegylated G-CSF [12, 22, 31].	Thrombocytopenia remains a concern, and historical studies raised safety concerns regarding CSF use during thoracic CRT [1, 24].
Radiotherapy toxicity	Contemporary evidence suggests that G-CSF does not consistently increase clinically significant RT-related toxicity in selected patients [24].	Historical concerns, particularly during thoracic RT, included potential enhancement of pulmonary and combined-treatment toxicity [1].
Patient selection	Selective use may be appropriate in patients at high risk of treatment-limiting neutropenia, including those with previous febrile neutropenia, limited marrow reserve, extensive marrow irradiation, or highly myelosuppressive chemotherapy [12, 13, 22, 31].	Major guidelines generally advise against routine prophylactic CSF during concurrent CRT, favoring individualized use based on clinical risk and treatment context.
Evidence quality	Recent prospective and retrospective studies in cervical cancer, nasopharyngeal carcinoma, and SCLC suggest feasibility and potential benefit, particularly with pegylated formulations.	Evidence remains heterogeneous, disease-specific, and predominantly nonrandomized; therefore, findings cannot be generalized to all RT/CRT settings.

equivalent to limited-volume treatment. The potential for thrombocytopenia, transfusion requirements, and impaired marrow recovery should be weighed against the risk of febrile neutropenia and treatment interruption.

6. Do not equate hematologic improvement with improved oncologic outcomes. Reductions in neutropenia or febrile neutropenia do not necessarily translate into improved tumor response, progression-free survival, or overall survival. G-CSF should therefore primarily be viewed as supportive therapy intended to improve the safety and feasibility of treatment.

7. Interpret GM-CSF and sargramostim separately. Historical studies of GM-CSF provide important safety information but should not be directly extrapolated to G-CSF. Studies of sargramostim have largely focused on immune modulation and potential antitumor effects rather than routine neutropenia prophylaxis. Current evidence does not support substituting GM-CSF or sargramostim for G-CSF as routine prophylaxis.

In conclusion, G-CSF effectively supports neutrophil recovery during or after RT and has an established role in the therapeutic management of clinically significant treatment-related neutropenia. However, improvement in hematologic parameters has not consistently translated into better tumor response, treatment efficacy, progression-free survival, overall survival, or long-term marrow preservation.

Evidence for routine prophylactic G-CSF during concurrent CRT remains heterogeneous and largely dependent on treatment setting. Although G-CSF may reduce neutropenia, febrile neutropenia, and treatment interruptions in selected settings, consistent oncologic benefits have not been demonstrated, and thrombocytopenia remains a concern in some patients. GM-CSF and sargramostim should be considered separately because evidence regarding their immunomodulatory or mucosal effects does not establish a role in routine neutropenia prophylaxis.

Overall, G-CSF use during concurrent CRT should be selective and risk-adapted rather than universal. Decisions should incorporate febrile-neutropenia risk, treatment intent, radiation field and irradiated marrow volume, baseline marrow reserve, chemotherapy intensity, and the potential consequences of treatment interruption. Particular caution is warranted during thoracic, large-field, and other marrow-intensive RT.

Declarations

Ethics approval

Not applicable.

Consent to participate

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

Alireza Javadinia serves as an Editor of Reports of Radiotherapy and Oncology. The authors declare no other competing interests.

Funding

This review was entirely self-funded by the authors. No external funding was received.

Authors' contributions (CRediT)

SS contributed to conceptualization, project administration, supervision, methodology, investigation,

data curation, writing the original draft, and review and editing of the final manuscript. SAJ contributed to supervision and review and editing of the final manuscript. AHR contributed to review and editing of the final manuscript.

Acknowledgments

Statement of Transparency and Principles

• The authors declare no conflict of interest.

• The study was approved by the Research Ethics Committee of the authors' affiliated institution.

• The study data are available upon reasonable request.

• All authors contributed to the implementation of this research.

References

1. Bunn PA, Jr., Crowley J, Kelly K, Hazuka MB, Beasley K, Upchurch C, et al. Chemoradiotherapy with or without granulocyte-macrophage colony-stimulating factor in the treatment of limited-stage small-cell lung cancer: a prospective phase III randomized study of the Southwest Oncology Group. J Clin Oncol. 1995;13(7):1632–41. https://doi.org/10.1200/JCO.1995.13.7.1632
2. Benna M, Guy JB, Bosacki C, Jmour O, Ben Mrad M, Ogorodniitchouk O, et al. Chemoradiation and granulocyte-colony or granulocyte macrophage-colony stimulating factors (G-CSF or GM-CSF): time to think out of the box? Br J Radiol. 2020;93(1109):20190147. https://doi.org/10.1259/bjr.20190147
3. Golden EB, Chhabra A, Chachoua A, Adams S, Donach M, Fenton-Kerimian M, et al. Local radiotherapy and granulocyte-macrophage colony-stimulating factor to generate abscopal responses in patients with metastatic solid tumours: a proof-of-principle trial. The Lancet Oncology. 2015;16(7):795–803. https://doi.org/10.1016/S1470-2045(15)00054-6
4. Sheikhmiri S, Jabbari K, Taghizadeh-Hesary F. Re-evaluating Skin Care Restrictions in Radiation Oncology: Evidence Over Tradition. Reports of Radiotherapy and Oncology. 2026;11(1):35–7. https://doi.org/10.31557/RRO.2025.11.1.35
5. Kalaghchi B, Kazemian A, Hassanloo J, Zendehdel K. Granulocyte colony stimulating factor for prevention of craniospinal radiation treatment interruption among central nervous system tumor patients. Asian Pac J Cancer Prev. 2010;11(6):1499–502.
6. Madan R, Kumar N, Gupta A, Gupta K, Salunke P, Khosla D, et al. Effect of prophylactic granulocyte-colony stimulating factor (G-CSF) on acute hematological toxicity in medulloblastoma patients during craniospinal irradiation (CSI). Clin Neurol Neurosurg. 2020;196:105975. https://doi.org/10.1016/j.clineuro.2020.105975
7. Mac Manus MP, Clarke J, McCormick D, Abram WP. Use of recombinant granulocyte-colony stimulating factor to treat neutropenia occurring during craniospinal irradiation. International Journal of Radiation Oncology*Biology*Physics. 1993;26(5):845–50. https://doi.org/10.1016/0360-3016(93)90500-u
8. Schmidberger H, Hess CF, Hoffmann W, Reuss-Borst MA, Bamberg M. Granulocyte colony-stimulating factor treatment of leucopenia during fractionated radiotherapy. European Journal of Cancer. 1993;29(14):1927–31. https://doi.org/10.1016/0959-8049(93)90445-l
9. Mac Manus MP, McCormick D, Trimble A, Abram WP. Value of granulocyte colony stimulating factor in radiotherapy induced neutropenia: clinical and laboratory studies. Eur J Cancer. 1995;31a(3):302–7. https://doi.org/10.1016/0959-8049(94)00488-q
10. Fyles AW, Manchul L, Levin W, Robertson JM, Sturgeon J, Tsuji D. Effect of filgrastim (G-CSF) during chemotherapy and abdomino-pelvic radiation therapy in patients with ovarian carcinoma. Int J Radiat Oncol Biol Phys. 1998;41(4):843–7. https://doi.org/10.1016/s0360-3016(98)00093-5
11. Zou D, Guo M, Zhou Q. A clinical study of pegylated recombinant human granulocyte colony stimulating factor (PEG-rhG-CSF) in preventing neutropenia during concurrent chemoradiotherapy of cervical cancer. BMC Cancer. 2021;21(1):661. https://doi.org/10.1186/s12885-021-08364-9
12. Chen H, Ma Y, Wang D, Wu H, Zhang M, Xu Y, et al. The efficacy and safety of the prophylactic application of PEG-rhG-CSF in radiotherapy with weekly concurrent chemotherapy for cervical cancer. BMC Cancer. 2024;24(1):1405. 10.1186/s12885-024-13148-y.
13. Yang L, Yu L, Du X, Cui Y, Du G. Study of PEG-rhG-CSF for the prevention of neutropenia in concurrent chemoradiotherapy for nasopharyngeal carcinoma. PLoS One. 2025;20(1):e0315001. https://doi.org/10.1371/journal.pone.0315001
14. Vokes EE, Haraf DJ, Mick R, McEvilly JM, Weichselbaum RR. Intensified concomitant chemoradiotherapy with and without filgrastim for poor-prognosis head and neck cancer. J Clin Oncol. 1994;12(11):2351–9. https://doi.org/10.1200/JCO.1994.12.11.2351
15. Tejedor M, Valerdi JJ, Arias F, Dominguez MA, Pruja E, Mendez L, et al. Hyperfractionated radiotherapy concomitant with cisplatin and granulocyte colony-stimulating factor (filgrastim) for laryngeal carcinoma. Cytokines Cell Mol Ther. 2000;6(1):35–9. https://doi.org/10.1080/13684730050515895
16. Su YB, Vickers AJ, Zelefsky MJ, Kraus DH, Shaha AR, Shah JP, et al. Double-blind, placebo-controlled, randomized trial of granulocyte-colony stimulating factor during postoperative radiotherapy for squamous head and neck cancer. Cancer J. 2006;12(3):182–8. https://doi.org/10.1097/00130404-200605000-00005
17. Gomes F, Faivre-Finn C, Mistry H, Bezjak A, Pourel N, Fournel P, et al. Safety of G-CSF with concurrent chemo-radiotherapy in limited-stage small cell lung cancer - Secondary analysis of the randomised phase 3 CONVERT trial. Lung Cancer. 2021;153:165–70. https://doi.org/10.1016/j.lungcan.2021.01.025
18. Ohtsu A, Boku N, Muro K, Chin K, Muto M, Yoshida S, et al. Definitive chemoradiotherapy for T4 and/or M1 lymph node squamous cell carcinoma of the esophagus. J Clin Oncol. 1999;17(9):2915–21. https://doi.org/10.1200/JCO.1999.17.9.2915
19. Bogart JA, Herndon JE, 2nd, Lyss AP, Watson D, Miller AA, Lee ME, et al. 70 Gy thoracic radiotherapy is feasible concurrent with chemotherapy for limited-stage small-cell lung cancer: analysis of Cancer and Leukemia Group B study 39808. Int J Radiat Oncol Biol Phys. 2004;59(2):460–8. https://doi.org/10.1016/j.ijrobp.2003.10.021
20. Sheikh H, Colaco R, Lorigan P, Blackhall F, Califano R, Ashcroft L, et al. Use of G-CSF during concurrent chemotherapy and thoracic radiotherapy in patients with limited-stage small-cell lung cancer safety data from a

phase II trial. Lung Cancer. 2011;74(1):75–9. https://doi.org/10.1016/j.lungcan.2011.01.020
21. Liu F, Du Y, Cai B, Yan M, Yang W, Wang Q. A clinical study of polyethylene glycol recombinant human granulocyte colony-stimulating factor prevention neutropenia syndrome in patients with esophageal carcinoma and lung cancer after concurrent chemoradiotherapy. J Cancer Res Ther. 2017;13(5):790–5. https://doi.org/10.4103/jcrt.JCRT_320_17
22. Wang C, Zhu S, Miao C, Wang Y, Chen J, Yuan S, et al. Safety and efficacy of pegylated recombinant human granulocyte colony-stimulating factor during concurrent chemoradiotherapy for small-cell lung cancer: a retrospective, cohort-controlled trial. BMC Cancer. 2022;22(1):542. https://doi.org/10.1186/s12885-022-09644-8.
23. Du R, Hu P, Liu Q, Zhang J, Deng G, Hu D, et al. Granulocyte Colony-Stimulating Factor Treatment During Radiotherapy Is Associated With Survival Benefit in Patients With Lung Cancer. Technol Cancer Res Treat. 2018;17:1533033818816076. https://doi.org/10.1177/1533033818816076
24. Zarpelão FF, Barbosa LIT, Sousa JdS, Napoleão L, De Souza AL, Vilbert M. Safety in the use of granulocyte-colony stimulating factor during concurrent chemotherapy and thoracic radiotherapy in patients with small-cell lung cancer: A meta-analysis. Journal of Clinical Oncology. 2024;42(16_suppl):e20124–e. https://doi.org/10.1200/jco.2024.42.16_suppl.e20124
25. Knox SJ, Fowler S, Marquez C, Hoppe RT. Effect of filgrastim (G-CSF) in Hodgkin's disease patients treated with radiation therapy. Int J Radiat Oncol Biol Phys. 1994;28(2):445–50. https://doi.org/10.1016/0360-3016(94)90069-8
26. Adamietz IA, Rosskopf B, Dapper FD, von Lieven H, Boettcher HD. Comparison of two strategies for the treatment of radiogenic leukopenia using granulocyte colony stimulating factor. Int J Radiat Oncol Biol Phys. 1996;35(1):61–7. https://doi.org/10.1016/s0360-3016(96)85012-7
27. Kolotas C, Zamboglou N, Schnabel T, Bojar H, Wintzer A, Vogt H-G, et al. Effect of recombinant human granulocyte colony stimulating factor (r-metHuG-CSF) as an adjunct to large-field radiotherapy: A phase I study. International Journal of Radiation Oncology*Biology*Physics. 1996;35(1):137–42. https://doi.org/10.1016/s0360-3016(96)85022-x
28. Pape H, Orth K, Heese A, Heyll A, Kobbe G, Schmitt G, et al. G-CSF during large field radiotherapy reduces bone marrow recovery capacity. Eur J Med Res. 2006;11(8):322–8.
29. Cao C, Wang L, Jiang F, Jin Q, Jin T, Huang S, et al. Granulocyte-macrophage colony-stimulating factor for newly diagnosed glioblastoma. Neoplasia. 2025;63:101156. https://doi.org/10.1016/j.neo.2025.101156
30. Gyawali B, Bohlke K, Dickter JK, Kelkar AH, Knopf KB, Rapoport BL, et al. WBC Growth Factors: ASCO Guideline Update. J Clin Oncol. 2026;44(9):812–24. https://doi.org/10.1200/JCO-25-02938
31. Li W, Dong M, Huang S, Shi L, Yang H, Zhang Y, et al. Efficacy and safety of PEG-rhG-CSF in preventing chemoradiotherapy-induced neutropenia in patients with locally advanced cervical cancer. Biomol Biomed. 2023;23(2):310–6. https://doi.org/10.17305/bjbms.2022.7859.

This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.