NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ

Quality in Sport. eISSN 2450-3118.

Journal Home Page
https://apcz.umk.pl/QS/index

PIETRZAK, Barbara PATELSKI, Mikołaj, KLIMCZAK, Adrianna, KOTLARZ, Wiktoria, KAMIŃSKA, Marta, KUCZMA, Matylda, MOLENDA, Jakub, CZAPLA, Maciej, SURMA, Mateusz, and MIKUSEK, Wiktoria. Granulocyte Colony-Stimulating Factor (G-CSF): Clinical Use and Oncological Concerns. Quality in Sport. 2026;54:70712. eISSN 2450-3118. https://doi.org/10.12775/QS.2026.54.70712

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 10.04.2026. Revised: 17.04.2026. Accepted: 22.04.2026. Published: 26.04.2026.

Granulocyte Colony-Stimulating Factor (G-CSF): Clinical Use and Oncological Concerns

Barbara Pietrzak

University Clinical Hospital in Poznań, Przybyszewskiego 49, 60-355 Poznan, PL

https://orcid.org/0009-0009-3822-0037

pietrzak.barbara@outlook.com

Mikołaj Patelski
University Clinical Hospital in Poznań, Przybyszewskiego 49, 60-355 Poznan, PL
https://orcid.org/0009-0000-6608-3978
mikolajpatelski@gmail.com

Adrianna Klimczak
University Clinical Hospital in Poznań,Przybyszewskiego 49, 60-355 Poznan, PL
https://orcid.org/0009-0000-3248-6795
klimczakadrianna@gmail.com

Wiktoria Kotlarz
Medical Center HCP, 28 Czerwca 1956 r. 194, 61-485 Poznan: Poznan, PL
https://orcid.org/0009-0001-4916-1062
wiktoriakotlarz00@gmail.com

Marta Kamińska
Medical Center HCP, 28 Czerwca 1956 r. 194, 61-485 Poznan: Poznan, PL
https://orcid.org/0009-0003-9439-7917
kaminska.marta00@o2.pl

Matylda Kuczma
Medical Center HCP, 28 Czerwca 1956 r. 194, 61-485 Poznan: Poznan, PL
https://orcid.org/0009-0007-9757-9344
matylda120100@gmail.com

Jakub Molenda
University Clinical Hospital in Poznań,Przybyszewskiego 49, 60-355 Poznan, PL
https://orcid.org/0009-0003-8120-9710
jakmolenda@gmail.com

Maciej Czapla
Prof. S.T Dąbrowski Hospital in Puszczykowo S.A, 11 Józefa Ignacego Kraszewskiego Street, 62-040 Puszczykowo, PL
https://orcid.org/0009-0008-3291-6028
maciej.czapla02@gmail.com

Mateusz Surma
Prof. S.T Dąbrowski Hospital in Puszczykowo S.A, 11 Józefa Ignacego Kraszewskiego Street, 62-040 Puszczykowo, PL
https://orcid.org/0009-0002-6323-8588
msurma1129@gmail.com

Wiktoria Mikusek
Poznan University of Medical Sciences: Poznan, Greater Poland, PL
https://orcid.org/0009-0004-3602-0908
mikusekwiktoria@gmail.com

ABSTRACT

Introduction. Granulocyte colony-stimulating factor is a hematopoietic cytokine mainly produced by myeloid cells. Its primary role is to stimulate and promote neutrophil proliferation, which is commonly used in oncology to prevent myelosuppression often caused by cytotoxic treatment. Growing evidence suggests that its biological activity may extend beyond hematopoiesis and modulate tumor dynamics. Several studies indicate that elevated G-CSF levels and receptor expression are associated with greater aggressiveness and a more unfavourable prognosis. The role of G-CSF in fostering an immunosuppressive microenvironment, supporting metastasis, and promoting tumor growth has become a common area of research. Furthermore, studies have already claimed a higher incidence of secondary malignancies, like acute myeloid leukemia (AML) and myelodysplastic syndrome, among patients receiving G-CSF along with cytotoxic treatment.

INTRODUCTION AND PURPOSE

Granulocyte colony-stimulating factor (G-CSF) is a hematopoietic cytokine. Its recombinant forms are commonly used in oncology to manage chemotherapy-induced myelosuppression and help reduce the risk of febrile neutropenia by stimulating neutrophil recovery. Its clinical introduction has markedly improved the safety of cytotoxic treatment by reducing infection-related complications, enabling adherence to dose-dense or dose-intensive chemotherapy protocols, thereby improving patient outcomes. Beyond its established hematopoietic role, emerging evidence indicates that G-CSF and its receptor are expressed in several solid tumors. This phenomenon has been associated with increased tumor aggressiveness, greater metastatic potential, and poorer prognosis across multiple cancer types. G-CSF may remodel the tumor microenvironment by mobilizing myeloid-derived suppressor cells, enhancing angiogenesis, and facilitating immune escape, thereby facilitating tumor growth, invasion and even therapy resistance. Additionally, clinical observations raise concerns about the link between G-CSF administration and secondary hematological malignancies. Overall, these observations highlight the importance of careful G-CSF administration and individual approach to each patient.

The aim of this study is to provide a comprehensive review of G-CSF, focusing on established data on its clinical use and emerging knowledge of its broader biological effects in cancer.

In particular, we seek to examine the mechanisms by which G-CSF may affect tumor aggressiveness, progression, and metastatic behavior. Additionally, we also investigate its potential role in the development of secondary malignancies such as AML and MDS and analyze real-world patterns of G-CSF administration, including adherence to evidence-based prophylactic guidelines. By bringing these perspectives together, this work intends to discuss the advantages and potential risks of using G-CSF and to highlight the aspects that still remain uncertain.

MATERIALS AND METHODS

A comprehensive literature search was performed using PubMed database to identify studies on granulocyte colony-stimulating factor (G-CSF). Under review were articles published between January 2007 and January 2024. We included earlier landmark papers to provide historical context. Titles and abstracts were screened manually. In total, 117 abstracts were screened, 51 full texts were assessed, and 43 studies were selected that addressed mechanistic

insights, clinical guidelines, case reports of G-CSF-producing tumors, and evaluations of G-CSF-related risks.

Keywords: Granulocyte colony-stimulating factor, G-CSF, tumor aggressiveness, secondary malignancies, AML, MDS

RESULTS: CURRENT STATE OF KNOWLEDGE

G-CSF - clinical application and benefits

Granulocyte colony-stimulating factor (G-CSF) is a glycoprotein that regulates the proliferation, differentiation, and activation of neutrophilic granulocyte precursors. G-CSF and its receptor (G-CSFR) were considered to be predominantly expressed by myeloid cells. However, studies have identified their presence in fibroblasts, endothelial cells, bone marrow stromal cells, and other tissues, such as the placenta, cardiomyocytes, and B cells [1,2,3].

In clinical practice, recombinant forms of G-CSF - such as filgrastim, pegfilgrastim, lenograstim, and lipegfilgrastim are widely used to prevent and treat neutropenia. Available forms differ primarily in their molecular structure and duration of action. Filgrastim and lenograstim are short-acting and require daily administration, while pegfilgrastim and lipegfilgrastim are long-acting and can be administered once per chemotherapy cycle.

Cytotoxic treatment causes myelosuppression, reduces neutrophil production, thereby strongly increasing the risk of infections. In serious cases, febrile neutropenia has been observed to develop, defined as the onset of fever (oral temperature ≥ 38,3°C once or ≥ 38°C for over 2 hours) in conjunction with an absolute neutrophil count (ANC) of less than <1500/µL or ANC expected to decline below this threshold. Morbidity and mortality rates in patients receiving cytotoxic treatment are highly influenced by profound neutropenia, indicated by ANC < 100/µL. which carries the highest risk of severe bacteremia [4,5]. G-CSF prophylaxis reduces the depth and duration of low ANC, thus significantly lowering the risk of febrile neutropenia. Improving neutrophil recovery prevents infections caused by critically low ANC, thereby reducing the number of hospital admissions requiring intravenous antibiotic treatment. Furthermore, adequate neutrophil counts enable chemotherapy to be conducted according to the planned therapeutic regimen, which is particularly important in high-dose-density or dose-intensity regimens. Maintaining appropriate dosage levels is key to the effectiveness of these strategies,

cause it enables us to deliver more effective cytotoxic pressure on rapidly dividing cancer cells[6].

Optimal Timing and Administration of G-CSF

Timing of G-CSF administration is critical for safety and efficacy. In 2022, a two-round Delphi procedure involving 36 oncologists established consensus supporting the most commonly used approach: administering long-acting G-CSF 24 to 72 hours after completing a treatment cycle. It is believed that starting propylaxis no earlier than 24 hours post-chemotherapy helps avoid exposing progenitor myeloid cells to residual cytotoxic agents, while administering it within 72 hours supports timely bone marrow recovery and optimal responsiveness to the treatment [7].

A recent systematic review examined the optimal timing of prophylactic G-CSF during chemotherapy. They focused on the commonly used 2-day versus 3–5-day schedules. According to the meta-analysis, febrile neutropenia occurred more frequently on days 3-5 compared with day 2. However, it showed no differences in overall survival or infection-related mortality. Severe adverse events appeared slightly less frequent with later dosing, although this difference was not statistically significant. Data on pain remained inconclusive. Overall, both schedules were only weakly recommended, highlighting the need for stronger evidence to clarify optimal timing [8].

Effective and safe use of G-CSF requires adherence to established clinical guidelines that evaluate the risk of febrile neutropenia. They are based on chemotherapy regimens and patient-specific factors. Key recommendations from major organizations include American Society of Clinical Oncology (ASCO), European Organisation for Research and Treatment of Cancer (EORTC) and National Comprehensive Cancer Network (NCCN). The indication for G-CSF in primary prophylaxis of febrile neutropenia is determined by the risk associated with a specific treatment regimen, as well as by patient-, disease-, and treatment-related risk factors (Table 1) [9].

Patient-specific	Disease-specific	Treatment-specific
● Female sex	● Cancer subtype	● Chemotherapy regimen ○ High risk of FN (>20%) ○ Low risk of FN (10-20%)
● Advanced age > 65 years	● Bone Marrow Infiltration	● Chemotherapy dose intensity
● Malnutrition	● Late-stage cancer	● Absence of G-CSF prophylaxis
● Coexisting medical conditions	● Ongoing infection	● Absence of prophylactic antibiotics
● History of prior febrile neutropenia		● Previous exposure to cytotoxic therapy
● Hepatic impairment		
● Kidney impairment		
● Leukopenia		

- Reduced functional capacity
- Anemia
    - Cardiovascular disease
    - Recent surgical procedures

Table 1. Risk Factors Influencing G-CSF Prophylaxis Decision-Making [7]

Tumors expressing G-CSF and their aggressiveness

Multiple malignancies have been shown to express G-CSF and its receptor (G-CSFR). Such expression in many cases correlates with increased tumor aggressiveness and poorer clinical outcomes. Diagnosing granulocyte colony-stimulating factor-producing tumors can involve both clinical and histological evaluations. Clinically, these tumors may manifest with substantial leukocytosis that subsides after surgical resection [10]. However, a more direct method to confirm the tumor's role in G-CSF production is immunohistochemical staining, which reveals intracellular G-CSF expression [11, 12]. Hepatocellular carcinoma producing G-CSF is associated with rapid tumor growth and unfavorable prognosis, due to poor differentiation observed in most cases [13]. Similarly, G-CSF has been shown to be present in breast cancer, particularly in triple-negative subtypes, where they exhibit enhanced invasiveness and they are more likely to metastasize [14]. In the gastrointestinal tract, tumors such as colon, gastric, and pancreatic cancers have been reported to secrete G-CSF, often leading to advanced disease stages and poor prognoses[15]. Furthermore, G-CSF production in lung, bladder, and cervical cancers has been linked to aggressive clinical courses and rapid disease progression [16, 17, 18, 19, 20]. These findings highlight outstanding questions about

the roles of G-CSF and its receptor in tumor biology. Research suggests that G-CSF may promote tumor growth and its microenvironment.

Reinforcement of cancer progression

Emerging evidence suggests that G-CSF may trigger protumorigenic effects and contribute to tumor progression and metastasis. One key mechanism by which G-CSF may promote tumor progression is by increasing the accumulation and activity of myeloid-derived suppressor cells (MDSCs). These cells originate from bone marrow precursors and are considered to facilitate tumor growth and spread, due to an immunosuppressive effect that inhibits anti-tumor immune response. Studies have reported that high levels of G-CSF in vivo correlate with a strong granulocytic MDSC response in various cancer models [21, 22, 23].

This phenomenon may have profound consequences on the effectiveness of cancer treatments. Recent studies have suggested that G-CSF may contribute to chemotherapy resistance in different cancers. In breast cancer models treated with paclitaxel, G-CSF-induced tumor angiogenesis has been linked to reduced chemotherapy efficacy. Similarly, in medulloblastoma, post-chemotherapy G-CSF administration increased the proportion of G-CSFR-positive tumor cells that exhibited resistance. Uterine cervical cancers producing high levels of G-CSF have also demonstrated resistance to cisplatin-based chemotherapy, possibly through mechanisms involving MDSCs [23,24]. Studies also suggest that G-CSF, acting via MDSCs, can possibly contribute to promoting VEGF-independent angiogenesis. This results in enhanced resistance to anti-VEGF therapies [25, 26]. Furthermore, in a clinical trial involving patients with advanced unresectable head and neck cancer receiving accelerated radiotherapy, prophylactic G-CSF was associated with a reduction in local tumor control [27].

Additionally, G-CSF has been shown to contribute to the upregulation of neutrophil extracellular traps (NETs) production. These are formations, resembling web-like structures made of extracellular DNA, histones, and antimicrobial proteins released by activated neutrophils in response to infection or inflammation. Although NETs play an important role in the human immunological system, studies suggest they may also promote tumor progression. By physically trapping circulating tumor cells, they support their adhesion to blood vessels. This mechanism directly contributes to metastatic spread. NETs have also been found to increase the production of proangiogenic factors, including VEGF-A, which promotes angiogenesis in the tumor microenvironment. Activated neutrophils release angiogenic factors,

including VEGF-A, ANGPT1, CXCL8, HGF, and MMP-9, all of which contribute to new blood vessel formation. This enhances endothelial cell migration and tube formation, essential for supporting tumor growth and metastasis [28, 29 , 30 , 31 , 32].

Secondary malignancies associated with G-CSF administration

The association between G-CSF use and the development of secondary malignancies has long been a subject of interest among researchers. As a hematopoietic cytokine, G-CSF increases bone marrow activity and can contribute to excessive cell proliferation, and increase the risk of secondary malignancies. An extensive meta-analysis of 68 randomized controlled trials with more than 31 000 patients revealed that while G-CSF support improved overall survival, it was also linked to a significantly higher risk of developing secondary malignancies, including acute myeloid leukemia (AM) as well as myelodysplastic syndrome (MDS) (RR=1,85; 95% CI: 1,9–2,88) [33]. On the other hand, in another large population-based cohort study involving 122 373 breast cancer survivors, those who received chemotherapy in conjunction with G-CSF, exhibited a non-significant increase risk of AML (aHR=1,3; 95% CI: 1,0–1,7) and MDS (aHR=1,3 ; 95% CI: 0,9–1,8). However, a higher risk of acute lymphoblastic leukemia or lymphocytic lymphoma (ALL/LL) was observed, especially among patients who received four or more G-CSF cycles (aHR=2,3; 95% CI: 1,0–5,1), indicating a potential dose-response relationship [34]. Deeper analysis indicates that the type of G-CSF may also influence the risk profile. Specifically, according to another research concerning non-Hodgkin lymphoma, patients who received 10 or more doses of filgrastim had a higher incidence of MDS/AML (HR=1,67; 95% CI: 1,25–2,23), while no significant risk increase was observed with pegfilgrastim [35]. Overall, current data suggest that if there is any additional risk, it is small and depends on the treatment context.

Real-world adherence to G-CSF prophylaxis guidelines

Established guidelines recommend prophylactic G-CSF for oncological patients at high risk of febrile neutropenia exist, however, in daily clinical conditions, the administration of G-CSF continues to be inconsistent. In a retrospective cohort study in the USA, only 48,5% of patients on high-risk chemotherapy regimens received G-CSF prophylaxis, and only 13,9% of those on intermediate-risk regimens with additional risk factors did so [36]. In Germany, a representative survey revealed that guideline adherence for high-risk lung cancer patients improved from 15,4%

up to 47,85%, yet still remained sub-optimal. In certified cancer treatment centers, higher compliance rates were demonstrated [37]. In Italy, a multicenter observational study found that G-CSF was frequently administered beyond the recommended 24-72 hours post-chemotherapy timeframe; outside this window, 42% of daily G-CSF cycles were initiated [38]. In another extensive review,regardless of established guidelines, nearly one-third of physicians reported using G-CSF prophylactically in patients with a low risk (<20%) of febrile neutropenia. Furthermore, 48% of physicians indicated using G-CSF alongside antibiotics for the management of febrile neutropenia, which is not routinely recommended [39]. Variation in practice indicates that more standardized guidance may help ensure greater consistency with evidence-based practice and benefit patient outcomes.

Emerging Alternatives to G-CSF in Neutropenia Prophylaxis

As G-CSF continues to be the standard practice for preventing chemotherapy-induced neutropenia, a number of alternative strategies are being explored and considered. Among them, granulocyte-macrophage colony-stimulating factor (GM-CSF), a hematopoietic cytokine that stimulates multiple myeloid lineages and strengthens innate and adaptive immune responses. Unfortunately, its broader effects have raised safety concerns in oncology [40]. Other factors under consideration include thrombopoietin (TPO) receptor agonists such as eltrombopag and romiplostim. They are widely used in immune thrombocytopenia and post-transplant aplasia, also promote multilineage hematopoiesis, and may shorten cytopenias after chemotherapy. Unfortunately, their use with regard to neutropenia prophylaxis is not as effective [41]. Another alternative option for G-CSF could be CXCR4 antagonists like plerixafor, currently used to prepare patients for stem cell transplants. They mobilize hematopoietic progenitors by disrupting CXCL12–CXCR4 signaling and are currently used to prepare patients for stem cell transplantation [42]. Lastly, researchers have been working toward predictive algorithms and machine learning, which can result in more careful and personalized patient selection and minimize unnecessary G-CSF exposure [43].

Studies on G-CSF substitutes continue to show a growing effort to develop more personalized, potentially safer strategies in supportive oncology.

DISCUSSION

Granulocyte colony-stimulating factor is still a significant clinical tool that effectively reduces the risk of febrile neutropenia and improves the safety of cytotoxic treatments in oncological patients. However, their role in fostering cancer spread and progression is still unclear. Exogenously administered as well as tumor-derived G-CSF has already been linked to increased tumor aggressiveness, chemotherapy or radiotherapy resistance and higher frequency of secondary hematologic malignancies. Studies also report that G-CSF enhances the formation of neutrophil extracellular traps (NETs), leading to increased production of proangiogenic proteins supporting angiogenesis within the tumor microenvironment. Additionally, cancer cells expressing G-CSF were found to promote the accumulation of myeloid-derived suppressor cells (MDSCs), resulting in enhanced immunosuppression and inhibited anti-tumor immune response. Nonetheless, adherence to guideline-recommended prophylaxis in real-world conditions is inconsistent and varies between clinical centres. These results demonstrate the need for a cautious risk assessment, a more thorough, evidence-based approach to G-CSF use, and further research into its possible impact on cancer development. Additional hope for safer, supportive care during oncological treatment comes in the form of emerging alternatives such as GM-CSF, TPO receptor agonists, CXCR4 antagonists, and peptide-based agents.

DISCLOSURE

Conceptualization: Barbara Pietrzak

Methodology: Adrianna Klimczak, Mikołaj Patelski

Software: Wiktoria Kotlarz

Check: Maciej Czapla, Jakub Molenda

Formal analysis: Jakub Molenda

Investigation: Barbara Pietrzak

Resources: Marta Kamińska, Wiktoria Mikusek, Maciej Czapla

Writing -rough preparation: Mateusz Surma, Matylda Kuczma

Writing -review and editing: Matylda Kuczma, Jakub Molenda

Visualization: Wiktoria Mikusek, Wiktoria Kotlarz

Supervision: Adrianna Klimczak, Marta Kamińska

Project administration: Adrianna Klimczak

All authors have read and agreed with the published version of the manuscript.

Funding Statement:

The study did not receive special funding.

Institutional Review Board Statement:

Not applicable.

Informed Consent Statement:

Not applicable.

Data Availability Statement:

Not applicable.

Acknowledgments:

Not applicable. As this article involves a review and synthesis of existing literature rather than original research involving human subjects, ethical assessment and institutional review board statements are not applicable.

Conflict of Interest Statement:

The authors report no conflicts of interest.

Declaration of generative AI and AI-assisted technologies in the writing process:

In preparing this work, the authors used ChatGPT (OpenAI) for language editing and grammar correction only. After using this tool, the authors reviewed and edited the text as needed and accept full responsibility for the substantive content of the publication.

REFERENCES

1. Nagata S, Fukunaga R. Granulocyte colony-stimulating factor and its receptor. *Prog Growth Factor Res*. 1991;3(2):131-141. doi:10.1016/s0955-2235(05)80004-3
2. Schneider A, Krüger C, Steigleder T, et al. The hematopoietic factor G-CSF is a neuronal ligand that counteracts programmed cell death and drives neurogenesis. *J Clin Invest*. 2005;115(8):2083-2098. doi:10.1172/JCI23559
3. Shimoji K, Yuasa S, Onizuka T, et al. G-CSF promotes the proliferation of developing cardiomyocytes in vivo and in derivation from ESCs and iPSCs. *Cell Stem Cell*. 2010;6(3):227-237. doi:10.1016/j.stem.2010.01.002
4. Klastersky J, de Naurois J, Rolston K, et al. Management of febrile neutropenia: ESMO Clinical Practice Guidelines. *Ann Oncol*. 2016;27(suppl 5):v111-v118. doi:10.1093/annonc/mdw325
5. Punnapuzha S, Edemobi PK, Elmoheen A. Febrile Neutropenia. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; March 30, 2023.
6. Gascón P, Awada A, Karihtala P, Lorenzen S, Minichsdorfer C. Optimal use of granulocyte colony-stimulating factor prophylaxis to improve survival in cancer patients receiving treatment : An expert view. *Wien Klin Wochenschr*. 2024;136(11-12):362-368. doi:10.1007/s00508-023-02300-6
7. Adamo V, Antonuzzo L, Danova M, et al. Supportive therapies in the prevention of chemotherapy-induced febrile neutropenia and appropriate use of granulocyte colony-stimulating factors: a Delphi consensus statement. *Support Care Cancer*. 2022;30(12):9877-9888. doi:10.1007/s00520-022-07430-7
8. Ozaki Y, Yokoe T, Yoshinami T, et al. Optimal timing of prophylactic pegylated G-CSF after chemotherapy administration for patients with cancer: a systematic review and meta-analysis from Clinical Practice Guidelines for the use of G-CSF 2022. *Int J Clin Oncol*. 2024;29(5):551-558. doi:10.1007/s10147-024-02499-y
9. Blayney DW, Schwartzberg L. Chemotherapy-induced neutropenia and emerging agents for prevention and treatment: A review. *Cancer Treat Rev*. 2022;109:102427. doi:10.1016/j.ctrv.2022.102427
10. Asano S, Urabe A, Okabe T, Sato N, Kondo Y. Demonstration of granulopoietic factor(s) in the plasma of nude mice transplanted with a human lung cancer and in the tumor tissue. *Blood*. 1977;49(5):845-852.

11. Schurmann G, Zweifel M, Giger R, et al. Granulocyte Colony-stimulating Factor Producing Oropharyngeal Squamous Cell Carcinoma. *In Vivo*. 2021;35(3):1785-1790. doi:10.21873/invivo.12438
12. Hirai K, Kumakiri M, Fujieda S, et al. Expression of granulocyte colony-stimulating factor and its receptor in epithelial skin tumors. *J Dermatol Sci*. 2001;25(3):179-188. doi:10.1016/s0923-1811(00)00131-6
13. Nagata H, Komatsu S, Takaki W, et al. Granulocyte colony-stimulating factor-producing hepatocellular carcinoma with abrupt changes. *World J Clin Oncol*. 2016;7(5):380-386. doi:10.5306/wjco.v7.i5.380
14. Liu L, Liu Y, Yan X, Zhou C, Xiong X. The role of granulocyte colony-stimulating factor in breast cancer development: A review. *Mol Med Rep*. 2020;21(5):2019-2029. doi:10.3892/mmr.2020.11017
15. Fan Z, Li Y, Zhao Q, et al. Highly Expressed Granulocyte Colony-Stimulating Factor (G-CSF) and Granulocyte Colony-Stimulating Factor Receptor (G-CSFR) in Human Gastric Cancer Leads to Poor Survival. *Med Sci Monit*. 2018;24:1701-1711. Published 2018 Mar 23. doi:10.12659/msm.909128
16. Samejima H, Ose N, Sakurai T, Nagata H, Morii E, Shintani Y. G-CSF-producing left lung squamous cell carcinoma positive for ROS1 rearrangements completely resected after neoadjuvant radiation chemotherapy: A case report. *Respir Med Case Rep*. 2022;38:101697. Published 2022 Jun 27. doi:10.1016/j.rmcr.2022.101697
17. Shiba S, Oike T, Ando K, Yoshimoto Y, Takayama Y, Ohno T. Granulocyte-colony stimulating factor-producing uterine cervical cancer treated with chemoradiotherapy: A case report with mutation analysis and literature review. *Clin Case Rep*. 2020;9(1):185-192. Published 2020 Nov 6. doi:10.1002/ccr3.3495
18. Choi KJ, Kim KC, Kim EJ. A case of granulocyte colony-stimulating factor producing lung adenocarcinoma with anaplastic lymphoma kinase gene rearrangements. *Respir Med Case Rep*. 2023;46:101885. Published 2023 Jun 5. doi:10.1016/j.rmcr.2023.101885
19. Morinaga R, Kawahara T, Kuroda S, Inayama Y, Uemura H. Granulocyte Colony-Stimulating Factor-Producing Bladder Cancer. *Case Rep Oncol*. 2019;12(2):603-607. Published 2019 Aug 6. doi:10.1159/000502174
20. Kowanetz M, Wu X, Lee J, et al. Granulocyte-colony stimulating factor promotes lung metastasis through mobilization of Ly6G+Ly6C+ granulocytes. *Proc Natl Acad Sci U S A*. 2010;107(50):21248-21255. doi:10.1073/pnas.1015855107

21. DuPre' SA, Hunter KW Jr. Murine mammary carcinoma 4T1 induces a leukemoid reaction with splenomegaly: association with tumor-derived growth factors. *Exp Mol Pathol*. 2007;82(1):12-24. doi:10.1016/j.yexmp.2006.06.007
22. Abe F, Dafferner AJ, Donkor M, et al. Myeloid-derived suppressor cells in mammary tumor progression in FVB Neu transgenic mice. *Cancer Immunol Immunother*. 2010;59(1):47-62. doi:10.1007/s00262-009-0719-2
23. Kawano M, Mabuchi S, Matsumoto Y, et al. The significance of G-CSF expression and myeloid-derived suppressor cells in the chemoresistance of uterine cervical cancer. *Sci Rep*. 2015;5:18217. Published 2015 Dec 15. doi:10.1038/srep18217
24. Paul MR, Huo Y, Liu A, et al. Characterization of G-CSF receptor expression in medulloblastoma. *Neurooncol Adv*. 2020;2(1):vdaa062. Published 2020 May 27. doi:10.1093/noajnl/vdaa062
25. Shojaei F, Wu X, Qu X, et al. G-CSF-initiated myeloid cell mobilization and angiogenesis mediate tumor refractoriness to anti-VEGF therapy in mouse models. *Proc Natl Acad Sci U S A*. 2009;106(16):6742-6747. doi:10.1073/pnas.0902280106
26. Phan VT, Wu X, Cheng JH, et al. Oncogenic RAS pathway activation promotes resistance to anti-VEGF therapy through G-CSF-induced neutrophil recruitment. *Proc Natl Acad Sci U S A*. 2013;110(15):6079-6084. doi:10.1073/pnas.1303302110
27. Staar S, Rudat V, Stuetzer H, et al. Intensified hyperfractionated accelerated radiotherapy limits the additional benefit of simultaneous chemotherapy--results of a multicentric randomized German trial in advanced head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2001;50(5):1161-1171. doi:10.1016/s0360-3016(01)01544-9
28. Demers M, Krause DS, Schatzberg D, et al. Cancers predispose neutrophils to release extracellular DNA traps that contribute to cancer-associated thrombosis. *Proc Natl Acad Sci U S A*. 2012;109(32):13076-13081. doi:10.1073/pnas.1200419109
29. Cools-Lartigue J, Spicer J, McDonald B, et al. Neutrophil extracellular traps sequester circulating tumor cells and promote metastasis. *J Clin Invest*. 2013;123(8):3446-3458. doi:10.1172/JCI67484
30. Hu W, Xu B, Zhang J, Kou L, Xu X. Neutrophil extracellular traps: biological functions and relevance in cancer metastasis and therapy. *Signal Transduct Target Ther*. 2022;7(1):305. doi:10.1038/s41392-022-01169-1
31. Poto R, Cristinziano L, Modestino L, et al. Neutrophil extracellular traps, angiogenesis and cancer. *Biomedicines*. 2022;10(2):431. doi:10.3390/biomedicines10020431

32. Xia X, Zhang Z, Zhu C, et al. Neutrophil extracellular traps promote metastasis in gastric cancer through TGF-β signaling. *Nat Commun.* 2022;13(1):4637. doi:10.1038/s41467-022-28492-5
33. Lyman GH, Yau L, Nakov R, Krendyukov A. Overall survival and risk of second malignancies with cancer chemotherapy and G-CSF support. *Ann Oncol.* 2018;29(9):1903-1910. doi:10.1093/annonc/mdy311
34. Jabagi MJ, Vey N, Goncalves A, Le Tri T, Zureik M, Dray-Spira R. Risk of secondary hematologic malignancies associated with breast cancer chemotherapy and G-CSF support: A nationwide population-based cohort. *Int J Cancer*. 2021;148(2):375-384. doi:10.1002/ijc.33216
35. Calip GS, Moran KM, Sweiss KI, et al. Myelodysplastic syndrome and acute myeloid leukemia after receipt of granulocyte colony-stimulating factors in older patients with non-Hodgkin lymphoma. *Cancer*. 2019;125(7):1143-1154. doi:10.1002/cncr.31914
36. Averin A, Silvia A, Lamerato L, et al. Risk of chemotherapy-induced febrile neutropenia in patients with metastatic cancer not receiving granulocyte colony-stimulating factor prophylaxis in US clinical practice. *Support Care Cancer*. 2021;29(4):2179-2186. doi:10.1007/s00520-020-05715-3
37. Link H, Kerkmann M, Holtmann L, Ortner P; Working Groups Supportive Care (ASORS now AGSMO) and Medical Oncology (AIO) within the German Cancer Society (DKG). G-CSF guideline adherence in Germany, an update with a retrospective and representative sample survey. *Support Care Cancer*. 2019;27(4):1459-1469. doi:10.1007/s00520-018-4481-x
38. Barni S, Lorusso V, Giordano M, et al. A prospective observational study to evaluate G-CSF usage in patients with solid tumors receiving myelosuppressive chemotherapy in Italian clinical oncology practice. *Med Oncol*. 2014;31(1):797. doi:10.1007/s12032-013-0797-z
39. Barnes G, Pathak A, Schwartzberg L. G-CSF utilization rate and prescribing patterns in United States: associations between physician and patient factors and GCSF use. *Cancer Med*. 2014;3(6):1477-1484. doi:10.1002/cam4.344\
40. Kumar A, Taghi Khani A, Sanchez Ortiz A, Swaminathan S. GM-CSF: A Double-Edged Sword in Cancer Immunotherapy. *Front Immunol*. 2022;13:901277. Published 2022 Jul 5. doi:10.3389/fimmu.2022.901277
41. Elsayed A, Elsayed B, Elmarasi M, et al. Thrombopoietin Receptor Agonists in Post-Hematopoietic Cell Transplantation Complicated by Prolonged Thrombocytopenia: A

Comprehensive Review. *Immunotargets Ther*. 2024;13:461-486. Published 2024 Sep 13. doi:10.2147/ITT.S463384

42. McDermott DH, Velez D, Cho E, et al. A phase III randomized crossover trial of plerixafor versus G-CSF for treatment of WHIM syndrome. *J Clin Invest*. 2023;133(19):e164918. Published 2023 Oct 2. doi:10.1172/JCI164918

43. Hughes JH, Tong DMH, Burns V, et al. Clinical decision support for chemotherapy-induced neutropenia using a hybrid pharmacodynamic/machine learning model. *CPT Pharmacometrics Syst Pharmacol*. 2023;12(11):1764-1776. doi:10.1002/psp4.13019