

WBC Growth Factors: ASCO Guideline Update

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ABSTRACT

ASCO Guidelines provide recommendations with comprehensive review and analyses of the relevant literature for each recommendation, following the guideline development process as outlined in the *ASCO Guidelines Methodology Manual*. ASCO Guidelines follow the *ASCO Conflict of Interest Policy for Clinical Practice Guidelines*.

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PURPOSE To update the ASCO guideline on use of hematopoietic colony-stimulating factors (CSFs) in patients with cancer.

METHODS A systematic review identified randomized controlled trials (RCTs), meta-analyses, and systematic reviews that addressed use of CSFs for the prevention or treatment of neutropenic events, or for mobilization of stem cells, in adults with cancer. PubMed and the Cochrane Library were searched for articles published from September 1, 2014, to August 22, 2025. ASCO convened an Expert Panel to review the evidence and formulate recommendations.

RESULTS The updated systematic review included 33 RCTs and 16 systematic reviews. Additions to the body of evidence include approval of new CSFs and additional biosimilars, and approval of an additional CXCR4 inhibitor that may be used with CSFs for the mobilization of hematopoietic stem cells.

RECOMMENDATIONS Prophylactic use of CSFs to reduce the risk of febrile neutropenia is warranted when the risk of febrile neutropenia from chemotherapy is approximately 20% or higher and no other equally effective and safe regimen that does not require CSFs is available. For patients receiving chemotherapy with a <20% risk of febrile neutropenia, primary prophylaxis with a CSF may be warranted if patients are at a high risk of febrile neutropenia based on age, medical history, or disease characteristics. For stem-cell mobilization, CSFs may be used either alone, after chemotherapy, or in combination with plerixafor or motixafortide. The guideline also provides information about the dosing and selection of CSFs. Additional information is available at www.asco.org/supportive-care-guidelines.

ACCOMPANYING CONTENT

 Appendix
 Data Supplement

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INTRODUCTION

Neutropenia and its complications, including febrile neutropenia and infection, remain important toxicities of myelosuppressive chemotherapy.¹ Neutropenic complications require prompt evaluation and treatment with empiric

antibiotics and often require hospitalization.² Hematopoietic colony-stimulating factors (CSFs) reduce the duration and severity of neutropenia and the risk of febrile neutropenia.³ These agents have been recommended by ASCO and other organizations for patients at high risk of neutropenia based on their chemotherapy regimen or factors such as age and

TARGET POPULATION AND AUDIENCE

Target Population

Adults with solid tumors or hematologic malignancies treated with systemic antineoplastic therapy.

Target Audience

Medical oncologists, hematologists, oncology nurses, oncology pharmacists, infectious disease specialists, and adults with cancer.

comorbidities.^{4,5} CSFs also play a role in stem-cell mobilization for hematopoietic stem-cell transplantation (SCT).

ASCO first provided guidance on CSF use in 1994 and has updated this guidance several times since then, with the latest update conducted in 2015.⁵ The current guideline updates and builds upon the previous reviews of the literature and provides guidance regarding the appropriate use of CSFs in adults receiving systemic antineoplastic therapy for cancer.

GUIDELINE QUESTIONS

This guideline update addresses seven overarching clinical questions pertaining to adults receiving systematic antineoplastic therapy for a solid tumor or hematologic malignancy: (1) What factors should influence the decision to administer primary prophylaxis of febrile neutropenia with a CSF? (2) What factors should influence the decision to administer secondary prophylaxis of febrile neutropenia with a CSF? (3) Are there circumstances in which CSFs may be administered for the treatment of febrile neutropenia? (4) What is the role of CSFs as adjuncts to progenitor-cell transplantation? (5) Should CSFs be avoided in patients receiving concomitant chemotherapy and radiation therapy? (6) Do CSFs differ in efficacy or safety? (7) What are recommendations for the initiation, duration, dosing, and administration of CSFs?

METHODS

Guideline Development Process

This systematic review-based guideline product was developed by a multidisciplinary Expert Panel, which included a patient representative and an ASCO guidelines staff member with health research methodology expertise (Appendix Table A1, online only).

The recommendations were developed by using a systematic review of evidence published between September 1, 2014, and August 22, 2025. PubMed and the Cochrane Library were searched for randomized controlled trials (RCTs), systematic

reviews, and meta-analyses. Articles were selected for inclusion in the systematic review based on the following criteria:

- Population: Adults with solid tumors or hematologic malignancies treated with systemic antineoplastic therapy
- Interventions: Granulocyte CSFs (G-CSFs) and granulocyte macrophage CSFs (GM-CSFs), including biosimilars
- Comparisons: Placebo, usual care, or different type or dose of CSF
- Outcomes: Neutropenia- and infection-related outcomes, adverse events (AEs), stem-cell mobilization

Articles were excluded from the systematic review if they were (1) meeting abstracts not subsequently published in peer-reviewed journals; (2) editorials, commentaries, letters, news articles, case reports, and narrative reviews; and (3) published in a non-English language. This guideline also does not address trilaciclib, a CDK 4/6 inhibitor that has been approved by the US Food and Drug Administration (FDA) to decrease the incidence of chemotherapy-induced myelosuppression in adults receiving certain types of chemotherapy for extensive-stage small cell lung cancer. Trilaciclib is addressed in the ASCO-Ontario Health guideline on systemic therapy for small-cell lung cancer.⁶

Two panel meetings were held, one of which was a full-day, in-person meeting. Members were asked to provide ongoing input on the updated guideline development protocol, quality and assessment of the evidence, generation of recommendations, draft content, as well as review and approve drafts during the entire development of the guideline. ASCO staff met routinely with the Expert Panel co-chairs and corresponded with the panel via e-mail to coordinate the process to completion. Ratings for strength of the recommendation and evidence quality are provided with each recommendation, defined in Appendix Table A2. The quality of the evidence for each outcome was assessed using the Cochrane Risk of Bias tool and elements of the GRADE quality assessment and recommendations development process.^{7,8} GRADE quality assessment labels (ie, high, moderate, low, very low) were assigned for each outcome by the project methodologist in collaboration with the Expert Panel co-chairs and reviewed by the full Expert Panel. All funding for the administration of the project was provided by ASCO.

Guideline Review and Approval

The draft recommendations were released to the public for open comment from May 1 through May 15, 2025. Response categories of “Agree as written,” “Agree with suggested modifications,” and “Disagree. See comments” were captured for every recommendation. Seven reviews were received, and the percentage of respondents who agreed or agreed with suggested modifications ranged from 83% to 100% across recommendations. Expert Panel members reviewed comments from all sources and determined whether to maintain original draft recommendations,

revise with minor language changes, or consider major recommendation revisions.

The draft was submitted to four external reviewers with content expertise. Comments were reviewed by the Expert Panel, and all changes were incorporated into the final manuscript prior to ASCO Evidence Based Medicine Committee (EBMC) review and approval. All ASCO guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO EBMC before submission to the *Journal of Clinical Oncology* for editorial review and consideration for publication.

Guideline Updating

The ASCO Expert Panel and guidelines staff will work with co-chairs to keep abreast of any substantive updates to the guideline. Based on a formal review of the emerging literature, ASCO will determine the need to update. The ASCO Guidelines Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the guideline update process. This is the most recent information as of the publication date.

RESULTS

Characteristics of Studies Identified in the Updated Literature Search

The updated literature search identified 414 publications. After applying the eligibility criteria, 49 publications (33 RCTs and 16 systematic reviews) were included and formed the evidentiary basis for the new and/or updated guideline recommendations.^{9-30,31-57} No new, eligible publications were identified for the question on use of CSFs for the treatment of febrile neutropenia. Included studies assessed the efficacy and safety of several new CSFs, including additional biosimilars of filgrastim and pegfilgrastim, as well as two novel agents, eflapegrastim and efbemalenogragstim. Characteristics and results of the included studies are provided in the Data Supplement (online only).

Evidence Quality Assessment

The quality of evidence was assessed for each outcome of interest. This rating includes factors such as study design, consistency of results, directness of evidence, precision, publication bias, and magnitude of effect, assessed by one reviewer. Evidence quality ratings accompany each recommendation and are illustrated in greater detail in the Data Supplement. Refer to Appendix [Table A2](#) for definitions for the quality of the evidence, and the Methodology Manual for more information.

RECOMMENDATIONS

All recommendations are available in [Table 1](#).

WHAT FACTORS SHOULD CONTRIBUTE TO DECISIONS REGARDING PRIMARY PROPHYLAXIS OF FEBRILE NEUTROPENIA WITH A CSF?

Literature Review Update and Analysis

Fifteen publications (seven RCTs and eight systematic reviews) addressed the risks and benefits of primary prophylaxis with a CSF versus no CSF or different CSF use.^{11,12,19,20,24,25,30,32,39,42,44-46,51,60} Compared with no CSF, primary prophylaxis with a CSF decreased the risk of febrile neutropenia from 68.8% to 1.2% in patients with early-stage breast cancer treated with docetaxel and cyclophosphamide⁶⁰; decreased the risk of grade 3 or 4 neutropenia from 11.6% to 1.2% in patients with non-small cell lung cancer (NSCLC) treated with adjuvant chemotherapy⁴⁴ and from 5.7% to 2.4% in patients with advanced colorectal cancer treated with bevacizumab plus first-line chemotherapy⁴²; and decreased the duration of severe neutropenia from 3.9 days to 1.3 days in patients with stages II to IV breast cancer treated with docetaxel and doxorubicin.²⁰ In a 2019 meta-analysis, pegfilgrastim and filgrastim were each more effective than placebo for reducing the risk of febrile neutropenia.⁵¹

The most common adverse effect of CSFs is bone pain. A 2021 systematic review noted that the frequency of bone pain among CSF-treated patients varies, but may range from 25% to 38%.³² A three-arm RCT evaluated naproxen 500 mg twice a day, loratadine 10 mg once a day, and no prophylaxis for bone pain in CSF-treated patients with newly diagnosed breast cancer. The primary outcome of all-grade bone pain did not differ significantly across study arms,³⁰ although some secondary bone pain outcomes improved in the naproxen and loratadine arms. Treatment-related AEs and discontinuations were less common with loratadine than with naproxen. This trial builds upon earlier findings showing reductions in bone pain with naproxen.⁶¹

A 2018 meta-analysis of RCTs in solid tumors or malignant lymphoma treated with conventional-dose chemotherapy assessed mortality and risk of second malignancies in relation to CSF use.³⁹ In studies where all patients received the same chemotherapy regimen, mortality was similar with and without CSFs (relative risk [RR], 0.97 [95% CI, 0.93 to 1.01]; 16 studies). In an analysis not restricted to patients who received the same chemotherapy regimen, risk of secondary malignancies was higher among those receiving CSFs (RR, 1.85 [95% CI, 1.19 to 2.88]).

The question of whether the risk of febrile neutropenia associated with specific chemotherapy regimens differs in RCTs and observational studies was explored by a 2016 meta-analysis.⁴⁵ Cumulative incidence of febrile neutropenia for specific regimens tended to be higher in observational studies than in RCTs (adjusted odds ratio [OR], 1.74; 95% CI, 1.15 to 2.62). The authors noted that a 13%

TABLE 1. Summary of Recommendations

Clinical Question	Recommendation
<i>General Note.</i> The following recommendations (strong or conditional/weak) and terminology (Data Supplement) represent reasonable options for patients depending on clinical circumstances and in the context of individual patient preferences. Recommended care should be accessible to patients whenever possible.	
What factors should influence the decision to administer primary prophylaxis of febrile neutropenia with a CSF?	1.1. Patients should be offered primary prophylaxis with a G-CSF when the risk of febrile neutropenia, secondary to a chemotherapy regimen, is equal to or greater than approximately 20%, unless an alternative chemotherapy regimen with comparable efficacy and safety that does not require G-CSF is available. (Evidence quality: High; Strength of recommendation: Strong) 1.2. Among patients who receive chemotherapy with a lower risk of febrile neutropenia, primary prophylaxis with a G-CSF should be offered if a patient is at high risk of complications from febrile neutropenia based on age, comorbidities, or disease characteristics, and no alternative chemotherapy regimen with comparable efficacy and safety that does not require G-CSF is available. (Evidence quality: Low; Strength of recommendation: Conditional; Box 1) 1.3. If G-CSF is not affordable or available, antibiotic prophylaxis may be offered. (Evidence quality: Low; Strength of recommendation: Conditional) <i>Qualifying statement for Recommendation 1.3:</i> Antibiotic prophylaxis is not a preferred option due to the risk of antimicrobial resistance, disturbance of gut microbiome, Clostridioides difficile infection, and other adverse effects, which may outweigh the benefits of antibiotic use in many cases.
What factors should influence the decision to administer secondary prophylaxis of febrile neutropenia with a CSF?	2.1. Secondary prophylaxis with a CSF is recommended for patients who experienced a neutropenic complication from a previous cycle of chemotherapy (for which primary prophylaxis was not received), in which a reduced dose or treatment delay may compromise cure rates or survival outcomes. In many clinical situations, dose reduction or delay may be a reasonable alternative or additional strategy. (Evidence quality: Low; Strength of recommendation: Conditional)
Are there circumstances in which CSFs may be administered for the treatment of febrile neutropenia?	3.1. A CSF should not be routinely used for patients with neutropenia who are afebrile. (Evidence quality: High; Strength of recommendation: Strong) 3.2. A CSF should not be routinely used as adjunctive treatment with antibiotic therapy for patients with fever and neutropenia. (Evidence quality: High; Strength of recommendation: Strong) 3.3. A CSF may be offered in patients with fever and neutropenia who are at high risk for infection-associated complications or who have prognostic factors that are predictive of poor clinical outcomes. (Evidence quality: Low; Strength of recommendation: Conditional; Box 2)
What is the role of CSFs as adjuncts to progenitor-cell transplantation?	4.1. A CSF should be used alone, after chemotherapy, or in combination with a CXCR4 inhibitor (plerixafor or motixafortide), to mobilize peripheral-blood progenitor cells. Choice of mobilization strategy depends in part on the type of cancer and type of transplantation. (Evidence quality: High; Strength of recommendation: Strong) 4.2. A CSF should be administered after autologous SCT to reduce the duration of severe neutropenia. (Evidence quality: High; Strength of recommendation: Strong) 4.3. A CSF may be administered after allogeneic SCT to reduce the duration of severe neutropenia. (Evidence quality: Low; Strength of recommendation: Conditional)
Should CSFs be avoided in patients receiving concomitant chemotherapy and radiation therapy?	5.1. CSFs are not recommended in patients receiving concomitant chemotherapy and radiation therapy, particularly involving the mediastinum. (Evidence quality: Low; Strength of recommendation: Conditional) <i>Note for Recommendation 5.1:</i> There is little evidence regarding use of CSFs in patients receiving radiation therapy alone.
Do CSFs differ in efficacy or safety?	6.1. Filgrastim, pegfilgrastim, efilgrastim, and biosimilars can be used for prophylaxis or treatment of febrile neutropenia. The choice of agent depends on cost, patient convenience, availability, accessibility, health system context, disease subtype, and treatment regimen. (Evidence quality: High; Strength of recommendation: Strong)
What are recommendations for the initiation, duration, dosing, and administration of CSFs?	Recommendations for the initiation, duration, dosing, and administration of CSFs are provided in Table 2 .

NOTE. The strength of the recommendation is defined as follows: Strong: In recommendations for an intervention, the desirable effects of an intervention outweigh its undesirable effects. In recommendations against an intervention, the undesirable effects of an intervention outweigh its desirable effects. All or almost all informed people would make the recommended choice for or against an intervention. Conditional/weak: In recommendations for an intervention, the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists. In recommendations against an intervention, the undesirable effects probably outweigh the desirable effects, but appreciable uncertainty exists. Most informed people would choose the recommended course of action, but a substantial number would not.

Abbreviations: CSF, colony-stimulating factor; G-CSF, granulocyte colony-stimulating factor; SCT, stem-cell transplantation.

cumulative incidence of febrile neutropenia in an RCT would translate into a 20% cumulative incidence of febrile neutropenia in the real world.

CSF prophylaxis in patients receiving chemotherapy with an intermediate febrile neutropenia risk (10%–20%)

was assessed in a 2023 cluster-randomized trial among patients receiving first-line therapy for breast cancer, colorectal cancer, or NSCLC.²⁴ Study sites were randomized to standard order entry for primary prophylaxis or to an alert not to prescribe. Standard order entry increased the use of primary prophylaxis (37.1% v 9.9%)

BOX 1. PATIENT RISK FACTORS FOR FEBRILE NEUTROPENIA^{58,59}

In addition to chemotherapy regimen and type of malignancy, consider these factors when estimating a patient's overall risk of febrile neutropenia.

- Age 65 years or older or frailty based on geriatric assessment
- Advanced disease
- Previous chemotherapy or radiation therapy
- Preexisting neutropenia or bone marrow involvement with tumor
- Active or recent infection
- Colonization with multidrug-resistant organisms
- Open wounds or recent surgery
- Poor performance status
- Poor nutritional status or low BMI
- Poor renal function
- Liver dysfunction, most notably elevated bilirubin
- Cardiovascular disease
- HIV
- Multiple comorbid conditions

but did not reduce the risk of febrile neutropenia (3.7% v 3.7%).

Finally, an RCT of 458 patients with early breast cancer treated with docetaxel and cyclophosphamide compared CSF with antibiotics for primary prophylaxis.¹² The composite outcome of febrile neutropenia and nonfebrile neutropenia treatment-related hospitalization did not differ significantly between study arms (risk difference, -6.7% [95% CI, -13.5 to 0.1]). However, febrile neutropenia risk, a secondary outcome, was lower in the G-CSF arm (5.7%) than in the antibiotic arm (15.8%).

Clinical Interpretation

There was some debate among the panel members regarding evidence for the 20% cutoff threshold to define the eligibility for primary prophylaxis. While this threshold has been consistently used in all previous guidelines from multiple societies, the Panel sought direct supporting evidence. The strongest evidence came from a 2023 cluster-randomized trial,²⁴ which showed that decreasing the threshold below 20% increased G-CSF use without improving outcomes such as the risk of febrile neutropenia. Based on these findings, the Panel recommendations maintain the 20% threshold and discourage prophylactic G-CSF when febrile neutropenia risk is <20%, unless other febrile neutropenia risk factors are present.

The Panel also recognizes that categorizing a given chemotherapy regimen into a certain percentage for the risk of

febrile neutropenia is based on trial results, and the use of G-CSF prophylaxis in new trials will have already been built into the protocols. Determining which risk factors, to what extent, and in what combination would substantially increase the febrile neutropenia risk to warrant G-CSF prophylaxis remains a subjective decision. Thus, the Expert Panel reiterates the statement of the 2015 guideline that, "The ASCO Panel looks forward to reviewing validated and tested, user-friendly risk-prediction tools when they are available, but at present, none can be fully recommended."

A 2021 trial¹² failed to show the superiority of prophylactic G-CSF over prophylactic ciprofloxacin among patients receiving chemotherapy for breast cancer and found that prophylactic G-CSF was not a cost-effective option. The Panel acknowledges that this provides evidence to use antibiotic prophylaxis where G-CSF is not accessible or affordable. However, the Panel cautions against associated risks, including the emergence of multidrug-resistant organisms, disruption of microbiome balance and diversity, and increased risk of *Clostridioides difficile* infection. With the introduction of biosimilars, the affordability of G-CSF is expected to improve, and G-CSF remains the preferred option over antibiotics.

WHAT FACTORS SHOULD INFLUENCE DECISIONS REGARDING SECONDARY PROPHYLAXIS OF FEBRILE NEUTROPENIA WITH A CSF?

Literature Review Update and Analysis

A single, 2015 trial was included in the updated systematic review.³³ The trial compared G-CSF with dose delay or dose reduction among 407 women with breast cancer who experienced a first neutropenic event. The likelihood of receiving at least 85% of the planned relative dose intensity was higher in the G-CSF arm than in the comparison arm (75% v 50%, $P < .0001$). Additional evidence came from a secondary analysis of an RCT that compared filgrastim with placebo in patients receiving chemotherapy for small cell lung cancer.^{62,63} Placebo-arm patients who developed febrile neutropenia crossed over to open-label filgrastim, and those patients experienced lower cumulative incidence of grade 4 neutropenia and shorter duration of grade 4 neutropenia than patients who remained in the placebo arm.⁶³ The incidence of febrile neutropenia after crossing from the placebo arm to the open-label filgrastim arm ranged from 6% to 21% across chemotherapy cycles.

Clinical Interpretation

New evidence continues to demonstrate that secondary prophylaxis with G-CSF reduces neutropenic events and helps maintain the dose intensity of chemotherapy. However, there is no evidence to date that secondary prophylaxis improves disease-free survival or overall survival (OS). Thus, the Panel reiterates that secondary prophylaxis with G-CSF can be used when maintaining dose intensity is of clinical importance. In other situations, dose reduction and/or

treatment delay are reasonable alternatives when maintaining dose intensity is not necessary.

ARE THERE CIRCUMSTANCES IN WHICH CSFs MAY BE USED FOR THE TREATMENT OF FEBRILE NEUTROPENIA?

Literature Review Update and Analysis

The updated literature review identified no new eligible publications. For patients with neutropenia and without fever, the strength of the recommendation against routine CSF increased in the 2000 ASCO guideline, based on a 1997 RCT of G-CSF versus placebo in patients with severe neutropenia and without fever.⁶⁴ Although G-CSF reduced the time to neutrophil recovery, it did not affect incidence of hospitalization, length of hospital stay, duration of parenteral antibiotics, or number of culture-positive infections.

For patients with febrile neutropenia, a meta-analysis described in the 2015 guideline reported that antibiotics plus a CSF did not reduce overall mortality compared with antibiotics alone (hazard ratio, 0.74 [95% CI, 0.47 to 1.16]).⁶⁵ However, the addition of a CSF shortened the duration of neutropenia, fever, and antibiotic use, and reduced the likelihood of prolonged (>10 days) hospital stays.

Clinical Interpretation

The Panel reiterates that CSFs should not be routinely used for patients without fever, as neutropenia alone does not require treatment. CSFs should also not be routinely used before chemotherapy solely to improve the neutrophil counts. Even for patients with febrile neutropenia, routine adjunctive use of CSF in addition to antibiotics is not recommended, as it does not improve mortality and only slightly reduces hospitalization length of stay. However, patients with fever at a high risk of poor clinical outcomes from febrile neutropenia may be offered CSFs. **Box 2** provides examples of factors associated with increased risk. Physicians should use their clinical judgment to decide whether these or other factors are sufficient to justify treatment with CSF in this context, as no validated risk-prediction tool for this purpose currently exists. Treatment of febrile neutropenia, including antimicrobial selection and outpatient treatment, is addressed in a separate ASCO guideline.²

WHAT IS THE ROLE OF CSFs AS ADJUNCTS TO PROGENITOR-CELL TRANSPLANTATION?

Literature Review Update and Analysis

Stem-Cell Mobilization

In the setting of stem-cell mobilization, the effects of G-CSF alone or in combination with other agents were assessed in three meta-analyses^{36,38,50} and three RCTs.^{16,22,27} Two CXCR4 inhibitors, plerixafor and motixafortide, each increase the yield of CD34⁺ cells when used in combination with G-CSF,

BOX 2. PATIENT RISK FACTORS FOR POOR CLINICAL OUTCOMES FROM FEBRILE NEUTROPENIA OR INFECTION²

- Sepsis syndrome
- Age 65 years or older or frailty based on geriatric assessment
- Severe neutropenia (absolute neutrophil count <100/mcL)
- Neutropenia expected to be more than 7 days in duration
- Prior episode of febrile neutropenia
- Pneumonia
- Invasive fungal infection
- Other clinically documented infections
- Hospitalization at the time of fever

relative to G-CSF alone. In a 2024 meta-analysis of RCTs and observational studies in patients with multiple myeloma and lymphoma, the likelihood of reaching a predetermined yield of CD34⁺ cells was 64.9% with a combination of plerixafor and G-CSF, compared with 33.8% with G-CSF alone ($P < .00001$).³⁶ The combination of plerixafor and G-CSF did not increase the frequency of all-grade treatment-emergent AEs relative to G-CSF alone. Information for grade 3 or 4 AEs was not provided. A benefit of motixafortide in combination with G-CSF was reported in a phase III RCT of 122 patients with multiple myeloma.¹⁶ The proportion of patients collecting $\geq 6 \times 10^6$ CD34⁺ cell kg⁻¹ within two apheresis procedures was 92.5% with motixafortide and G-CSF compared with 26.2% with G-CSF plus placebo. There were no grade 4 or 5 AEs, but the frequency of grade 3 AEs was higher in the motixafortide arm (27.5% v 4.8%).

Studies also reported on the combination of chemotherapy with G-CSF for stem-cell mobilization. A meta-analysis of RCTs and observational data reported that cyclophosphamide plus G-CSF improved stem-cell yield in multiple myeloma but also increased the risk of admission and fever compared with G-CSF alone.⁵⁰ A network meta-analysis of RCTs also reported improved stem-cell yield with chemotherapy (cyclophosphamide or intermediate-dose cytarabine) plus G-CSF in multiple myeloma.³⁸

Use of CSFs After Hematopoietic SCT

The updated literature review included two RCTs of G-CSF after hematopoietic SCT, neither of which changed previous recommendations. In the autologous setting, a noninferiority trial of G-CSF starting 3 days post-transplant compared with no G-CSF demonstrated a 4-day difference in median length of stay favoring the G-CSF arm, resulting in early closure of the trial.²³ Patients in the G-CSF arm also had fewer days of febrile neutropenia and fewer days on antibiotics. There was no significant difference between study arms in platelet recovery, documented infections, hospital readmissions, or 1-year OS.

In the allogeneic setting, post-transplant use of a CSF was added as an option in the 2015 guideline. A 2006 meta-analysis of RCTs found that CSF use after allogeneic SCT reduced the risk of documented infections and did not have a statistically significant effect on grade 2 to 4 acute graft-versus-host disease (GVHD) or treatment-related mortality.⁶⁶ These results differ from some large, observational studies, which have reported that use of CSFs after allogeneic SCT may increase the risk of adverse effects such as GVHD.⁶⁷⁻⁶⁹

Clinical Interpretation

For peripheral blood stem-cell mobilization, a CXCR4 inhibitor, either motixafortide or plerixafor, in combination with G-CSF is recommended, as both agents are associated with higher rates of successful collection compared with G-CSF alone. These agents have not been directly compared in a randomized trial, so the choice of agent should be based on institutional experience, availability, and patient-specific factors. Mobilization with chemotherapy (eg, cyclophosphamide, intermediate-dose cytarabine) plus G-CSF also yields higher CD34⁺ cell collections than G-CSF alone, but at the cost of increased toxicities associated with chemotherapy, including hospitalization and fever; this strategy remains an appropriate option in selected patients. Thus, the optimal mobilization strategy depends on several patient- and disease-specific considerations.

Recent data support the administration of G-CSF after autologous hematopoietic cell transplantation in most patients, given that its addition shortens time to neutrophil engraftment, the number of days of febrile neutropenia, and hospital length of stays. After allogeneic hematopoietic cell transplantation, G-CSF may lower risk of infection, while safety concerns regarding GVHD have not been consistently demonstrated across studies. Therefore, CSFs may be used in this setting as well.

SHOULD CSFs BE AVOIDED IN PATIENTS RECEIVING CONCOMITANT CHEMOTHERAPY AND RADIATION THERAPY?

Literature Review Update and Analysis

The literature review identified two RCTs.^{54,57} A 2025 trial compared pegylated recombinant human granulocyte colony-stimulating factor (PEG-rhG-CSF) with no PEG-rhG-CSF among 88 patients undergoing chemoradiotherapy for nasopharyngeal cancer.⁵⁴ The primary outcome of interest was grade 3 or 4 neutropenia, and incidence was lower in the pegfilgrastim arm (grade 3: 0 v 13.6%, $P = .03$, no grade 4 events), with 34.1% in the pegfilgrastim arm experiencing mild bone pain. No patients developed febrile neutropenia in either arm. Platelet levels did not differ significantly between study arms. A 2021 trial randomly assigned 58 patients undergoing chemoradiotherapy for cervical cancer to PEG-rhG-CSF (40 participants) or no PEG-rhG-CSF (18 patients).⁵⁷ The

small number of patients in the control arm and some imbalances in baseline characteristics make it difficult to draw firm conclusions, but patients in the intervention arm had a lower incidence of grade 3 or 4 neutropenia. Decreased platelets (grade not reported) occurred in one patient in the intervention arm and no patients in the control arm. These trials add to a 1995 RCT of GM-CSF in patients with limited-stage small cell lung cancer treated with chemoradiotherapy. Patients in the GM-CSF arm reported an increased frequency of grade 3 and 4 thrombocytopenia.⁷⁰

Clinical Interpretation

The major concern regarding CSF use with concomitant chemotherapy and radiation therapy is the potential for deleterious effects on platelet counts, as described in a 1995 RCT.⁷⁰ In addition, there is little evidence of clinical benefit in this context, including reduction in the incidence of febrile neutropenia. Secondary analyses of two RCTs were reviewed in a 2023 Ontario Health (Cancer Care Ontario)-ASCO guideline on systemic therapy for small cell lung cancer.⁶ In both studies, patients with limited-stage small cell lung cancer were randomly assigned to chemoradiotherapy with once-daily versus twice-daily radiation; G-CSF use was based on local protocols and was not randomly assigned. The first study was a phase II trial in which 13 of 38 patients received G-CSF. In the G-CSF-treated patients, 54% experienced grade 3 or 4 thrombocytopenia and 38% experienced grade 3 or 4 anemia.⁷¹ In the larger, phase III CONVERT trial, 180 of 487 received G-CSF prophylaxis, 60 as primary prophylaxis and 120 as secondary prophylaxis.⁷² Across all chemotherapy cycles, risk of febrile neutropenia was 17% without G-CSF, 18% with primary prophylaxis, and 35% with secondary prophylaxis. Blood transfusions were more common in both G-CSF groups, occurring in 53% and 50% of the primary and secondary prophylaxis groups, respectively, compared with 31% in the no G-CSF group. OS and progression-free survival were similar regardless of G-CSF use. Although firm conclusions cannot be drawn from these studies due to the nonrandomized use of G-CSF, these studies indicate potential adverse effects of G-CSF use during chemoradiotherapy without clear evidence of benefit.

G-CSF use was randomly assigned in the 2025 trial of PEG-rhG-CSF versus no PEG-rhG-CSF among patients undergoing chemoradiotherapy for nasopharyngeal cancer.⁵⁴ The trial supported reduction in neutropenia through use of G-CSF, but not in febrile neutropenia, which is the primary outcome of interest.

IS THERE A PREFERRED CSF FOR PROPHYLAXIS OR TREATMENT OF FEBRILE NEUTROPENIA?

Literature Review Update and Analysis

Since the previous guideline update, additional G-CSF biosimilars have become available, with meta-analyses supporting their efficacy and safety relative to reference

biologics.^{41,53,73} Studies have also continued to compare the efficacy of short-acting G-CSF and long-acting (PEGylated) forms, with mixed results. A 2021 meta-analysis of 10 RCTs conducted in China among adults with cancer found no difference in incidence of febrile neutropenia between PEGylated G-CSF and G-CSF (RR, 0.82 [95% CI, 0.57 to 1.17]). PEGylated G-CSF was associated with a lower risk of severe neutropenia (RR, 0.86 [95% CI, 0.76 to 0.96]) and bone and/or muscle pain (RR, 0.75 [95% CI, 0.58 to 0.98]).⁴⁹ By contrast, a 2019 meta-analysis evaluating 11 CSFs found PEGylated G-CSF was associated with a lower risk of febrile neutropenia than G-CSF in both direct pairwise meta and network meta-analysis, with no significant differences in severe neutropenia or bone pain.⁵¹ Finally, a 2020 meta-analysis of nine breast cancer RCTs found no significant differences in incidence and duration of grade 3 or worse neutropenia or bone and/or muscle pain between the two formulations.³⁵

Two new long-acting agents—eflapegrastim-xnst and efbemalenogristim alfa—have been compared with pegfilgrastim and/or filgrastim. In two RCTs of patients with breast cancer, eflapegrastim-xnst was noninferior to pegfilgrastim for duration of severe neutropenia.^{14,43} However, grade 3 or 4 AEs were numerically higher with eflapegrastim-xnst than with pegfilgrastim in both studies (14% v 7%¹⁴ and 18% v 11%⁴³). Efbemalenogristim alfa was noninferior to filgrastim in phase III trial,⁵⁶ noninferior to pegfilgrastim in a phase II trial,²¹ and superior to placebo in a phase III trial, with respect to duration of moderate and/or severe neutropenia in patients being treated for breast cancer.²⁰ Serious AEs were similar between fixed-dose (20 mg) efbemalenogristim alfa and filgrastim (5.0% v 6.7%).⁵⁶ Eflapegrastim-xnst and efbemalenogristim alfa have both been approved by the FDA, but efbemalenogristim alfa was not yet commercially available in the United States at the time of writing this guideline.

Clinical Interpretation

Choice of G-CSF agents (short-acting v PEGylated) and among biosimilar products should be based on patient preference, convenience, cost, availability, and health system context. There is no strong evidence-based rationale to prefer one approved agent over another.

WHAT ARE THE RECOMMENDATIONS FOR THE INITIATION, DURATION, DOSING, AND ADMINISTRATION OF CSFs?

Literature Review Update and Analysis

Two RCTs compared reduced doses of PEGylated rhG-CSF with the 6-mg dose commonly used in the United States. In a trial conducted in China among patients receiving adjuvant chemotherapy for breast cancer, the 3-mg dose was noninferior to the 6-mg dose with respect to ANC recovery before the second chemotherapy cycle.⁵⁵ A phase II dose-finding trial conducted in Japan evaluated three doses of

PEG-rhG-CSF, 1.8 mg, 3.6 mg, and 6 mg, in patients receiving chemotherapy for breast cancer, reporting durations of severe neutropenia of 2.2 days, 1.5 days, and 1.4 days, respectively, concluding that the 3.6-mg dose may be safe and effective.⁴⁰

A noninferiority trial among 466 patients with early breast cancer assessed different durations of filgrastim for primary prophylaxis.¹³ For the primary composite outcome of either febrile neutropenia or treatment-related hospitalization, 5 days of filgrastim was noninferior to 7–10 days of filgrastim.

Timing of initiation of G-CSF was evaluated in two RCTs.^{29,52} Sixty patients undergoing adjuvant docetaxel, doxorubicin, and cyclophosphamide chemotherapy for breast cancer started filgrastim on either day 2 or day 5 after chemotherapy.²⁹ Across all cycles, patients in the day 2 arm had a lower incidence of febrile neutropenia than patients in the day 5 arm (6.4% v 22.2%, $P < .0001$). Timing of PEG-rhG-CSF (day 7 v day 3) was evaluated in a trial of 160 patients with breast cancer.⁵² In the first cycle, patients in the day 7 arm had a lower incidence of grade 3 or 4 neutropenia than patients in the day 3 arm (15.8% v 29.9%, $P = .04$). Incidence of febrile neutropenia did not differ significantly between the two arms (4.0% v 6.5%, $P = .72$).

Clinical Interpretation

The doses recommended in [Table 2](#) are consistent with product labeling in the United States. However, several practical considerations merit attention. For feasibility reasons, some patients receive same-day pegfilgrastim, which may offer reduced efficacy compared with pegfilgrastim administered 1–3 days after chemotherapy.⁷⁴ In such situations, the intent of G-CSF use (primary v secondary prophylaxis), the patient's risk of febrile neutropenia, the risk of complications, and the appropriateness of alternative strategies such as dose reduction or treatment delay should be considered. Given that the benefits of routine G-CSF use are modest, same-day administration might further diminish efficacy. More recently, an RCT presented at the 2025 Congress of the European Society for Medical Oncology compared pegfilgrastim injections at 24, 48, and 72 hours post chemotherapy and found that receiving pegfilgrastim at 72 hours post chemotherapy significantly reduced the incidence of bone pain without compromising efficacy.⁷⁵

Many patients are capable of self-administering pegfilgrastim at home, thus avoiding return to the treatment facility solely for injection. Similarly, data from recent trials support shorter filgrastim courses (5 days v 7–10 days)¹³ or lower pegfilgrastim doses^{40,55} as potentially effective strategies. These options should be considered through shared decision making between patients and their physicians since these strategies could improve quality of life and reduce costs without compromising efficacy or safety.

TABLE 2. Recommendations for the Initiation, Duration, Dosing, and Administration of CSFs

Agent	Dosing and Administration
Filgrastim, including biosimilars	Filgrastim should be started 24-72 hours after the administration of myelotoxic chemotherapy. In the setting of high-dose therapy and autologous stem-cell rescue, filgrastim can be started 1-5 days after administration of high-dose therapy. For peripheral blood progenitor cell mobilization, filgrastim should be started at least 4 days before the first leukapheresis procedure and continued until the last leukapheresis. In adults, the recommended filgrastim dose is 5 µg/kg once per day for all clinical settings other than peripheral blood stem-cell mobilization. In the setting of peripheral blood stem-cell mobilization, a dose of 10 µg/kg once per day may be preferable. The preferred route of filgrastim administration is subcutaneous.
Pegfilgrastim, including biosimilars	Pegfilgrastim 6 mg should be given once per chemotherapy cycle, 24-72 hours after chemotherapy. Pegfilgrastim is also available in a timed auto-inject device that delivers 6 mg of pegfilgrastim subcutaneously, 27 hours after it is placed on the skin and activated. Pegfilgrastim is not currently indicated for stem-cell mobilization. The 6-mg formulation should not be used in infants, children, or small adolescents who weigh <45 kg.
Eflapegrastim-xnst	Eflapegrastim-xnst 13.2 mg should be given once per chemotherapy cycle, approximately 24 hours after chemotherapy. The route of administration is subcutaneous. Eflapegrastim-xnst is not currently indicated for stem-cell mobilization.
Sargramostim	Because sargramostim (GM-CSF) has been licensed specifically for use in mobilization and after transplantation of autologous PBPCs, after autologous or allogeneic bone marrow transplantation, and for AML, the manufacturer's instructions for administration are limited to those clinical settings. GM-CSF should be initiated on the day of bone marrow infusion, not <24 hours after the last chemotherapy, and 12 hours after the most recent radiotherapy. GM-CSF should be continued until an ANC >1.5 × 10 ⁹ /L for 3 consecutive days. The drug should be discontinued early or the dose reduced by 50% if the ANC increases to > 20 × 10 ⁹ /L. The recommended dose for adults is 250 µg/m ² once per day.

Abbreviations: ANC, absolute neutrophil count; GM-CSF, granulocyte macrophage colony-stimulating factor; PBPCs, peripheral blood progenitor cells.

LIMITATIONS OF THE EVIDENCE AND PRIORITIES FOR FUTURE RESEARCH

The Panel believes that the “risk factors” that elevate a patient’s risk to develop complications from febrile neutropenia have not been soundly studied. A validated tool to determine who is at a higher risk to develop complications from febrile neutropenia may help improve the risk benefit of CSFs even more, and to personalize the therapy.⁷⁶ The Expert Panel encourages more research into “biomarkers” or personalization of risks of febrile neutropenia and its complications that enables physicians to tailor the use of CSF even more judiciously. With several biosimilar options, the price of CSF products has fallen in several countries globally; however, prices remain high and unaffordable in many other regions. Future research could also further refine de-escalation opportunities with routine CSF administration.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

PATIENT AND CLINICIAN COMMUNICATION

See the Discussion Points Between Patients and Clinicians box. For additional recommendations and strategies to optimize patient-clinician communication, see Patient-Clinician Communication: ASCO Consensus Guideline.⁷⁷

PATIENT ACCESS CONSIDERATIONS

Several factors can influence a patient’s ability to access and use CSFs. Long-acting CSFs, for example, are typically administered the day after chemotherapy, which involves a return to the treatment facility. For patients in rural areas or

without ready means of transportation, this may be a barrier to care. Home administration of a short-acting CSF may be an easier option for these patients. Indeed, many patients have reported that they can also self-administer this product.

Although short-acting CSFs allow many patients to self-treat at home, home treatment is not feasible for everyone. Filgrastim and its biosimilars need to be refrigerated, and the patient or their caregivers should be able to understand and follow the instructions for home treatment. Patients who do not have the resources for at-home treatment may be offered a long-acting CSF, as discussed previously, or clinic- or hospital-based administration of a short-acting CSF.

The most appropriate type of CSF (short-acting or long-acting) will vary by patient circumstances. Patients should

DISCUSSION POINTS BETWEEN PATIENTS AND CLINICIANS

- Why am I a candidate for a WBC growth factor?
- What are the potential benefits? What are the potential risks? Are there ways to manage the risks?
- What are the alternatives if I do not want a WBC growth factor?
- How do different CSFs vary in terms of factors such as cost and ease of use?
- What considerations are important for patients with limited access to care, due to factors such as distance from the treatment facility or insurance status?

also be informed about how costs may vary across available options.

MULTIPLE CHRONIC CONDITIONS

Creating evidence-based recommendations to inform treatment of patients with additional chronic conditions, a situation in which the patient may have two or more such conditions—referred to as multiple chronic conditions (MCC)—is challenging. Patients with MCC are a complex and heterogeneous population, making it difficult to account for all of the possible permutations to develop specific recommendations for care. In addition, the best available evidence for treating index conditions, such as cancer, is often from clinical trials whose study selection criteria may exclude these patients in order to avoid potential interaction effects or confounding of results associated with MCC. As a result, the reliability of outcome data from these studies may be limited, thereby creating constraints for expert groups to make recommendations for care in this heterogeneous patient population.

As many patients for whom guideline recommendations apply present with MCC, any treatment plan needs to take into account the complexity and uncertainty created by the presence of MCC and highlights the importance of shared decision making regarding guideline use and implementation. Therefore, in consideration of recommended care for the target index condition, clinicians should review all other chronic conditions present in the patient and take those conditions into account when formulating the treatment and follow-up plan.

COST IMPLICATIONS

Cost of care has become an important consideration both for patients and health systems due to its relationship with patient outcomes. Studies have shown that patients who experience financial toxicity due to cancer treatment are at a higher risk of foregoing or delaying care, not adhering to recommended cancer treatments, decreased satisfaction with care, poor quality of life, and potentially worse survival.⁷⁸ This is even more pronounced in low- and middle-income regions, where even biosimilar CSFs can be unaffordable for many patients paying out-of-pocket.⁷⁹

Health technology assessment, including cost-effectiveness analysis, is increasingly used by payers, governments, and policymakers to inform coverage decisions for supportive care interventions such as CSFs.^{80–82} In high-income regions, these assessments can influence whether a given agent (eg, originator v biosimilar) is placed on formularies or subject to prior authorization, whereas in low- and middle-income regions, they may determine whether any CSF is available through public health systems at all.

Health technology assessment approaches can vary substantially between countries, and their outcomes depend on local willingness-to-pay thresholds, health care budget constraints, and burden-of-disease considerations. While cost-effectiveness analysis can promote efficient resource allocation, strict application in resource-limited settings may unintentionally restrict access if high upfront drug costs are weighed more heavily than long-term benefits such as reduced hospitalizations.

Discussion of cost should be an integral part of shared decision making.⁸³ Clinicians should discuss with patients the use of less expensive alternatives when practical and feasible for treatment of the patient's disease, provided there are two or more treatment options that are comparable in terms of benefits and risks.⁸³

Patient out-of-pocket costs may vary depending on insurance coverage. Coverage may be provided under either the medical or pharmacy benefit, which may have different cost-sharing arrangements. Patients should be made aware that different products may be preferred or covered by their specific insurance plan, and that even within the same insurance plan, the price may vary between different pharmacies or health care contexts (eg, hospital or clinic infusion room). When discussing financial issues and concerns, patients should be informed of any financial counseling services available to help navigate this complex and heterogeneous landscape.⁸³

GUIDELINE IMPLEMENTATION

ASCO guidelines are developed for implementation across health settings. Each ASCO guideline includes a community oncologist member on the panel. The additional role of this community oncologist member on the guideline panel is not only to assess the suitability of the recommendations for implementation in the community setting, but also to identify any other barriers to implementation that a reader should be aware of. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners, as well as survivors of cancer and caregivers, and also to provide adequate services in the context of limited resources. The guideline recommendations table and accompanying tools (available at www.asco.org/supportive-care-guidelines) were designed to facilitate implementation of recommendations. This guideline will be distributed widely. ASCO guidelines are posted on the ASCO website and most often published in the *Journal of Clinical Oncology*.

ADDITIONAL RESOURCES

For current information, including selected updates, supplements, and clinical tools and resources, visit www.asco.org/supportive-care-guidelines. The Data Supplement for this

guideline includes additional evidence tables and systematic review search details. Guideline recommendations and algorithms are also available in the free ASCO Guidelines app (available for download in the [Apple App Store](#) and [Google Play Store](#)). Listen to key recommendations and insights from panel members on the [ASCO Guidelines podcast](#). The Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the methods used to develop this guideline. Patient information is available at www.cancer.org.

ASCO welcomes your comments on this guideline, including implementation challenges, new evidence, and how this guideline impacts you. To provide feedback, contact us at guidelines@asco.org. Comments may be incorporated into a future guideline update. To submit new evidence or suggest a topic for guideline development, complete the form available at www.asco.org/guidelines.

INCLUSIVE LANGUAGE

ASCO is committed to promoting the health and well-being of all patients. ASCO guidelines are intended to apply to, and be discussed clearly and compassionately with, all patients. For this reason, guideline authors use appropriately

RELATED ASCO GUIDELINES

- Palliative Care for Patients With Cancer⁸⁴ (<https://ascopubs.org/doi/10.1200/JCO.24.00542>)
- Patient-Clinician Communication⁷⁷ (<https://ascopubs.org/doi/10.1200/JCO.2017.75.2311>)
- Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Systemic Cancer Therapy⁸⁵ (<https://ascopubs.org/doi/10.1200/JCO.23.00933>)
- Outpatient Management of Fever and Neutropenia² (<https://ascopubs.org/doi/10.1200/JCO.2017.77.6211>)
- Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression⁵⁸ (<https://ascopubs.org/doi/10.1200/JCO.18.00374>)

inclusive language. In instances in which the guideline draws upon data based on research in a specified population (eg, studies regarding women with ovarian cancer), the guideline authors describe the characteristics and results of the research as reported.

including a supplement with additional evidence tables, clinical tools and resources, and links to patient information at www.cancer.org, is available at www.asco.org/supportive-care-guidelines.

EQUAL CONTRIBUTION

B.G. and T.C. were Expert Panel co-chairs.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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EDITOR'S NOTE

This ASCO Clinical Practice Guideline Update provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information,

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REFERENCES

- Boccia R, Glaspy J, Crawford J, et al: Chemotherapy-induced neutropenia and febrile neutropenia in the US: A beast of burden that needs to be tamed? *Oncologist* 27:625-636, 2022
- Taplitz RA, Kennedy EB, Bow EJ, et al: Outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology and infectious diseases Society of America Clinical Practice Guideline update. *J Clin Oncol* 36:1443-1453, 2018
- Bennett CL, Djulbegovic B, Norris LB, et al: Colony-stimulating factors for febrile neutropenia during cancer therapy. *N Engl J Med* 368:1131-1139, 2013
- National Comprehensive Cancer Network: NCCN Guidelines Version 1.2025 Hematopoietic Growth Factors (ed 01.2025), 2024. <https://www.nccn.org>
- Smith TJ, Bohlke K, Lyman GH, et al: Recommendations for the use of WBC growth factors: American Society of Clinical Oncology Clinical Practice Guideline update. *J Clin Oncol* 33:3199-3212, 2015
- Khurshid H, Ismail N, Bian J, et al: Systemic therapy for small-cell lung cancer: ASCO-Ontario Health (Cancer Care Ontario) Guideline. *J Clin Oncol* 41:5448-5472, 2023
- Higgins J, Thomas J, Chandler J, et al (eds): *Cochrane Handbook for Systematic Reviews of Interventions* (ed 2). Chichester, United Kingdom, Wiley, 2019
- Balshem H, Helfand M, Schünemann HJ, et al: GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 64:401-406, 2011
- Blackwell K, Gascon P, Krendyukov A, et al: Safety and efficacy of alternating treatment with EP2006, a filgrastim biosimilar, and reference filgrastim: A phase III, randomised, double-blind clinical study in the prevention of severe neutropenia in patients with breast cancer receiving myelosuppressive chemotherapy. *Ann Oncol* 29:244-249, 2018
- Bozzoli V, Tisi MC, Maiolo E, et al: Four doses of unpegylated versus one dose of pegylated filgrastim as supportive therapy in R-CHOP-14 for elderly patients with diffuse large B-cell lymphoma. *Br J Haematol* 169:787-794, 2015
- Chambers P, Jani Y, Wei L, et al: Patient factors and their impact on neutropenic events: A systematic review and meta-analysis. *Support Care Cancer* 27:2413-2424, 2019
- Clemons M, Fergusson D, Joy AA, et al: A multi-centre study comparing granulocyte-colony stimulating factors to antibiotics for primary prophylaxis of docetaxel-cyclophosphamide induced febrile neutropenia. *Breast* 58:42-49, 2021
- Clemons M, Fergusson D, Simos D, et al: A multicentre, randomised trial comparing schedules of G-CSF (filgrastim) administration for primary prophylaxis of chemotherapy-induced febrile neutropenia in early stage breast cancer. *Ann Oncol* 31:951-957, 2020
- Cobb PW, Moon YW, Mezei K, et al: A comparison of efilgrastim to pegfilgrastim in the management of chemotherapy-induced neutropenia in patients with early-stage breast cancer undergoing cytotoxic chemotherapy (RECOVER): A phase 3 study. *Cancer Med* 9:6234-6243, 2020
- Cornes P, Gascon P, Chan S, et al: Systematic review and meta-analysis of short- versus long-acting granulocyte colony-stimulating factors for reduction of chemotherapy-induced febrile neutropenia. *Adv Ther* 35:1816-1829, 2018
- Crees ZD, Rettig MP, Jayasinghe RG, et al: Motixafortide and G-CSF to mobilize hematopoietic stem cells for autologous transplantation in multiple myeloma: A randomized phase 3 trial. *Nat Med* 29:869-879, 2023
- Ding X, Ding J, Gu H, et al: Long-acting granulocyte colony-stimulating factor in primary prophylaxis of early infection in patients with newly diagnosed multiple myeloma. *Support Care Cancer* 30:4049-4054, 2022
- Do T, Medhekar R, Bhat R, et al: The risk of febrile neutropenia and need for G-CSF primary prophylaxis with the docetaxel and cyclophosphamide regimen in early-stage breast cancer patients: A meta-analysis. *Breast Cancer Res Treat* 153:591-597, 2015
- Fernandes R, Mazzarello S, Stober C, et al: Primary febrile neutropenia prophylaxis for patients who receive FEC-D chemotherapy for breast cancer: A systematic review. *JCO Glob Oncol* 10.1200/JGO.2016.008540
- Glaspy J, Bondarenko I, Burdaeva O, et al: Efbemalenograstim alfa, an Fc fusion protein, long-acting granulocyte-colony stimulating factor for reducing the risk of febrile neutropenia following chemotherapy: Results of a phase III trial. *Support Care Cancer* 32:34, 2023
- Glaspy J, Bondarenko I, Krasnozhan D, et al: Efbemalenograstim alfa not inferior to pegfilgrastim in providing neutrophil support in women with breast cancer undergoing myelotoxic chemotherapy: Results of a phase 2 randomized, multicenter, open-label trial. *Support Care Cancer* 32:91, 2024
- Goto H, Sawa M, Fujiwara SI, et al: Impact of single dose of pegfilgrastim on peripheral blood stem cell harvest in patients with multiple myeloma or malignant lymphoma. *Sci Rep* 15:14523, 2025
- Grosso D, Leiby B, Wilde L, et al: A prospective, randomized trial examining the use of G-CSF versus no G-CSF in patients post-autologous transplantation. *Transplant Cell Ther* 28:831.e1-831.e7, 2022
- Hershman DL, Bansal A, Sullivan SD, et al: A pragmatic cluster-randomized trial of a standing order entry intervention for colony-stimulating factor use among patients at intermediate risk for febrile neutropenia. *J Clin Oncol* 41:590-598, 2023
- Hoshina H, Takei H: Granulocyte-colony stimulating factor-associated aortitis in cancer: A systematic literature review. *Cancer Treat Res Commun* 29:100454, 2021
- Huang X, Li S, Shi W, et al: A prospective, randomized clinical trial of emergency treatment of chemotherapy-induced neutropenia and febrile neutropenia by pegylated recombinant human granulocyte colony-stimulating factor (PEG-rhG-CSF). *Br J Clin Pharmacol* 89:372-379, 2023
- Jeker B, Thalmann L, Bacher U, et al: Comparing stem cell mobilization with chemotherapy and cytokine (G-CSF) versus cytokine alone in myeloma patients (MOCCCA): A randomized phase II, open-label, non-inferiority trial. *Bone Marrow Transpl* 60:270-276, 2025
- Ji X, Xu L, Pan P, et al: Efficacy and safety of 3 mg pegylated recombinant human granulocyte colony-stimulating factor as support to chemotherapy for lung cancer. *Thorac Cancer* 13:117-125, 2022
- Kim Z, Hur SM, Lee JE, et al: The optimal timing and duration of daily G-CSF for the primary prevention of febrile neutropenia in breast cancer patients undergoing adjuvant TAC chemotherapy. *Asia Pac J Clin Oncol* 21:383-391, 2025
- Kirshner JJ, McDonald MC, 3rd, Kruter F, et al: NOLAN: A randomized, phase 2 study to estimate the effect of prophylactic naproxen or loratadine vs no prophylactic treatment on bone pain in patients with early-stage breast cancer receiving chemotherapy and pegfilgrastim. *Support Care Cancer* 26:1323-1334, 2018
- Kowalyszyn RD, Fein LE, Richardet ME, et al: Biosimilar versus originator pegfilgrastim for preventing chemotherapy-induced neutropenia: A phase III randomized, multicenter, evaluator-blinded, noninferiority study. *JCO Glob Oncol* 10.1200/JGO.21.00276
- Lapidari P, Vaz-Luis I, Di Meglio A: Side effects of using granulocyte-colony stimulating factors as prophylaxis of febrile neutropenia in cancer patients: A systematic review. *Crit Rev Oncol Hematol* 157:103193, 2021
- Leonard RC, Mansi JL, Keerie C, et al: A randomised trial of secondary prophylaxis using granulocyte colony-stimulating factor ('SPROG' trial) for maintaining dose intensity of standard adjuvant chemotherapy for breast cancer by the Anglo-Celtic Cooperative Group and NCRN. *Ann Oncol* 26:2437-2441, 2015
- Li W, Dong M, Huang S, et al: Efficacy and safety of PEG-rhG-CSF in preventing chemoradiotherapy-induced neutropenia in patients with locally advanced cervical cancer. *Biomol Biomed* 23:310-316, 2023
- Li X, Zheng H, Yu MC, et al: Is PEGylated G-CSF superior to G-CSF in patients with breast cancer receiving chemotherapy? A systematic review and meta-analysis. *Support Care Cancer* 28:5085-5097, 2020
- Li Y, Qiu X, Lei Y, et al: G-CSF + plerixafor versus G-CSF alone mobilized hematopoietic stem cells in patients with multiple myeloma and lymphoma: A systematic review and meta-analysis. *Ann Med* 56:2329140, 2024
- Link H, Illerhaus G, Martens UM, et al: Efficacy and safety of lipegfilgrastim versus pegfilgrastim in elderly patients with aggressive B cell Non-Hodgkin lymphoma (B-NHL): Results of the randomized, open-label, non-inferiority AVOID neutropenia study. *Support Care Cancer* 29:2519-2527, 2021
- Luo C, Wu G, Huang X, et al: Efficacy of hematopoietic stem cell mobilization regimens in patients with hematological malignancies: A systematic review and network meta-analysis of randomized controlled trials. *Stem Cell Res Ther* 13:123, 2022
- Lyman GH, Yau L, Nakov R, et al: Overall survival and risk of second malignancies with cancer chemotherapy and G-CSF support. *Ann Oncol* 29:1903-1910, 2018
- Masuda N, Tokuda Y, Nakamura S, et al: Dose response of pegfilgrastim in Japanese breast cancer patients receiving six cycles of docetaxel, doxorubicin, and cyclophosphamide therapy: A randomized controlled trial. *Support Care Cancer* 23:2891-2898, 2015
- Na H, Kwon SH, Son KH, et al: Comparative safety profiles of oncology biosimilars: A systematic review and network meta-analysis. *BioDrugs* 37:205-218, 2023

42. Pinter T, Klippel Z, Cesas A, et al: A phase III, randomized, double-blind, placebo-controlled trial of pegfilgrastim in patients receiving first-line FOLFOX/bevacizumab or FOLFIRI/bevacizumab for locally advanced or metastatic colorectal cancer: Final results of the Pegfilgrastim and Anti-VEGF Evaluation Study (PAVES). *Clin Colorectal Cancer* 16:103-114.e3, 2017
43. Schwartzberg LS, Bhat G, Peguero J, et al: Eflapegrastim, a long-acting granulocyte-colony stimulating factor for the management of chemotherapy-induced neutropenia: Results of a phase III trial. *Oncologist* 25:e1233-e1241, 2020
44. Sun XS, Wang Z, Ren SH, et al: PEG-rhG-CSF for prophylaxis of neutropenia after chemotherapy in patients with non-small cell lung cancer: A multicenter, prospective, randomized study. *Thorac Cancer* 13:2429-2435, 2022
45. Truong J, Lee EK, Trudeau ME, et al: Interpreting febrile neutropenia rates from randomized, controlled trials for consideration of primary prophylaxis in the real world: A systematic review and meta-analysis. *Ann Oncol* 27:608-618, 2016
46. Van Belle H, Hurvitz SA, Gilbar PJ, et al: Systematic review and meta-analysis of febrile neutropenia risk with TCH(P) in HER2-positive breast cancer. *Breast Cancer Res Treat* 190:357-372, 2021
47. Waller CF, Ranganna GM, Pennella EJ, et al: Randomized phase 3 efficacy and safety trial of proposed pegfilgrastim biosimilar MYL-1401H in the prophylactic treatment of chemotherapy-induced neutropenia. *Ann Hematol* 98:1217-1224, 2019
48. Wan L, Zhang Y, Lai Y, et al: Effect of granulocyte-macrophage colony-stimulating factor on prevention and treatment of invasive fungal disease in recipients of allogeneic stem-cell transplantation: A prospective multicenter randomized phase IV trial. *J Clin Oncol* 33:3999-4006, 2015
49. Wang G, Zhang Y, Wang X, et al: Long-acting versus short-acting granulocyte colony-stimulating factors among cancer patients after chemotherapy in China: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 100:e28218, 2021
50. Wang L, Xiang H, Yan Y, et al: Comparison of the efficiency, safety, and survival outcomes in two stem cell mobilization regimens with cyclophosphamide plus G-CSF or G-CSF alone in multiple myeloma: A meta-analysis. *Ann Hematol* 100:563-573, 2021
51. Wang Y, Chen L, Liu F, et al: Efficacy and tolerability of granulocyte colony-stimulating factors in cancer patients after chemotherapy: A systematic review and Bayesian network meta-analysis. *Sci Rep* 9:15374, 2019
52. Xu Y, Huang L, Wang J, et al: Exploring optimal administration timing of pegylated recombinant human granulocyte colony-stimulating factor for chemotherapy-induced neutropenia in early breast cancer treated with pharmacubincin and endoxan: A prospective randomized controlled clinical trial. *BMC Cancer* 24:1387, 2024
53. Yang J, Yu S, Yang Z, et al: Efficacy and safety of supportive care biosimilars among cancer patients: A systematic review and meta-analysis. *BioDrugs* 33:373-389, 2019
54. Yang L, Yu L, Du X, et al: Study of PEG-rhG-CSF for the prevention of neutropenia in concurrent chemoradiotherapy for nasopharyngeal carcinoma. *PLoS One* 20:e0315001, 2025
55. Yang S, Chen SS, Zhang CG, et al: Low-dose pegylated recombinant human granulocyte-colony stimulating factor as hematopoietic support for adjuvant chemotherapy in Chinese patients with breast cancer: An open-label, randomized, non-inferiority trial. *Br J Clin Pharmacol* 90:2621-2629, 2024
56. Zhang Q, Wang Z, Yao W, et al: A randomized, multicenter phase III study of once-per-cycle administration of efbemalenogristim alfa (F-627), a novel long-acting rhG-CSF, for prophylaxis of chemotherapy-induced neutropenia in patients with breast cancer. *BMC Cancer* 24:1143, 2024
57. 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* 21:661, 2021
58. Taplitiz RA, Kennedy EB, Bow EJ, et al: Antimicrobial prophylaxis for adult patients with cancer-related immunosuppression: ASCO and IDSA Clinical Practice Guideline update. *J Clin Oncol* 36:3043-3054, 2018
59. Lyman GH, Abella E, Pettengell R: Risk factors for febrile neutropenia among patients with cancer receiving chemotherapy: A systematic review. *Crit Rev Oncol Hematol* 90:190-199, 2014
60. Kosaka Y, Rai Y, Masuda N, et al: Phase III placebo-controlled, double-blind, randomized trial of pegfilgrastim to reduce the risk of febrile neutropenia in breast cancer patients receiving docetaxel/cyclophosphamide chemotherapy. *Support Care Cancer* 23:1137-1143, 2015
61. Kirshner JJ, Heckler CE, Janelins MC, et al: Prevention of pegfilgrastim-induced bone pain: A phase III double-blind placebo-controlled randomized clinical trial of the university of Rochester cancer center clinical community oncology program research base. *J Clin Oncol* 30:1974-1979, 2012
62. Crawford J, Ozer H, Stoller R, et al: Reduction by granulocyte colony-stimulating factor of fever and neutropenia induced by chemotherapy in patients with small-cell lung cancer. *N Engl J Med* 325:164-170, 1991
63. Crawford J, Glaspy JA, Stoller RG, et al: Final results of a placebo-controlled study of filgrastim in small-cell lung cancer: Exploration of risk factors for febrile neutropenia. *Support Cancer Ther* 3:36-46, 2005
64. Hartmann LC, Tschetter LK, Habermann TM, et al: Granulocyte colony-stimulating factor in severe chemotherapy-induced afebrile neutropenia. *N Engl J Med* 336:1776-1780, 1997
65. Mhaskar R, Clark OA, Lyman G, et al: Colony-stimulating factors for chemotherapy-induced febrile neutropenia. *Cochrane Database Syst Rev* 2014:CD003039, 2014
66. Dekker A, Bulley S, Beyene J, et al: Meta-analysis of randomized controlled trials of prophylactic granulocyte colony-stimulating factor and granulocyte-macrophage colony-stimulating factor after autologous and allogeneic stem cell transplantation. *J Clin Oncol* 24:5207-5215, 2006
67. Remberger M, Naseh N, Aschan J, et al: G-CSF given after haematopoietic stem cell transplantation using HLA-identical sibling donors is associated to a higher incidence of acute GVHD II-IV. *Bone Marrow Transpl* 32:217-223, 2003
68. Ringden O, Hassan Z, Karlsson H, et al: Granulocyte colony-stimulating factor induced acute and chronic graft-versus-host disease. *Transplantation* 90:1022-1029, 2010
69. Ringden O, Labopin M, Gorin NC, et al: Treatment with granulocyte colony-stimulating factor after allogeneic bone marrow transplantation for acute leukemia increases the risk of graft-versus-host disease and death: A study from the Acute Leukemia Working Party of the European Group for Blood and Marrow Transplantation. *J Clin Oncol* 22:416-423, 2004
70. Bunn PA, Jr., Crowley J, Kelly K, 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* 13(7):1632-1641, 1995
71. Sheikh H, Colaco R, Lorigan P, 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* 74:75-79, 2011
72. Gomes F, Faivre-Finn C, Mistry H, 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* 153:165-170, 2021
73. Rodriguez G, Mancuso J, Lyman GH, et al: ASCO policy statement on biosimilar and interchangeable products in oncology. *JCO Oncol Pract* 19:411-419, 2023
74. Burris HA, Belani CP, Kaufman PA, et al: Pegfilgrastim on the same day versus next day of chemotherapy in patients with breast cancer, non-small-cell lung cancer, ovarian cancer, and non-hodgkin's lymphoma: Results of four multicenter, double-blind, randomized phase II studies. *JCO Oncol Pract* 6:133-140, 2010
75. Wang K, Li P, Yang C, et al: Timing of Pegfilgrastim Administration and Pegfilgrastim-Induced Bone Pain: A Prospective, Randomized Phase 3 Trial. Abstract 297MO. Presented at the ESMO Congress 2025, Berlin, Germany, 2025
76. Wijeratne DT, Wright K, Gyawali B: Risk-stratifying treatment strategies for febrile neutropenia-tools, tools everywhere, and not a single one that works? *JCO Oncol Pract* 17:651-654, 2021
77. Gilligan T, Coyle N, Frankel RM, et al: Patient-clinician communication: American Society of Clinical Oncology Consensus Guideline. *J Clin Oncol* 35:3618-3632, 2017
78. Desai A, Gyawali B: Financial toxicity of cancer treatment: Moving the discussion from acknowledgement of the problem to identifying solutions. *EClinicalMedicine* 20:100269, 2020
79. Raptis SG, Shkabar B, Bandy S, et al: Defining and measuring financial toxicity in Low- and middle-income countries. *JCO Oncol Pract* 21:57-68, 2025
80. Apro MS, Chaplin S, Cornes P, et al: Cost-effectiveness of granulocyte colony-stimulating factors (G-CSFs) for the prevention of febrile neutropenia (FN) in patients with cancer. *Support Care Cancer* 31:581, 2023
81. Tseng TH, Chiang SC, Hsu JC, et al: Cost-effectiveness analysis of granulocyte colony-stimulating factors for the prophylaxis of chemotherapy-induced febrile neutropenia in patients with breast cancer in Taiwan. *PLoS One* 19:e0303294, 2024
82. Kelkar AH, Abel GA: Decoding cost-effectiveness of PNH therapies. *Blood* 145:8-10, 2025
83. Meropol NJ, Schrag D, Smith TJ, et al: American Society of Clinical Oncology guidance statement: The cost of cancer care. *J Clin Oncol* 27:3868-3874, 2009
84. Sanders JJ, Temin S, Ghoshal A, et al: Palliative care for patients with cancer: ASCO guideline update. *J Clin Oncol* 42:2336-2357, 2024
85. Dale W, Klepin HD, Williams GR, et al: Practical assessment and management of vulnerabilities in older patients receiving systemic cancer therapy: ASCO Guideline update. *J Clin Oncol* 41:4293-4312, 2023

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

WBC Growth Factors: ASCO Guideline Update

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APPENDIX 1. GUIDELINE DISCLAIMER

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APPENDIX 2. GUIDELINE AND CONFLICTS OF INTEREST

The Expert Panel was assembled in accordance with ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at <http://www.asco.org/guideline-methodology>). All members of the Expert Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

TABLE A1. WBC Growth Factors Guideline Update Expert Panel Membership

Name	Affiliation	Role or Area of Expertise
Bishal Gyawali, MD, PhD, FASCO	Queen's University, Kingston, ON, Canada	Medical oncology, public health sciences
Tessa Cigler, MD, MPH	Weill Cornell Medicine, New York, NY	Medical oncology
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Sally Schott	Patient Advocate, Medford, OR	Advocacy
Madhav R. Seshadri, MD	University of California San Francisco, San Francisco, CA	Hematology, hematopoietic stem-cell transplantation
Ramila Shilpakar, MD, DM	Bir Hospital, National Academy of Medical Sciences, Kathmandu, Nepal	Medical oncology
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Dario Trapani, MD	University of Milan, European Institute of Oncology, Milan, Italy	Medical oncology
Amy B. Woodard, PharmD	Moffitt Cancer Center, Tampa, FL	Pharmacy
Kari Bohlke, ScD	ASCO, Alexandria, VA	ASCO Practice Guideline Staff (Health Research Methods)

TABLE A2. Recommendation Rating Definitions

Term	Definition
Quality of evidence	
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect
Strength of recommendation	
Strong	In recommendations for an intervention, the desirable effects of an intervention outweigh its undesirable effects In recommendations against an intervention, the undesirable effects of an intervention outweigh its desirable effects All or almost all informed people would make the recommended choice for or against an intervention
Conditional/Weak	In recommendations for an intervention, the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists In recommendations against an intervention, the undesirable effects probably outweigh the desirable effects, but appreciable uncertainty exists Most informed people would choose the recommended course of action, but a substantial number would not

NOTE. Schünemann H, Brożek J, Guyatt G, et al: GRADE handbook for grading quality of evidence and strength of recommendations. 2013. <https://gdt.gradepro.org/app/handbook/handbook.html>.