STUDY GUIDE

Evidence-based AGIHO guideline update on prophylaxis of infectious complications with granulocyte-stimulating factors (G-CSF) for the treatment of adult patients with cancer.

Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO) · 2026

Study Guide: Prophylaxis of Infectious Complications with G-CSF in Cancer Patients

This study guide provides a comprehensive overview of the updated evidence-based guidelines from the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO). It focuses on the use of Granulocyte Colony-Stimulating Factor (G-CSF) to prevent febrile neutropenia (FN) and other infectious complications in adult cancer patients.

I. Key Concepts and Clinical Guidelines

1. Fundamentals of G-CSF Prophylaxis

- **Purpose:** G-CSF is used to reduce the incidence and duration of severe neutropenia and febrile neutropenia (FN), thereby decreasing the need for hospitalization and antibiotic treatment.
- **Risk Assessment for Solid Tumors:**
  - **High Risk (>20%):** Strong indication for G-CSF.
  - **Intermediate Risk (10–20%):** Indication for G-CSF if additional clinical risk factors are present.
  - **Low Risk (<10%):** No routine indication for G-CSF.
- **Timing of Administration:** For non-Hodgkin lymphoma and solid tumors, G-CSF should ideally be administered **2–4 days after** completing cytotoxic treatment. Administration on the same day as chemotherapy is associated with a higher incidence of FN.

2. Recommendations by Disease Entity

Hematological Malignancies

- **Non-Hodgkin Lymphoma (NHL):** Secondary use of G-CSF is associated with more treatment delays compared to primary use. Primary prophylaxis is recommended to maintain dose intensity, though a clear benefit for overall survival (OS) by increasing dose intensity has not been definitively proven.
- **Hodgkin Lymphoma (HL):**
  - **ABVD Regimen:** Routine G-CSF is **not** recommended and may increase bleomycin-induced lung toxicity.
  - **BV+AVD Regimen:** Primary G-CSF prophylaxis is recommended for both younger and elderly patients.
  - **BEACOPP/BrECADD:** Prophylactic G-CSF is mandatory for all patients.
- **Acute Myeloid Leukemia (AML):** G-CSF safely shortens neutropenia and hospitalization. However, it should generally be avoided before day 14 of induction therapy if early blast clearance needs to be assessed.
- **Acute Lymphoblastic Leukemia (ALL):** Routine use of G-CSF is recommended, with conventional G-CSF preferred during frequent repetitive chemotherapy (induction).

Emerging Immunotherapies

- **CAR T Cell Therapy:** G-CSF is recommended for treating immune effector cell-associated hematotoxicity (ICAHT). It has not been associated with an increase in severe cytokine release syndrome (CRS) or neurotoxicity (ICANS).
- **Bispecific Antibodies (BsAb):** G-CSF may be considered for treatment-related neutropenia. However, it should be avoided during step-up dosing or when the patient is at risk for/experiencing CRS, as FN and CRS symptoms can overlap.

3. Formulations and Stewardship

- **Biosimilars:** These are therapeutic alternatives that are non-inferior to originator G-CSF in terms of efficacy and survival. They are highly recommended due to their cost-effectiveness.
- **Efbemalenograstim alfa (EMGA):** A third-generation, non-pegylated, long-acting G-CSF. It is non-inferior to pegfilgrastim and avoids the risk of anti-PEG antibody induction.
- **Antibiotic Stewardship:** G-CSF is preferred over prophylactic antibiotics for preventing FN to reduce long-term detrimental effects and overall antibiotic consumption.

II. Short-Answer Practice Questions

1. **What are the three primary clinical benefits of G-CSF prophylaxis identified in the 2014 and 2026 guidelines?**

2. **According to the ESCMID criteria used in the guidelines, what does a Strength of Recommendation (SoR) grade of 'A' signify?**
3. **Why is G-CSF prophylaxis not routinely recommended for patients undergoing the ABVD protocol for Hodgkin lymphoma?**
4. **What is the recommended timing for G-CSF administration relative to chemotherapy, and why?**
5. **What is a significant advantage of Efbemalenograstim alfa over pegylated G-CSF formulations?**
6. **In the context of AML treatment, when should the administration of G-CSF be restricted?**
7. **How does the use of G-CSF impact the incidence of Cytokine Release Syndrome (CRS) in CAR T cell therapy according to current data?**
8. **What is the "secondary application" of G-CSF?**
9. **True or False: Biosimilar G-CSF is considered inferior to originator G-CSF regarding overall survival rates.**
10. **In patients receiving bispecific antibodies (BsAb), why should G-CSF be avoided during CRS?**

III. Essay Prompts for Deeper Exploration

1. **The Evolution of G-CSF Guidelines:** Compare the 2014 AGIHO guidelines with the 2026 update. Discuss how the introduction of immunotherapies like CAR T cell therapy and bispecific antibodies has necessitated new clinical strategies for managing neutropenia.
2. **Economic and Systemic Impacts of Biosimilars:** Analyze the role of biosimilar G-CSF in modern oncology. How does the evidence for non-inferiority support the transition toward these agents, and what are the implications for healthcare costs and patient access to treatment?
3. **The Intersection of G-CSF and Antibiotic Stewardship:** Evaluate the argument for using G-CSF as a tool for antibiotic stewardship. Discuss the potential long-term benefits of reducing antibiotic consumption in cancer patients and the evidence supporting G-CSF over prophylactic antibiotics.
4. **Risk-Benefit Analysis in Hodgkin Lymphoma:** Critically examine the use of G-CSF across different HL treatment regimens (ABVD vs. BrECADD vs. BV+AVD). Discuss the clinical factors—such as lung toxicity risks and the necessity of dose intensity—that influence these conflicting recommendations.

IV. Glossary of Important Terms

Term	Definition
ANC	Absolute Neutrophil Count; a measure of the number of neutrophil granulocytes in the blood.
Biosimilar	A biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference ("originator") product.
BsAb	Bispecific Antibody; a type of immunotherapy that targets two different antigens simultaneously.
CAR T Cell Therapy	Chimeric Antigen Receptor T cell therapy; a treatment where a patient's T cells are genetically engineered to attack cancer cells.
CRS	Cytokine Release Syndrome; a systemic inflammatory response that can be triggered by certain types of immunotherapy.
EMGA	Efbemalenograstim alfa; a third-generation, long-acting, non-pegylated recombinant fusion protein G-CSF.
ESCMID	European Society of Clinical Microbiology and Infectious Diseases; the body providing the criteria for Level of Evidence (LoE) and Strength of Recommendation (SoR).
Febrile Neutropenia (FN)	The occurrence of a fever during a period of significantly low neutrophil counts; a serious complication of chemotherapy.
G-CSF	Granulocyte Colony-Stimulating Factor; a glycoprotein that stimulates the bone marrow to produce granulocytes and stem cells.
ICAHT	Immune Effector Cell-Associated Hematotoxicity; blood-related toxicities (like neutropenia) following CAR T cell therapy.
ICANS	Immune Effector Cell-Associated Neurotoxicity Syndrome; a clinical syndrome of neurologic symptoms that can occur after immunotherapy.
LoE	Level of Evidence; a ranking system (I to III) indicating the quality and source of clinical data.
PEG	Polyethylene glycol; a compound used to prolong the half-life of drugs, which can sometimes induce anti-PEG antibodies.
SoR	Strength of Recommendation; a grade (A to D) indicating the level of support a medical group provides for a specific intervention.