

Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update Summary


Randy A. Taplitz, Erin B. Kennedy, and Christopher R. Flowers

UC San Diego Health, La Jolla, CA; American Society of Clinical Oncology, Alexandria, VA; and Emory University School of Medicine, Atlanta, GA

Patients who undergo cytotoxic chemotherapy and hematopoietic stem cell transplantation are at risk for infection, particularly during the period of neutropenia.¹ Neutrophils are critical to provide host defense against infection, particularly bacterial and fungal infection. The risk of infection increases with the depth and duration of neutropenia, and the greatest risk occurs in patients who experience profound, prolonged neutropenia after chemotherapy, which is most likely to occur in the period before engraftment during hematopoietic cell transplantation and after induction chemotherapy for acute leukemia.² Fever can be an important indicator and is often the only sign or symptom of infection, although clinicians should also be mindful that patients who are severely or profoundly neutropenic may present with suspected infection in an afebrile, or even hypothermic, state. Prevention and appropriate management of febrile neutropenia are important, because the rate of major complications (eg, hypotension, acute renal, respiratory or heart failure) in the context of febrile neutropenia is approximately 25% to 30%, and mortality may reach 11%.^{3,4} In the setting of severe sepsis or septic shock, the hospital mortality rate may be as high as 50%.⁵ In addition to depth and duration of neutropenia, other factors that contribute to

immunosuppression and/or risk of infection in this patient population include the following: impaired integrity of mucocutaneous barriers (eg, catheters, mucositis), the type of treatment or conditioning regimens, metabolic perturbations (eg, diabetes, uremia), the presence of immunomodulating viruses, the presence of graft-versus-host disease, and perturbation of the microbiome.

Antimicrobial prophylaxis is an intervention that can reduce the risk of infection in immunosuppressed patients. However, because of drug-related adverse effects as well as concerns with antimicrobial resistance, cost considerations, and the physiologic importance to the host of maintenance of equilibrium in the diversity and density of the host microbiome, the decision to administer prophylaxis requires a balance of benefits versus harms. The previous version of this guideline recommended antibacterial and antifungal prophylaxis for higher-risk patients and recommended that there was not a high enough baseline risk of febrile neutropenia and infection-related mortality in lower-risk patients to warrant routine administration of these agents.⁶ This version of the guideline includes updated meta-analyses of antimicrobial interventions for the prevention of febrile neutropenia.

 DOI: <https://doi.org/10.1200/JOP.18.00366>; published online ahead of print at jop.ascopubs.org on September 4, 2018.

THE BOTTOM LINE

Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update Summary

Guideline Question

What antimicrobial prophylaxis is appropriate for immunosuppressed patients with cancer?

Target Population

Patients receiving treatment of cancer as inpatients or outpatients who are experiencing immune suppression or increased susceptibility to infection.

Target Audience

Oncologists, infectious disease specialists, emergency medicine physicians, nurses, and advanced practice providers who may treat patients with immunosuppression that results from cancer treatment.

Methods

An Expert Panel convened to update clinical practice guideline recommendations based on a systematic review of the medical literature.

Key Recommendations

Antimicrobial prophylaxis:

Recommendation 1.1 Risk of febrile neutropenia should be systematically assessed (in consultation with infectious disease specialists as needed), including patient-, cancer- and treatment-related factors (see Table 1). (Type of recommendation: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.2 Antibiotic prophylaxis with a fluoroquinolone is recommended for patients who are at high risk for febrile neutropenia or profound, protracted neutropenia (eg, most patients with acute myeloid leukemia/myelodysplastic syndromes [AML/MDS] or hematopoietic stem cell transplantation [HSCT] treated with myeloablative conditioning regimens). Antibiotic prophylaxis is not routinely recommended for patients with solid tumors. (Type of recommendation: evidence-based; benefits outweigh harms; Evidence quality: high; Strength of recommendation: moderate).

Recommendation 2.1 Antifungal prophylaxis with an oral triazole or parenteral echinocandin is recommended for patients at risk for profound, protracted neutropenia (eg, most patients with AML/MDS or HSCT). Antifungal prophylaxis is not routinely recommended for patients with solid tumors. Further distinctions between recommendations for invasive candidiasis and invasive mold infection are provided within the full text of the guideline. (Type of recommendation: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Other recommended prophylactic measures for microbial infections include the following:

Recommendation 2.2 Prophylaxis (eg, trimethoprim-sulfamethoxazole [TMP-SMX]) is recommended for patients receiving chemotherapy regimens associated with > 3.5% risk for pneumonia from *Pneumocystis jirovecii* (eg, those with ≥ 20 mg prednisone equivalents daily for ≥ 1 month or those based on purine analog use). (Type of

THE BOTTOM LINE

recommendation: evidence-based; benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).⁷

Recommendation 3.1 Herpes simplex virus (HSV)–seropositive patients undergoing allogeneic HSCT or leukemia induction therapy should receive prophylaxis with a nucleoside analog (eg, acyclovir). (Type of recommendation: evidence-based; benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).⁷

Recommendation 3.2 Treatment with a nucleoside reverse transcription inhibitor (eg, entecavir, tenofovir) is recommended for patients at high risk of hepatitis B reactivation. (Type of recommendation: consensus-based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 3.3 Yearly influenza vaccination with inactivated vaccine is recommended for all patients receiving chemotherapy for malignancy, for all family and household contacts, and for health care providers. (Type of recommendation: consensus-based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 3.4 The Expert Panel also supports other vaccination recommendations for immunosuppressed adult oncology patients that are contained within the IDSA guideline for vaccination of the immunosuppressed host.^{12,13} (Type of recommendation: consensus-based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Additional recommended precautions:

Recommendation 4.1 All health care workers should comply with hand hygiene and respiratory hygiene/cough etiquette guidelines to reduce the risk for aerosol- and direct or indirect contact-based transmission of pathogenic microorganisms in the health care setting. (Type of recommendation: consensus-based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 4.2 Outpatients with neutropenia from cancer therapy should avoid prolonged contact with environments that have high concentrations of airborne fungal spores (eg, construction and demolition sites, intensive exposure to soil through gardening or digging, household renovation). (Type of recommendation: consensus-based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

*Please see the complete guideline document for further details and qualifying statements to the recommendations.*¹⁴

Additional Resources

More information, including a Data Supplement with additional evidence tables, a Methodology Supplement with information about evidence quality and strength of recommendations, slide sets, and clinical tools and resources, is available at www.asco.org/supportive-care-guidelines. Patient information is available at www.cancer.net.

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.

The update of the 2013 ASCO Guidelines for Antimicrobial Prophylaxis for Immunosuppression in Adults Treated for Malignancy is being carried out in partnership with the Infectious Diseases Society of America (IDSA).^{6,7} ASCO methodology relies on analysis of strength and quality of evidence; IDSA employs the grading of recommendations assessment, development and evaluation (ie, GRADE) system to assess quality of evidence and to develop evidence-based recommendations.⁸ This guideline employs the ASCO methodology and grading system. This guideline cannot be considered a comprehensive resource for the prevention of infection in patients with cancer. For guidance on outpatient management of febrile neutropenia, please consult the recently updated joint ASCO/IDSA guideline, Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy.⁹ For recommendations about the use of colony-stimulating factors in patients with solid tumors or lymphoma, please refer to the Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update.¹⁰ For more specific guidelines about the prevention and treatment of infections in recipients of stem-cell transplantations, please consult the American Society for Blood and Marrow Transplantation/IDSA guidelines.¹¹ Additional information is available at www.asco.org/supportive-care-guidelines. Patient information is available at www.cancer.net. **JOP**

Acknowledgment

Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update was developed and written by the following: Randy A. Taplitz, Erin B. Kennedy, Eric J. Bow, Jennie Crews, Charise Gleason, Douglas K. Hawley, Amelia A. Langston, Loretta J. Nastoupil, Michelle Rajotte, Kenneth Rolston, Lynne Strasfeld, and Christopher R. Flowers

Authors' Disclosures of Potential Conflicts of Interest

Disclosures provided by the authors are available with this article at jop.ascopubs.org.

Author Contributions

Conception and Design: Randy A. Taplitz, Christopher R. Flowers
Collection and Assembly of Data: Randy A. Taplitz, Christopher R. Flowers
Data Analysis and Interpretation: All authors

Manuscript Writing: All authors

Final Approval: All authors

Accountable for All Aspects of Work: All authors

Corresponding author: Erin B. Kennedy, American Society of Clinical Oncology, 2318 Mill Rd, Suite 800, Alexandria, VA 22314; e-mail: guidelines@asco.org.

References

1. Sievers EL, Dale DC, Bolyard AA, et al: Types of severe chronic neutropenia. <https://www.neutropenia.ca/about/types-of-neutropenia>
2. Bow E, Marr KA, Thorner AR: Overview of neutropenic fever syndrome. <https://www.uptodate.com/contents/overview-of-neutropenic-fever-syndromes>
3. Carmona-Bayonas A, Jiménez-Fonseca P, Virizuela Echaburu J, et al: Prediction of serious complications in patients with seemingly stable febrile neutropenia: Validation of the clinical index of stable febrile neutropenia in a prospective cohort of patients from the FINITE study. *J Clin Oncol* 33:465-471, 2015
4. Kuderer NM, Dale DC, Crawford J, et al: Mortality, morbidity, and cost associated with febrile neutropenia in adult cancer patients. *Cancer* 106:2258-2266, 2006
5. Legrand M, Max A, Peigne V, et al: Survival in neutropenic patients with severe sepsis or septic shock. *Crit Care Med* 40:43-49, 2012
6. Flowers CR, Seidenfeld J, Bow EJ, et al: Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol* 31:794-810, 2013
7. Freifeld AG, Bow EJ, Sepkowitz KA, et al: Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis* 52:e56-e93, 2011
8. Brożek JL, Akl EA, Compalati E, et al: Grading quality of evidence and strength of recommendations in clinical practice guidelines, part 3 of 3: The GRADE approach to developing recommendations. *Allergy* 66:588-595, 2011
9. 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
10. 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
11. Tomblyn M, Chiller T, Einsele H, et al: Guidelines for preventing infectious complications among hematopoietic cell transplant recipients: A global perspective—Preface. *Bone Marrow Transplant* 44:453-455, 2009
12. Rubin LG, Levin MJ, Ljungman P, et al: 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis* 58:e44-100, 2014
13. Kim DK RL, Hunter P: Advisory Committee on Immunization Practices Recommended Immunization schedule for Adults Aged 19 Years or Older—United States, 2018. *MMWR Morb Mortal Wkly Rep* 67:158-160, 2018
14. Taplitz 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* DOI: <https://doi.org/10.1200/JCO.18.00374>

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update Summary

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jop/site/ifc/journal-policies.html.

Randy A. Taplitz

Consulting or Advisory Role: Merck

Research Funding: Chimerix (Inst)

Travel, Accommodations, Expenses: Merck

Erin B. Kennedy

No relationship to disclose

Christopher R. Flowers

Consulting or Advisory Role: OptumRx, Seattle Genetics, Bayer, Gilead Sciences, Spectrum Pharmaceuticals, Avvie, Celgene, Denovo Biopharma, BeiGene, AstraZeneca, Karyopharm Therapeutics, Pharmacyclics, Janssen

Research Funding: Acerta Pharma (Inst), Infinity Pharmaceuticals (Inst), Onyx (Inst), Janssen Oncology (Inst), Gilead Sciences (Inst), Celgene (Inst), TG Therapeutics (Inst), Genentech (Inst), Roche (Inst), Pharmacyclics (Inst), Abbvie (Inst), Immune Design (Inst), BeiGene (Inst)

Travel, Accommodations, Expenses: Gilead Sciences, Celgene, Genentech, Roche