Clinical Implications of Febrile Neutropenia Guidelines in the Cancer Patient Population

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Febrile neutropenia is a medical emergency that requires urgent evaluation, the timely administration of empiric broad-spectrum antimicrobials, and careful monitoring to optimize patient outcomes and mitigate the risk of complications. Fever in the setting of neutropenia can affect subsequent chemotherapy dosing and scheduling, which, in turn, affects treatment efficacy and overall prognosis. Febrile neutropenia remains a significant cause of morbidity, mortality, and cost burden in patients with cancer. ASCO and the Infectious Disease Society of America (IDSA) have published clinical practice guidelines for the effective triage, risk stratification, and standardized management of this vulnerable patient population with a focus on patients who can safely be managed in the outpatient setting. The IDSA guideline on the general management of neutropenic patients with cancer was first published in 1997 and last updated in 2011. In the article that accompanies this commentary, Zimmer and Freifeld address an important gap in the literature regarding the management of most patients who will require inpatient care. As the authors note, there is no set of diagnostics or grading criteria that can precisely distinguish bacteremia from uninfected febrile neutropenia; therefore, treatment is indicated in all cases. Antibiotic regimens must primarily target gram-negative pathogens that carry the highest risk for morbidity and mortality.

In specific groups, such as patients undergoing high-dose cytotoxic chemotherapy and hematopoietic stem cell transplantation, antimicrobial prophylaxis is indicated for patients with cancer who are at high risk of infection during prolonged neutropenia to prevent febrile neutropenia and reduce infectious risk. Another recent IDSA/ASCO clinical practice guideline delineates the judicious application of such measures. Risk for febrile neutropenia should be assessed on the basis of patient characteristics, underlying malignancy, and treatment-related criterion, with prophylactic antimicrobial selection, timing, and duration administered accordingly. However, as Zimmer and Freifeld note, fluoroquinolone prophylaxis is increasingly associated with multidrug resistance and potential toxicity, which must be considered in both the use of prophylactic regimens and the diagnostic workup and treatment selection when febrile neutropenia occurs in the setting of prophylaxis. Prophylaxis regimens vary by institutional practice as there is no uniform evidence that suggests enhanced survival with use. Supportive measures, including respiratory hygiene/cough etiquette, hand hygiene, vaccination administration, and limiting hazardous environmental exposures, are modalities that are intended to augment infection prevention.

Upon evaluating patients with febrile neutropenia, clinicians must differentiate between patients who can be safely treated and monitored as outpatients versus individuals who require inpatient hospitalization. ASCO/IDSA recently published updated recommendations for the identification of patients with febrile neutropenia who may be considered for outpatient management. This approach was endorsed by Zimmer and Freifeld. Validated tools, such as Talcott’s rules, the Multinational Association for Supportive Care in Cancer score, and the Clinical Index of Stable Febrile Neutropenia, support risk stratification for decision making. In treatment centers that have the resource capacity to provide prompt triage, empiric treatment, and ongoing evaluation, an empiric oral and/or outpatient antibiotic management strategy is possible for low-risk patients with solid tumors who have undergone mild- to moderate-intensity chemotherapy and otherwise seem to be clinically stable. Patients with hematologic malignancies or who undergo hematopoietic stem cell transplantation are unlikely to be appropriate candidates for outpatient therapy, nor are patients known or suspected to be infected by fluoroquinolone-resistant or other resistant pathogens, such as methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus, and extended-spectrum β-lactamase gram-negative organisms. Multiorgan system involvement with accompanying derangements in examination findings or laboratory diagnostics also exclude patients from outpatient management. As the authors recommend, site-specific antibiograms and susceptibility patterns related to a patient’s presenting history and physical examination should guide differential diagnosis and treatment.

The initial diagnostic approach for patients with febrile neutropenia must include timely and thorough evaluation and laboratory, microbiologic, and...
radiologic diagnostics as indicated with expanded workup in the setting of hematologic malignancy and hematopoietic stem cell transplantation. Time from triage to the delivery of antibiotics should not exceed 1 hour as delays are associated with complications and decreased survival. For patients who develop febrile neutropenia while receiving oral fluoroquinolone prophylaxis, monotherapy with an antipseudomonal B-lactam agent is recommended, with the addition of other antimicrobials if other complications arise, such as hemodynamic instability, or if antimicrobial resistance is suspected or proven. Consideration of logistic and psychosocial support, access to 24/7 emergency services, transportation, compliance, and mutually developed patient-provider understanding of the care plan must be ensured. Although the article by Zimmer and Freifeld fills an important gap, an updated, evidence-based guideline specifically geared toward the inpatient management of febrile neutropenia for patients with cancer is needed.

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AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT
Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI https://doi.org/10.1200/JOP.18.00718.

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AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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

No other potential conflicts of interest were reported.