Communicating Safe Outpatient Management of Fever and Neutropenia

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The ASCO Clinical Practice Guidelines Committee identified outpatient management of febrile neutropenia (FN) as a priority new topic. The resulting guideline, “Antimicrobial Prophylaxis and Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy,”¹ provides evidence-based recommendations on preventing infection of afebrile adult oncology outpatients with neutropenia, and on selection of and initial empiric therapy for individuals with fever and neutropenia who can be treated safely in the outpatient setting. The guideline is based on a systematic review that yielded 47 articles published in English from 43 studies that met selection criteria. The recommendations of an expert panel emerged from extracted data and informal consensus when data were lacking. A brief summary of the main recommendations is provided in Table 1; an executive summary of the guideline is published in *Journal of Clinical Oncology*¹; and the full guideline, evidence tables, and clinical tools are posted at www.asco.org/guidelines/outpatientfn. In addition, *Journal of Clinical Oncology* recently published an evidence-based guideline developed by an international panel of experts on management of fever and neutropenia in pediatric patients with cancer or undergoing hematopoietic stem-cell transplantation.² Most recommendations on risk stratification and outpatient treatment in this guideline agree with ASCO’s guideline for adult oncology outpatients.

ASCO’s Guideline Panel considers inpatient treatment to be the standard approach to managing an FNE because medical complications of fever and neutropenia occur in up to 10% to 11% of patients identified as low risk by presently available risk indices or scoring systems.¹ However, outpatient treatment may be acceptable for carefully selected patients who are systematically evaluated beginning with a validated risk assessment tool. In summary, the Panel’s major recommendations are (1) For afebrile outpatients with neutropenia, antibacterial and antifungal prophylaxis is only recommended if absolute neutrophil count is expected to be less than 100/ μ L for more than 7 days, unless other factors (see guideline text) increase risks for complications or mortality to similar levels. (2) Risk for medical complications in patients with fever and neutropenia should be assessed systematically using either the Multinational Association for Supportive Care in Cancer (MASCC) score or Talcott’s rules. (3) Patients with MASCC scores ≥ 21 or in Talcott’s group 4 and without other risk factors (see guideline text) may be treated safely with outpatient empiric therapy. (4) Febrile

neutropenic patients should receive their initial dose of empiric antibacterial therapy within 1 hour of triage. (5) An oral fluoroquinolone plus amoxicillin/clavulanate (or plus clindamycin for those with penicillin allergy) is recommended as initial empiric therapy, unless fluoroquinolone prophylaxis was used before fever developed (see guideline text for alternatives).

Disseminating guideline recommendations and supporting evidence to practicing clinicians and effectively communicating recommendations and their underlying rationale to patients are crucial components of implementing evidence-based guidelines.³ To improve adherence to this new guideline, we discuss communication strategies for patients (plus their relatives and/or volunteer caregivers) and stress the need to coordinate across primary, specialist, and emergency care settings, to aid in managing FN in adult oncology outpatients. A summary of key issues for patient-clinician communication is provided in Table 2, and sample key messages for patients are provided in Table 3. The literature we cite (identified separately from the guideline’s systematic review) is from targeted searches and our personal files; the communication strategies discussed here have not been evaluated in randomized clinical trials.

In 2008, the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) studied care delivered to patients who died within 30 days of chemotherapy and identified several significant issues related to FN management.⁴ They highlighted the need to communicate management guidelines to all concerned, including patients, their relatives, and primary and secondary care staff. Because oncology nurses play a vital role in educating patients about FN, expanded dissemination and implementation of clinical practice guidelines to nursing professionals would support patient education goals.^{5,6}

Additional research shows that effective patient-clinician communication can influence treatment outcome. A study⁷ of communication on cancer treatment and adverse events (AEs) surveyed 508 cancer patients (of whom 67% had low WBC counts) and found that discussions alone did not appear to provide patients with sufficient understanding or skills to deal with AEs. These findings suggest that efforts to improve cancer care should include development of tools to improve patients’ understanding of AEs (and by extension interventions such as treatment for FN) and to make these resources available to patients. Such tools could include patient handouts, videos, and Internet-based resources.

Table 1. Summary of Key Recommendations

Clinical Question	2012 Recommendations
<p>A. What interventions are appropriate to prevent infections in patients with a malignancy who have received chemotherapy in inpatient or outpatient settings and who are, or are anticipated to become, neutropenic as outpatients?</p> <p>A-1. How should risk of developing a febrile neutropenic episode (FNE) be assessed in such patients who are not yet febrile? What clinical characteristics identify patients who should be offered antimicrobial prophylaxis?</p> <p>A-2. What antimicrobial drug classes should be used to prevent infection in outpatients who should be offered prophylaxis?</p> <p>A-3. What additional precautions are appropriate to prevent exposure of neutropenic but afebrile outpatients with a malignancy to infectious agents or organisms?</p>	<ul style="list-style-type: none"> FNE risk should be systematically assessed (in consultation with infectious disease specialists as needed) including patient-related, cancer-related, and treatment-related factors. G-CSF prophylaxis should be used before neutropenia develops for patients defined as appropriate in ASCO's WBC growth factors guideline Clinicians should consider antibacterial prophylaxis only for patients expected to experience profound neutropenia (defined as ANC < 100/μL) likely to last for ≥ 7 d Limit antifungal prophylaxis to patients receiving chemotherapy expected to cause profound neutropenia (ANC < 100/μL) for ≥ 7 d, which confers substantial risk (> 6%–10%) for IFI Patients receiving chemotherapy regimens associated with > 3.5% risk for pneumonia due to <i>Pneumocystis jirovecii</i> (eg, those with ≥ 20 mg of prednisone equivalents daily for ≥ 1 mo, or those based on purine analogs) are eligible for prophylaxis Antiviral prophylaxis is recommended for some patient groups (see details in guideline) Seasonal influenza immunization is recommended for all patients undergoing treatment for malignancy, and for all family and household contacts For antibacterial prophylaxis, use an orally administered, systemically absorbed fluoroquinolone See guideline for recommendations on antifungal, <i>Pneumocystis jirovecii</i>, and antiviral prophylaxis in higher-risk patients Influenza immunization should utilize trivalent inactivated vaccine All health care workers should follow hand hygiene guidelines including handwashing practices to reduce exposure through contact transmission, and respiratory hygiene/cough etiquette guidelines to reduce exposure through droplet transmission Outpatients with neutropenia due to cancer therapy should avoid prolonged contact with environments that have high concentrations of airborne fungal spores (eg, construction and demolition sites)
<p>B. Which oncology patients with fever and neutropenia are appropriate candidates for outpatient management?</p> <p>B-4. What clinical characteristics should be used to select patients for outpatient empiric therapy?</p> <p>B-5. Should outpatients with fever and neutropenia at low risk for medical complications receive their initial dose(s) of empiric antimicrobial(s) in the hospital or clinic and be observed, or can some selected for outpatient management be discharged immediately after evaluation?</p> <p>B-6. What psychosocial and logistical requirements must be met to permit outpatient management of patients with fever and neutropenia?</p>	<ul style="list-style-type: none"> Because medical complications occurred in up to 11% of patients identified as low-risk for medical complications of FN in studies validating risk indices or scoring systems, the Panel considers inpatient treatment the standard approach for managing an FNE. However, outpatient management may be acceptable for carefully selected patients When considering a patient with an FNE for outpatient management, the Panel recommends beginning the evaluation with a systematic risk assessment using a validated index such as the MASCC score or Talcott's Rules to identify those at low risk who can be treated safely outside the hospital with oral empirical antibiotic therapy Patients with any major abnormality or significant clinical worsening of organ dysfunction, comorbid conditions, or other risk factors should be managed initially in the hospital even if their MASCC score is above the threshold for low risk (i.e., ≥ 21) or they are in Talcott's group 4 Since evidence from direct comparisons was lacking, the Panel relied on expert opinion to recommend that the first dose of empiric therapy be administered within 1 hr after triage from initial presentation in the clinic, emergency room, or hospital department, after fever has been documented in a neutropenic patient and pretreatment blood samples have been drawn Similarly, the Panel also recommends that patients identified as low risk and selected for outpatient management be observed for at least 4 hr before discharge, to verify they are stable and can tolerate the regimen they will receive <p>Because direct comparative evidence was unavailable for any of these factors, the Panel relied on members' expert opinion to recommend that oncology patients with fever and neutropenia should meet the following criteria to receive empiric therapy as outpatients:</p> <ol style="list-style-type: none"> Residence ≤ 1 h or ≤ 30 miles (48 km) from clinic or hospital Patient's primary care physician agrees to outpatient management Able to comply with logistical requirements, including frequent clinic visits Family member or care giver at home 24 h each day 24-h a day access to a telephone and transportation No prior history of noncompliance with treatment protocols
<p>C. What interventions are indicated for oncology patients with an FNE who can be managed as outpatients?</p> <p>C-7. What diagnostic procedures are recommended?</p>	<p>Based on members' expert opinion, the Panel recommends that in the absence of an alternative explanation, fever in a patient with neutropenia from cancer therapy should be assumed to be due to a bacterial infection. The initial diagnostic approach should maximize the chances of establishing a clinical and microbiologic diagnosis that may affect antibacterial choice and prognosis (see details in full guideline online)</p>

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Table 1. (Continued)

Clinical Question	2012 Recommendations
C-8. What antibacterials are recommended for outpatient empiric therapy?	<ul style="list-style-type: none"> Patients with cancer, fever, and neutropenia and at low risk for medical complications may be given oral empiric therapy with a fluoroquinolone (ciprofloxacin or levofloxacin) plus amoxicillin/clavulanate (or plus clindamycin for those with penicillin allergy). However, a fluoroquinolone is not recommended for initial empiric therapy of neutropenic cancer patients who develop fever after receiving fluoroquinolone-based antibacterial prophylaxis, or in environments where the prevalence of fluoroquinolone resistance is >20% For patients with fever and neutropenia from cancer therapy who are at high risk for medical complications, the Panel recommends hospitalization for intravenous antimicrobial therapy and endorses the most recent (2010) recommendations from IDSA
C-9. What additional measures are recommended for outpatient management?	<ol style="list-style-type: none"> Frequent evaluation for at least 3 d, in clinic or at home Daily or frequent telephone contact to verify (by home thermometry) that fever resolves Monitoring of ANC and platelet count for myeloid reconstitution Frequent return visits to clinic Patients should be evaluated for admission to the hospital if any of the following occur: persistent neutropenic fever syndrome, fever recurs, new signs or symptoms of infection appear, use of oral medications is no longer possible or tolerable, a change in the empiric regimen or an additional antimicrobial drug becomes necessary, microbiologic tests identify species not susceptible to initial regimen
C-10. How should the persistent neutropenic fever syndrome be managed?	Low-risk patients who fail to defervesce after 2-3 d of an initial empirical broad-spectrum antibiotic regimen should be re-evaluated to detect and treat a new or progressing anatomical site of infection and considered for hospitalization

Abbreviations: ANC, absolute neutrophil count; G-CSF; granulocyte colony-stimulating factor; IDSA, Infectious Disease Society of America; IFI, invasive fungal infection; MASCC, Multinational Association for Supportive Care in Cancer.

Table 2. Summary of Patient-Clinician Communications

Communicate need for knowing and acting on the early symptoms of febrile neutropenia to all concerned, from patients at risk and their relatives, to primary and secondary care staff.
Use communication approaches tailored to individual patient needs according to health literacy and numeracy, living circumstances, language barriers, and decision-making capacity.
Provide clear written instructions about when and how to contact health care practitioners.
Expand dissemination and implementation of clinical practice guidelines to oncology nursing professionals in all care settings.
Recognize that coordination of care among primary care practitioners, specialists, and emergency departments is essential to ensure a rapid response when febrile neutropenia is suspected.
Encourage and support patients to advocate for their care in emergency situations so they are not put at greater risk.
Give patients access to written and/or electronic copies of their febrile neutropenia management plans.

The effectiveness of patient-clinician communication can be as important as that of a diagnostic or treatment intervention. Its scope encompasses patient, caregiver, and clinician roles, responsibilities, and expectations for health care; sharing all necessary information; and tailoring communication to individual patient needs according to health literacy, numeracy, living circumstances, language barriers, and decision-making capacity.^{7,8} Communication strategies developed for patients with limited health literacy can benefit patients of all literacy levels.⁹ Improving communication regarding outpatient management of FN must involve adapting the guideline's main recommendations to patient education resources tailored for patients with limited or poor health literacy.

Successful management of FN in adult oncology outpatients requires that they be educated to promptly recognize and act on signs and symptoms of possible infection. Effective education about monitoring body temperature and other symptoms of infection is vital. In addition, communications should acknowledge and address the reality that many patients are reluctant to seek help outside of office hours. It

Table 3. Sample Key Messages for Patients

Define neutropenia.
Explain that neutropenia is a major risk factor for infections in patients with cancer undergoing chemotherapy.
Convey that infections during chemotherapy can be life threatening and may delay future chemotherapy treatments.
Explain that there are effective strategies used by the health care team to anticipate, prevent, and manage infections.
Discuss the roles of the clinician and patient in managing febrile neutropenia.
Explain how risk will be assessed.
Explain that patients will be kept informed about when their risk of infection is highest.
Tell patients who are neutropenic that fever may be a sign of infection, even in the absence of other symptoms. Therefore, if fever is present, they need to seek immediate medical attention.
Provide information about other signs of infection and tell them to seek medical attention immediately in the presence of any signs of infection.
Provide information about hand washing, mouth care, skin changes and skin care, protection from cuts and scrapes, wound care, pet care, and gardening.

is essential that patients and caregivers receive clear written instructions on when and how to contact health care practitioners.¹⁰ Clinicians also are encouraged to inform patients of evidenced-based infection control guidelines to minimize unnecessary restrictions.^{11,12}

Although knowledge of how best to manage FN in adult oncology outpatients has grown significantly during the last several decades, new challenges to effective communication have arisen. These include the increasing numbers of patients immunocompromised after chemotherapy and immunotherapy, the changing epidemiology of infection, and the growing resistance of bacteria to commonly used antimicrobial agents. Moreover, as new chemotherapy regimens are developed, and as new antibiotics are introduced for prophylaxis or therapy, new infection risks have been defined,¹³ and the outpatient management of FN has become increasingly complex. Coordination of care among primary and specialist settings and emergency departments is essential

to ensure a rapid response when FN is suspected. Patients should be both encouraged and supported to advocate for their care in emergency situations so they are not put at greater risk. Patients should also have access to written and/or electronic copies of their FN management plans so that health care providers making treatment decisions are fully aware of the patient's needs.^{10,14}

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