ASCO Issues New Guideline on Fever and Neutropenia Management for Adult Patients with Cancer; Endorses International Pediatric Neutropenia Guideline

Guidelines Will Help Physicians Identify Patients at Highest Risk of Neutropenia-related Complications and Reduce Overtreatment

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ALEXANDRIA, Va. – Today, the American Society of Clinical Oncology (ASCO) issued a new clinical practice guideline on the management of neutropenia with fever and preventing related infections in patients with cancer. Neutropenia is a common condition among patients with cancer. It is caused by low levels of a type of white blood cells called neutrophils. The Society also endorsed a related guideline for children with cancer developed by the International Pediatric Fever and Neutropenia Guideline Panel. The guidelines will help doctors identify patients who are at high risk of medical complications related to neutropenia with fever, clarify when preventive treatment for infection is needed, and provide guidance on which patients can be managed safely at home during a febrile neutropenia episode.

Neutropenia can be caused by the cancer itself or by the types of chemotherapy drugs that kill cancer cells and some blood-forming cells. People with neutropenia are about 50 times more likely to develop an infection compared with those with normal blood counts. Febrile neutropenia is diagnosed when a patient with neutropenia develops a fever — a sign of possible infection — and typically is treated by immediate hospitalization and intravenous antibiotics to prevent life-threatening complications, such as sepsis. However, select patients who are at low risk of complications related to febrile neutropenia may be eligible for outpatient treatment.

“A priority of this evidence-based guideline was to help doctors identify patients with febrile neutropenia who do not need to be hospitalized,” said Christopher R. Flowers, MD, MS, Co-Chair
of the ASCO Expert Panel that drafted the guideline, and Associate Professor of Pediatrics and Hematology and Medical Oncology at Emory School of Medicine. “This guideline will help spare select patients from discomfort and risks of hospitalization, such as exposure to treatment-resistant microbes, and has the potential to save substantial resources.”

ASCO’s new guideline describes how well-validated scoring systems, such as the Multinational Association for Supportive Care in Cancer (MASCC) score and Talcott’s Rules, can be applied to assess the risk of complications from febrile neutropenia.

“Patients who don’t have a fever and have very low absolute neutrophil counts (less than 100 per microliter for more than 7 days) can also be managed safely at home with oral antibiotics and antifungals to prevent infection,” said Scott Ramsey, MD, PhD, Co-Chair of the ASCO Expert Panel that drafted the guideline, and Professor of Medicine at University of Washington School of Medicine. “Outcomes can be better for people if we identify those who can be safely managed at home.”

To develop this clinical practice guideline, an ASCO Expert Panel conducted a formal systematic review of evidence from relevant medical literature. The review yielded 47 articles published from 43 studies.

The guideline for adult patients specifically recommends the following:

- **Prevention of infection for patients with neutropenia but no fever:** Preventive treatment with antibacterial and antifungal drugs is only recommended for patients with profound neutropenia that will last for more than seven days, unless other factors increase the risk of complications. Overuse of preventive regimens contributes to the development of treatment resistant strains of microbes. The preferred preventive drugs are an oral fluoroquinolone for bacteria and an oral triazole for fungi.

- **Prompt initial treatment for febrile neutropenia:** Patients with neutropenia who develop a fever should go to the hospital, outpatient clinic, or doctor’s office immediately to receive initial antibacterial treatment.

- **Assessment of risk for complications in patients with febrile neutropenia using the MASSC score system or Talcott’s Rules:** Patients who are at lowest risk of complications have a MASCC score greater than 21 and fall into the Talcott’s Group 4. However, literature review showed that medical complications occurred in up to 11 percent of patients who are identified by these methods as having low risk of medical complications from febrile neutropenia.

- **Management of febrile neutropenia at home:** A subset of the patients who are identified as being at low risk of medical complications and are also without other risk factors listed in the guideline can be managed safely at home with oral antibacterial and antifungal regimens after receiving the initial treatment in the hospital, clinic, or doctor’s office. Outpatient management of febrile neutropenia is appropriate only for patients who are able to comply with frequent clinic visits, live within 1 hour or less than 30 miles from a hospital, have a caretaker present at home 24 hours a day, and have 24-hour a day access to a telephone and transportation to get to the hospital. Patients that experience a clinical worsening of their condition, organ dysfunction, or certain comorbid conditions should be managed in the hospital.

- **Medications for management of febrile neutropenia at home:** Because fever in a patient with
neutropenia is assumed to be due to bacterial infection, the first treatment should be with oral antibacterial drugs, typically a fluoroquinolone antibiotic plus amoxicillin/clavulanate. These treatments are given to prevent serious infection when there is a fever but doctors do not yet know what the infection is. Intravenous antibiotics given in the hospital are recommended for patients who are at high risk of complications.

In addition, the guideline aligns with ASCO’s “Top Five” opportunities to improve the quality and value of cancer care by curbing the use of common tests and treatments that are not supported by clinical evidence. ASCO developed this list through its participation in the Choosing Wisely® campaign, an effort by nine founding medical specialty societies and the American Board of Internal Medicine (ABIM) Foundation to help patients choose evidence-based and truly necessary care. A 2006 ASCO guideline on white blood cell growth factors, also known as colony-stimulating factors, recommended against their use for patients who have a very low risk for febrile neutropenia (less than 20 percent). These factors boost the body's production of white blood cells, which can be destroyed during certain chemotherapy regimens and thus cause neutropenia. By endorsing the 2006 recommendation, this new guideline remains consistent with ASCO's list of "Top Five" opportunities.

ASCO Endorses International Guideline for Managing Pediatric Febrile Neutropenia
The pediatric guideline endorsed by ASCO today was developed by the International Pediatric Fever and Neutropenia Guideline Panel, composed of experts in pediatric oncology and infectious disease, as well as patient advocates. The guideline provides recommendations related to diagnosis, ongoing management, and initial antifungal and antibacterial treatment of febrile neutropenia in children with cancer and/or those undergoing blood stem-cell transplantation. In addition to incorporating evidence from pediatric clinical trials, the authors adapted evidence from the adult population to the pediatric population. Febrile neutropenia is a common complication in children with cancer who receive chemotherapy. The guideline was published online September 17, 2012 in the Journal of Clinical Oncology. ASCO's endorsement of the guideline offers ASCO members guidance on management of febrile neutropenia in children as well as adults with cancer.

“This is the first comprehensive, evidence-based guideline to specifically address the management of febrile neutropenia in children with cancer,” said Flowers.

ASCO's guideline endorsement process involves assessing the clarity and clinical utility of the recommendations, and their consistency with the reviewers’ interpretation of the available data. Through guideline endorsements, ASCO will increase the scope of high-quality, ASCO-vetted guidance available to its members and the oncology community.

The results of clinical trials play a vital role in the development of ASCO’s guidelines and the guidelines it endorses. 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.

More information on the new guideline and clinical tools and resources are available.

For copies of both guidelines, please contact Aaron Tallent at aaron.tallent@asco.org or 571-483-1371.

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**About ASCO:**

Founded in 1964, the American Society of Clinical Oncology (ASCO) is the world’s leading professional organization representing physicians who care for people with cancer. With more than 35,000 members, ASCO is committed to improving cancer care through scientific meetings, educational programs and peer-reviewed journals. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation, which funds groundbreaking research and programs that make a tangible difference in the lives of people with cancer. For ASCO information and resources, visit asco.org. Patient-oriented cancer information is available at Cancer.Net.