Infectious Complications in Patients with Cancer - 2015
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General Reviews/Guidelines

Freifeld AG. 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 2011;52:e56-e93. *[Recently updated evidence-based guidelines developed by expert members of the IDSA that provide guidance for the approach to diagnosing and treating infections in neutropenic patients]*.

Lee DG. Evidence-based guidelines for empirical therapy of neutropenic fever in Korea. Korean J Intern Med 2011;26:220-52. *[Another set of evidence-based guidelines that address a few additional topics not covered by the IDSA guidelines]*

NCCN clinical practice guidelines in oncology. Prevention and treatment of cancer-related infections. V.1.2014. http://www.nccn.org/professionals/physician_gls/PDF/infections.pdf. *[An exhaustive & rational set of guidelines recently updated and developed by the National Comprehensive Cancer Network that address all aspects of cancer-related infections]*.

Flowers CR. 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 2013;31:794-810. *[Recently published guidelines that outline the approach to prophylaxis and treatment of infections in low risk outpatient cancer patients]*.

Granwehr B. The impact of infectious diseases consultation on oncology practice. Curr Opin Oncol 2013;25:353-9. *[Infectious diseases consultants contribute value in various inpatient and outpatient infections, decreasing mortality, cost, and complications]*.

Raghavendra M. Management of neutropenic fever during a transition from traditional hematology/oncology service to hospitalist care. Wisc Med J 2014;113:53-8.

Infection Risk/Clinical Presentation

Bodey GP. Quantitative relationships between circulating leukocytes and infection in patients with acute leukemia. Ann Intern Med 1966;64:328-40. *[The milestone description of the relationship between the absolute granulocyte count and risk of infection]*.

Taur Y. The intestinal microbiota and susceptibility to infection in immunocompromised patients. Curr Opin Infect Dis 2013;26:332-7. *[Commensal bacteria, largely anaerobic, serve to maintain microbial stability and colonization resistance by preventing overgrowth or domination with more pathogenic bacteria]*.

Sickles EA. Clinical presentation of infection in granulocytopenic patients. Arch Intern Med 1975;135:715-9.

Bodey GP. Unusual presentations of infection in neutropenic patients. Int J Antimicrob Agents 2000;16:93-5.

Nauseef WM. A study of the value of simple protective isolation in patients with granulocytopenia. N Engl J Med 1981;304:448-53. *[Description of a comparative trial of routine care versus protective isolation in neutropenic patients; demonstrated that routine care was equivalent to more elaborate protective isolation measures]*.

Antibiotic Prophylaxis

Leibovici L. Antibiotic prophylaxis in neutropenic patients. New evidence, practical decisions. Cancer 2006;107:1743-51.

Gafter-Gvili. Meta-analysis: antibiotic prophylaxis reduces mortality in neutropenic patients. Ann Intern Med 2005;142:979-95.

Pascoe J. Antibiotics for the prevention of febrile neutropenia. Curr Opin Hematol 2009;16:48-52.

Bow EJ. Antifungal prophylaxis for severely neutropenic chemotherapy recipients. A meta-analysis of randomized-controlled clinical trials. Cancer 2002;94:3230-46.

Empiric Antibiotic Therapy

Paul Ml. Beta lactam monotherapy versus beta lactam-aminoglycoside combination therapy for fever with neutropenia. Systematic review and meta-analysis. BMJ 2003;326:1111. *[Beta lactam monotherapy was marginally better for survival and was associated with fewer adverse events]*.

Paul M. Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia (review). Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD003038. DOI: 10.1002/14651858. CD003038.pub2. *[Beta-lactam monotherapy is advantageous compared with beta-lactam-aminoglycoside combination therapy with regard to survival, adverse events and fungal super-infections]*.

Corey L. Persistent fever in patients with neutropenia . N Engl J Med 2002;346:222-4.

Yahav D. Efficacy and safety of cefepime: a systematic review and meta-analysis. Lancet Infect Dis 2007;7:338-48.

Goulenok T. Antimicrobial treatment of febrile neutropenia: Pharmacokinetic-pharmacodynamic considerations. Clin Pharmacokinet 2013;52:869-83. *[Pharmacokinetic & pharmacodyanmic parameters are substantially changed in patients with febrile neutropenia; clinicians risk under-dosing antibiotic therapy in this group of patients]*.

Oral & Outpatient Antibiotic Management

Klastersky J. The Multinational Association for Supportive Care in Cancer Risk Index: a multinational scoring system for identifying low-risk febrile neutropenic cancer patients. J Clin Oncol 2000;18:3038-51. *[Article that describes the derivation of the MASCC risk index]*.

http://www.qxmd.com/calculate-online/hematology/febrile-neutropenia-mascc *[Online calculator for the MASCC index]*.

Freifeld A. A double-blind comparison of empirical oral and intravenous antibiotic therapy for low-risk febrile patients with neutropenia during cancer chemotherapy. N Engl J Med 1999;341:305-11 *[In hospitalized low-risk patients who have fever and neutropenia during cancer chemotherapy, empirical therapy with oral ciprofloxacin and amoxicillin-clavulanate is safe and effective]*.

Kern WV. Oral versus intravenous empirical antimicrobial therapy for fever in patients with granulocytopenia who are receiving cancer chemotherapy. N Engl J Med 1999;341:312-8 *[In low-risk patients with cancer who have fever and granulocytopenia, oral therapy with ciprofloxacin plus amoxicillin-clavulanate is as effective as intravenous therapy]*.

Vidal L. Oral versus intravenous antibiotic treatment for febrile neutropenia in cancer patients: a systematic review and meta-analysis of randomized trials. J Antimicrob Chemother 2004;54:29-37.

Talcott JA. Safety of early discharge for low-risk patients with febrile neutropenia: a multicenter randomized controlled trial. J Clin Oncol 2011;29:3977-83 *[No evidence of adverse medical consequence resulted from home care, despite a protocol designed to detect evidence of clinical deterioration]*.

Empiric Glycopeptide (vancomycin) Use

EORTC-IATCG. Vancomycin added to empirical combination antibiotic therapy for fever in granulocytopenic cancer patients. J Infect 1991;163:951-8. *[Trial that showed no additional benefit from the addition of vancomycin to empiric piperacillin-tazobactam in febrile neutropenic patients]*.

Micozzi A. Piperacillin/tazobactam/amikacin versus piperacillin/amikacin/teicoplanin in the empirical treatment of neutropenic patients. Eur J Clin Microbiol Infect Dis 1993;12:1-8.

Antifungal Therapy

Pizzo PA. Empiric antibiotic and antifungal therapy for cancer patients with prolonged fever and granulocytopenia. Am J Med 1982;72:101.

EORTC-IATCG. Empiric antifungal therapy in febrile granulocytopenic patients. Am J Med 1989;86:668.

Duarte RF. Phase 1b study of new posaconazole tablet for the prevention of invasive fungal infections in high-risk patients with neutropenia. Antimicrob Agents Chemother 2014 Jul 21 [Epub ahead of print]. *[Posaconazole tablets at a dose of 300 mg once daily achieved the desired exposure target and was generally well tolerated in high-risk neutropenic patients]*.

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Clinical Aspects & Therapy for Specific Infectious Syndromes

Nesher L. Neutropenic entercolitis, a growing concern in the era of widespread use of aggressive chemotherapy. Clin Infect Dis 2013;56:711-7. *[Management of neutropenic entercolitis includes bowel rest, correction of cytopathies and coagulopathies, and broad spectrum antibiotics and antifungal agents. Surgical intervention may be necessary to manage complications, but should be delayed if possible]*.

Walsh TJ. Treatment of aspergillosis: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis 2008;46:327-60.

Marr KA. Combination antifungal therapy for invasive aspergillosis. A randomized trial. Ann Intern Med 2015;162:81-9. *[Compared with voriconazole monotherapy, combination therapy with anidulafungin led to higher survival in subgroups of patients with invasive aspregillosis]*.

Nucci M. How we treat invasive fungal disease in patient with acute leukemia: the importance of an individualized approach. Blood 2014;124:3858-69. [*Patients are stratified as high, intermediate, or low risk for invasive fungal diseases and risk-adapted antifungal strategies are applied, including primary or secondary prophylaxis and diagnostic-based preemptive or empiric therapy]*.

Kontoyiannis DP. Hepatosplenic candidiasis. A manifestation of chronic disseminated candidiasis. Infect Dis Clin North Am 2000;14:721-39.

Kontoyiannis DP. How I treat mucormycosis. Blood 2011;118:1216-24. *[Review of potential diagnostic modalities and summation of recent evidence regarding newer potential modalities for the treatment of mucormycosis]*.

Perfect JR. Update on epidemiology of and preventive strategies for invasive fungal infections in cancer patients. Clin Infect Dis 2014;59:S352-5.

Kim SW. Diagnostic value of bronchoscopy in patient with hematologic malignancy and pulmonary infiltrates. Ann Hematol 2015;94:153-9. *[Retrospective analysis of 206 bronchoscopies in 187 patients with hematologic malignancies & pulmonary infiltrates. Bacteria found in 41.3%; fungi in 23.8%; viruses in 28.6%. Treatment was modified in 30.1% as a result of the bronchoscopy results]*.

Maschmeyer G. Diagnosis and antimicrobial therapy of lung infiltrates in febrile neutropenic patients (allogeneic SCT excluded): updated guidelines of the Infectious Disease Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO). Ann Oncol 2015;26:21-33. *[Evidence-based clinical practice guideline that addresses diagnosis & therapy]*.

Wingard JR. How I manage pulmonary nodular lesions and nodular infiltrates in patients with hematologic malignancies or undergoing hematopoietic cell transplantation. Blood 2012;120:1791-800.

Kumar D. Respiratory viral infections in transplant and oncology patients. Infect Dis Clin N Am 2010;24:395-412. *[Nice review of the importance of frequently-ignored respiratory viral infections in immunosuppressed patients. The authors emphasize the importance of prevention through infection control measures and appropriate immunization of patients and personnel]*.

Sandherr M. Antiviral prophylaxis in patients with solid tumours and haematological malignancies-update of the guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO). Ann Hematol 2015;94:1441-50. *[Provides some direction about antiviral prophylaxis for HSV, VZV, hepatitis B virus, and various respiratory viruses]*.

Chemaly RF. Respiratory viral infections in adults with hematological malignancies and human stem cell transplantation recipients. Medicine 206;85:278-87. *[Influenza, parainfluenza and RSV similar in frequency. Infection progresses to LRTI in 35% and overall mortality of 15%. Specific therapy may be of benefit]*.

Chemaly RF. Management of respiratory viral infections in hematopoietic cell transplant recipients and patients with hematologic malignancies. Clin Infect Dis 2014;59:S344-51. *[Increasing evidence suggests ribavirin may have some benefit in patients with RSV. Ribavirin & investigational agent DAS181 may be of some benefit for parainfluenza virus. Neuraminidase inhibitors have not been carefully examined in oncology patients but do have a role in therapy]*.

Kamboj M. Nosocomial infections in patients with cancer. Lancet Oncol 2009;10:589-97. *[9-12% of patients being treated in the hospital for cancer develop nosocomial infections]*.

Almyroudis NG. Prevention and treatment of invasive fungal disease in neutropenic patients. Curr Opin Infect Dis 2009;22:385-93.

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Pfeiffer CD. Diagnosis of invasive aspergillosis using a galactomannan assay: a meta-analysis. Clin Infect Dis 2006;42:1417-27.

Karageorgopoulos DE. β-D-glucan assay for the diagnosis of invasive fungal infections: a meta-analysis. Clin Infect Dis 2011;52:75-70.

Mulanovich VE. Fungal pneumonia in patients with hematologic malignancies: current approach and management. Curr Opin Infect Dis 2011;24:323-32.

Mihu CN. Does combination of lipid formulation of amphotericin B and echinocandins improve outcome of invasive aspergillosis in hematological malignancy patients? Cancer 2010;116:5290-6. *[The combination of liposomal amphotericin B and echinocandins offered no advantage in terms of improving response or reducing mortality over either drug alone in a study of 159 patients at MDACC]*.

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Vos FJ. ^{18}F-FDG PET/CT for diagnosing infectious complications in patients with severe neutropenia after intensive chemotherapy for haematological malignancy or stem cell transplantation. Eur J Nucl Med Mol Imaging 2012;39:120-8.

Hirsch HH. Fourth European Conference on Infection in Leukaemia (ECIL-4): guidelines for diagnosis and treatment of human respiratory syncytial virus, parainfluenza virus, metapneumovirus, rhinovirus, and coronavirus. Clin Infect Dis 2013;56:258-66.

Shomali W. Can procalcitonin distinguish infectious fever from tumor-related fever in non-neutropenic cancer patients? Cancer 2012;May 17 [Epub ahead of print] *[Baseline procalcitonin levels are markedly elevated in patients with blood stream infections, but also elevated in patients with tumor fever from widespread malignancy; there is considerable overlap in values such that the utility of this marker is suspect]*.

Catheter-related Infections

Raad I. Differential time to positivity: a useful method for diagnosing catheter-related bloodstream infections. Ann Intern Med 2004;140:18-25.

Raad I. Advances in prevention and management of central line-associated bloodstream infections in patients with cancer. Clin Infect Dis 2014;59:S340-3.

Mermel LA. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009; 49:1–45.

Picardi M. Early ultrasonographic finding of septic thrombophlebitis is the main indicator of central venous catheter removal to reduce infection-related mortality in neutropenic patients with bloodstream infection. Ann Oncol 2012;23:2122-8. *[With an ultrasonographic-driven strategy, early septic thrombophlebitis detection and prompt CVC removal decreased infection-related mortality, whereas clinically-driven strategy led to inappropriate number, reasons, and timeliness of CVC removal]*.

Colony Stimulating Factors

Otavio ACC. Colony-stimulating factors for chemotherapy-induced febrile neutropenia: a meta-analysis of randomized controlled trials. J Clin Oncol 2005;23:4198-4214.

Gurion R. Colony-stimulating factors for prevention and treatment of infectious complications in patients with acute myelogenous leukemia. Cochrane Database Syst Rev 2012;Jun 13;6:CD008238.

Smith TJ. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 2015;33[Epub ahead of print]. *[Prophylactic use of CSFs to reduce the risk of febrile neutropenia is warranted when the risk of febrile neutropenia is approximately 20% or higher and no other equally effective & safe regimen that does not require CSFs is available. Primary prophylaxis is recommended for the prevention of febrile neutropenia in patient who are at high risk on the basis of age, medical history, disease characteristics & myelotoxicty of the regimen]*.