Table 1. Overall Summary of Recommendations*

	Risk Stratification	Evaluation	Treatment
INITIAL PRESENTATION OF FN	Adopt a validated risk stratification strategy and incorporate it into routine clinical management (1C).	Obtain blood cultures at the onset of FN from all lumens of central venous catheters (1C). Consider peripheral blood culture concurrent with obtaining central venous catheter cultures (2C). Consider urinalysis and urine culture in patients where a clean-catch, midstream specimen is readily available (2C). Obtain chest radiography only in symptomatic patients (1B).	**High-Risk FN** Use monotherapy with an anti-pseudomonal *β*-lactam or a carbapenem as empiric therapy in pediatric high-risk FN (1A). Reserve addition of a second Gram-negative agent or a glycopeptide for patients who are clinically unstable, when a resistant infection is suspected, or for centers with a high rate of resistant pathogens (1B). **Low-Risk FN** In children with low-risk FN, consider initial or step-down outpatient management if the infrastructure is in place to ensure careful monitoring and follow-up (2B). In children with low-risk FN, consider oral antibiotic administration if the child is able to tolerate this route of administration reliably (2B).
		Modification of Treatment	**Cessation of Treatment**
ONGOING MANAGEMENT OF FN: 24 to 72 hours or more after initiation of empiric antibacterial treatment		In patients who are responding to initial empiric antibiotic therapy, discontinue double coverage for Gram-negative infection or empiric glycopeptide (if initiated) after 24 to 72 hours if there is no specific microbiologic indication to continue combination therapy (1B). Do not modify the initial empiric antibacterial regimen based solely on persistent fever in children who are clinically stable (1C). In children with persistent fever who become clinically unstable, escalate the initial empiric antibacterial regimen to include coverage for resistant Gram-negative, Gram-positive, and anaerobic bacteria (1C).	**All Patients** Discontinue empiric antibiotics in patients who have negative blood cultures at 48 hours, who have been afebrile for at least 24 hours and who have evidence of marrow recovery (1C). **Low-Risk FN** Consider discontinuation of empiric antibiotics at 72 hours in low-risk patients who have negative blood cultures and who have been afebrile for at least 24 hours, irrespective of marrow recovery status, as long as careful follow-up is ensured (2B).

	Risk Stratification	Evaluation	Treatment
EMPIRIC ANTIFUNGAL TREATMENT: 96 hours or more after initiation of empiric antibacterial treatment	Patients at IFD high-risk are those with AML, relapsed acute leukemia, those receiving highly myelosuppressive chemotherapy for other malignancies, and allogeneic hematopoietic stem cell transplant recipients with persistent fever despite prolonged (≥ 96 hours) broad-spectrum antibiotic therapy and expected prolonged neutropenia (>10 days). All others should be categorized as IFD low-risk (1B).	**All Patients** Consider galactomannan in bronchoalveolar lavage and cerebrospinal fluid to support the diagnosis of pulmonary or central nervous system aspergillosis (2C). In children, do not use ß-D-glucan testing for clinical decisions until further pediatric evidence has accumulated (1C). **IFD High Risk** Consider prospective monitoring of serum galactomannan twice per week in IFD high-risk hospitalized children for early diagnosis of invasive aspergillosis (2B). In IFD high-risk children with persistent FN beyond 96 hours, perform evaluation for IFD. Evaluation should include CT of the lungs and targeted imaging of other clinically suspected areas of infection (1B). Consider CT of the sinuses in children 2 years of age or older (2C). **IFD Low Risk** In IFD low-risk patients, do not implement routine galactomannan screening (1C).	**All Patients** Use either caspofungin or liposomal amphotericin B for empiric antifungal therapy (1A). **IFD High Risk** In neutropenic IFD high-risk children, initiate empiric antifungal treatment for persistent or recurrent fever of unclear etiology that is unresponsive to prolonged (≥ 96 hours) broad-spectrum antibacterial agents (1C). **IFD Low Risk** In neutropenic IFD low-risk children, consider empiric antifungal therapy in the setting of persistent FN (2C).

*Parenthesis indicates the GRADE strength of recommendation (1=strong, 2=weak) and quality of the evidence (A=high, B=moderate, C=low or very-low).

Abbreviations: AML – acute myeloid leukemia; CT – computed tomography; FN – fever and neutropenia; GRADE – Grades of Recommendation Assessment, Development and Evaluation; IFD – invasive fungal disease; CNS –central nervous system