Neutropenic Fever Inpatient Adult Treatment (Solid Tumors)

Patient presents with fever or develops fever at MD Anderson

Does patient exhibit ≥ 2 qSOFA criteria?

Yes → See Adult Sepsis Management algorithm and use sepsis order set

No → See Neutropenic Fever Outpatient Treatment for Solid Tumor Patients algorithm

Does patient meet outpatient therapy criteria?

Yes → See Neutropenic Fever Outpatient Treatment for Solid Tumor Patients algorithm

No → See Pneumonia in Adult Patients with Cancer algorithm

See Page 2 for antibiotic regimen

CVAD = central venous access device

PERG = percutaneous endoscopic gastrostomy

1 ANC < 1 K/microliter and temperature either ≥ 38.3°C or equal to 38°C for 1 hour or longer

2 qSOFA criteria:
- Altered mental status
- Respiratory rate ≥ 22 bpm
- Systolic blood pressure ≤ 100 mmHg

3 Patient must meet all of the following criteria for outpatient treatment:
- Solid tumor
- Able to tolerate oral medications
- Able to tolerate fluids
- Does not use PEG as primary route for nutrition and medications
- No confirmed focus of infection
- Lives within 1 hour travel time of MDACC
- Has a 24 hour caregiver
- Has access to transportation and telephone at residence

4 Complete physical exam
- Start IV fluids
- CBC with differential, BMP, lactic acid
- Blood cultures (with a set collected from each lumen simultaneously if CVAD present and 1 peripheral site); other cultures (e.g., sputum culture, urinalysis with culture and sensitivity) only if clinically indicated
- Chest x-ray or other tests as clinically indicated

5 Not currently on antibiotics
- 15 years old or older
- No quinolone allergy for oral regimens
- Patient is considered low risk
- No multi-resistant organism colonization

Note: This algorithm should not be used for patients receiving chimeric antigen receptor (CAR) cell therapy.
Consider the following when selecting antibiotics:
- Recent culture and sensitivity
- History of multi-drug resistant organism (MDRO)
- Infection or colonization
- Suspected line infection
- Antibiotic history and prophylaxis
- Source of infection if identified
- Antibiotic allergies
- Organ dysfunction
- Mucositis

Routine use of therapeutic G-CSF is not recommended.

Documented beta-lactam allergy (i.e., hives or anaphylaxis)

No

Yes

ANTIMICROBIAL THERAPY RECOMMENDATIONS
(Adjust doses for patients with renal/hepatic dysfunction)
Gram negative coverage antibiotics should be given first
Antibiotics should be given within 2 hours

Neutropenic fever:
- Cefepime 2 grams IV every 8 hours

If mucositis greater than or equal to grade 2, suspected intra-abdominal infection, or other indication for anaerobic coverage:
- Add metronidazole 500 mg IV every 8 hours

If clinically suspected line infection, bacteremia, skin/soft tissue infection, and/or MRSA colonization:
- Add vancomycin 15 mg/kg (round to nearest 250 mg dose) IV every 12 hours

If history of MDRO infection:
- Consider ID consult
- Consider meropenem 1 gram IV every 8 hours if clinically appropriate in place of cefepime/metronidazole

Neutropenic fever:
- Aztreonam 2 grams IV every 6 hours (preferred) or
- Ciprofloxacin 400 mg IV every 8 hours if no quinolone prophylaxis or therapy in past 90 days

Plus:
- Vancomycin 15 mg/kg (round to nearest 250 mg dose) IV every 12 hours

If mucositis greater than or equal to grade 2, suspected intra-abdominal infection, or other indication for anaerobic coverage:
- Add metronidazole 500 mg IV every 8 hours

If history of MDRO infection:
- Consider ID consult

See Page 3 for re-assessment

MDROs include:
- Enterococcus resistant to vancomycin
- Staphylococcus aureus resistant to meticillin (oxacillin)
- S. pneumoniae resistant to penicillin and streptococci resistant to cephalosporin
- Stenotrophomonas maltophilia
- Any extended spectrum beta-lactamase (ESBL)-producing gram negative bacilli
- Any carbapenem resistant gram negative bacilli
- All other gram negative bacilli that are resistant to usual recommended first-line agents

Chills, rigors with infusion through catheter, cellulitis or discharge around the line entry site

Continue G-CSF if patient was receiving as daily prophylaxis. Consider therapeutic use if risk factor(s) present: sepsis, age > 65 years old, pneumonia or other documented infection, invasive fungal infection, ANC < 100 K/microliter, expected neutropenia duration > 10 days, uncontrolled primary disease, hospitalization at the time of fever or prior episode of NF.

Consider meropenem if patient has any of the following:
- Non-IgE-mediated allergy to alternative agents
- Recent treatment (≥ 3 days duration) with cefepime or piperacillin/tazobactam within past 30 days
- Infection with ESBL organism
- Infection with organism only susceptible to carbapenem

1 MDROs include:
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- Staphylococcus aureus resistant to meticillin (oxacillin)
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2 Chills, rigors with infusion through catheter, cellulitis or discharge around the line entry site

3 Continue G-CSF if patient was receiving as daily prophylaxis. Consider therapeutic use if risk factor(s) present: sepsis, age > 65 years old, pneumonia or other documented infection, invasive fungal infection, ANC < 100 K/microliter, expected neutropenia duration > 10 days, uncontrolled primary disease, hospitalization at the time of fever or prior episode of NF.

4 Consider meropenem if patient has any of the following:
- Non-IgE-mediated allergy to alternative agents
- Recent treatment (≥ 3 days duration) with cefepime or piperacillin/tazobactam within past 30 days
- Infection with ESBL organism
- Infection with organism only susceptible to carbapenem

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. Local microbiology and susceptibility/resistance patterns should be taken into consideration when selecting antibiotics. This algorithm should not be used to treat pregnant women.
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RE-ASSESSMENT

72-hour evaluation

Patient afebrile

Has source of fever been identified?

Yes

- Treat for appropriate duration based on nature of infection (e.g., urinary tract infection, cellulitis)
- Disposition per MD

No

- Continue treatment for 2 days after ANC > 0.5 K/microliter and rising
- Disposition per MD

Patient febrile

- Re-evaluate antibiotics
- Repeat cultures
- Imaging as clinically indicated
- Evaluate thoroughly for non-infectious causes of fever (e.g., medications, thrombosis, tumor, necrosis)
- Consult Infectious Diseases

Disposition based on Infectious Diseases consult recommendations and/or diagnostic test results

1 Consider narrowing therapy based on cultures and sensitivities (e.g., discontinue vancomycin if no gram positive organisms are identified and patient does not have cellulitis)
SUGGESTED READINGS


SUGGESTED READINGS - continued


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SUGGESTED READINGS - continued


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DEVELOPMENT CREDITS

This practice consensus algorithm is based on majority expert opinion of the Neutropenic Fever Work Group at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

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