Optimizing Antimicrobial Use in Special Populations: Neutropenic Patients and the “Surviving the Sepsis Campaign”

Keith S. Kaye, MD, MPH
Professor of Medicine
University of Michigan Medical School
Ann Arbor, MI

Overview

• Sepsis
  – Definitions, CMS and SSCG and controversies
  – Impact on antibiotics
  – Opportunities for stewardship
• Febrile neutropenia
  – Guideline recommendations
  – Stewardship opportunities
    • Antibiotic selection
    • De-escalation
    • Duration
• Unanswered question/research opportunities
Surviving Sepsis: What’s the Concern

- Increasing national interest
  - SCCM, ESICM: Surviving Sepsis Campaign Guidelines (SSCG)
  - CDC: Get Ahead of Sepsis Campaign
  - CMS: SEP-1 Core Measure (began in 2015)
    - Public reporting began July, 2018

Image taken from CDC Get Ahead of Sepsis Educational Materials.
Rising Incidence . . .
But Decreasing Mortality In Septic Patients (?)

• According to claims-based data appears to be the case
  – But not as clear according to clinical data (Sepsis-3 criteria)


Outlining the Controversies

• SSCG (antibiotics [abx] within 1 hour) vs. SEP-1 (abx within 3 hours)
  – Different criteria used to define sepsis
    • SSCG recommends Sepsis-3 criteria: sepsis or septic shock using SOFA or qSOFA
    • SEP-1 recommends SIRS (≥ 2 criteria) + organ dysfunction ± refractory to fluid resuscitation
      – Severe sepsis or septic shock
  – 1-hour bundle vs 3- and 6-hour bundles
    • SCCM and ACEP re-evaluating appropriateness of “1-hour”

Crit Care Med 2017;45:486–552.
SEP-1 Compliance Associated with Reduced Mortality?

- Retrospective cohort study of sepsis cases from seven hospitals reported to CMS for the SEP-1 measure
- Of the 851 cases of sepsis, only 33% SEP-1 compliant

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate OR (95% CI)</th>
<th>Multivariate OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (continuous)</td>
<td>1.61 (1.00–2.63)</td>
<td>1.62 (1.02–2.59)</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.03 (0.71–1.50)</td>
<td>0.98 (0.65–1.49)</td>
</tr>
<tr>
<td>White race</td>
<td>0.78 (0.35–1.70)</td>
<td>0.66 (0.27–1.66)</td>
</tr>
<tr>
<td>Elixhauser score (continuous)</td>
<td>1.06 (1.04–1.09)</td>
<td>1.05 (1.03–1.08)</td>
</tr>
<tr>
<td>Acute care hospital bed community</td>
<td>1.64 (1.13–2.46)</td>
<td>0.91 (0.59–1.40)</td>
</tr>
<tr>
<td>Study year 2 vs year 1</td>
<td>0.84 (0.59–1.20)</td>
<td>0.71 (0.47–1.07)</td>
</tr>
<tr>
<td>Discharging service</td>
<td>0.39</td>
<td>0.39</td>
</tr>
<tr>
<td>Medical</td>
<td>1.41 (0.69–2.91)</td>
<td>1.03 (0.49–2.17)</td>
</tr>
<tr>
<td>Surgical</td>
<td>0.49 (0.30–0.81)</td>
<td>0.31 (0.18–0.53)</td>
</tr>
<tr>
<td>Hospital-acquired sepsis</td>
<td>5.13 (3.11–8.47)</td>
<td>4.41 (2.69–7.14)</td>
</tr>
<tr>
<td>Hypotension at sepsis onset</td>
<td>1.21 (0.83–1.77)</td>
<td>0.69 (0.39–1.22)</td>
</tr>
<tr>
<td>Septic shock (end-stage renal disease)</td>
<td>1.76 (1.08–2.84)</td>
<td>1.49 (0.91–2.43)</td>
</tr>
<tr>
<td>Respiratory failure at sepsis onset</td>
<td>0.98 (0.56–1.73)</td>
<td>0.98 (0.56–1.73)</td>
</tr>
<tr>
<td>Vague symptoms</td>
<td>3.16 (2.00–4.94)</td>
<td>2.13 (1.35–3.33)</td>
</tr>
<tr>
<td>Body weight (continuous)</td>
<td>0.99 (0.98–1.01)</td>
<td>0.99 (0.98–1.01)</td>
</tr>
<tr>
<td>Urinary</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Renal failure</td>
<td>3.49 (1.85–6.55)</td>
<td>2.03 (1.14–3.63)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>2.98 (1.29–5.21)</td>
<td>1.24 (0.54–2.88)</td>
</tr>
<tr>
<td>Other</td>
<td>403 (2.12–7.53)</td>
<td>428 (206–959)</td>
</tr>
</tbody>
</table>

After adjustment no association between compliance and death
- Time to antibiotics > 3 hrs predicted death, OR 1.94, p=0.04

CMS Still Supports SEP-1

- Although several groups have raised concerns about the SEP-1 measure, CMS has not changed the criteria
- Reporting of institutional compliance to CMS started in October 2015
- Compliance with SEP-1 is now publicly reported
- Which parts of the metric are most relevant for antimicrobial stewardship programs?
  - Initiation of antibiotics within 3 hours
  - Initiation (and continuation?) of “broad-spectrum” antibiotics

Crit Care Med. 2018;46(10):1585-1591
Broad-Spectrum Antibiotics Recommended by SEP-1

**Monotherapy**
- Ampicillin/sulbactam, cefepime, cefotaxime, ceftaroline fosamil, ceftazidime, ceftriaxone, doripenem, imipenem/cilastatin, levofloxacin, meropenem, moxifloxacin, piperacillin-tazobactam, ticarcillin-clavulanate

**Combination Therapy**
- Aminoglycoside OR Aztreonam OR Ciprofloxacin
- Cephalosporins (first and second generation) OR Clindamycin OR Daptomycin OR Glycopeptides OR Linezolid OR Macrolides OR Penicillins

https://www.nhfca.org/psf/resources/Updates1/SEP-1%20Measure%20Information%20Form%20(MIF).pdf

Recommendations for Changes to SEP-1: Monotherapy
- Considerations from a multi-stakeholder workgroup (IDSA, SCCM, SHP, ACEP)
- Clinical, resistance and adverse effects concerns considered

<table>
<thead>
<tr>
<th>SEP-1 Generic Name</th>
<th>MATS WG Recommendation Generic Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin/sulbactam</td>
<td>Removed</td>
</tr>
<tr>
<td>Cefepime</td>
<td>Cefepime</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>Cefotaxime</td>
</tr>
<tr>
<td>Ceftaroline fosamil</td>
<td>Ceftaroline fosamil</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>Ceftazidime</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Ceftriaxone</td>
</tr>
<tr>
<td>Doripenem</td>
<td>Doripenem</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>Ertapenem</td>
</tr>
<tr>
<td>Imipenem/cilastatin</td>
<td>Imipenem-cilastatin</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Removed</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Meropenem</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>Removed</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>Piperacillin-tazobactam</td>
</tr>
<tr>
<td>Ticarcillin-clavulanate</td>
<td>Removed</td>
</tr>
<tr>
<td>...</td>
<td>Ceftazidime-avibactam</td>
</tr>
<tr>
<td>...</td>
<td>Ceftolozane-tazobactam</td>
</tr>
</tbody>
</table>

Recommendations for Changes to SEP-1: Combination Therapy

- Considerations from a multi-stakeholder workgroup (IDSA, SCCM, SHP, ACEP)

**Antibiotics Recommended by SSCG**

- Empiric broad therapy with ≥1 antimicrobials for sepsis, shock
- Septic shock: Definitive treatment - rec combo rx with ≥ 2 abx, different classes

**TABLE 8. Important Terminology for Antimicrobial Recommendations**

<table>
<thead>
<tr>
<th><strong>Empiric therapy</strong></th>
<th>Initial therapy started in the absence of definitive microbiologic pathogen identification. Empiric therapy may be mono-, combination, or broad-spectrum, and/or multidrug in nature.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Targeted/definitive therapy</strong></td>
<td>Therapy targeted to a specific pathogen (usually after microbiologic identification). Targeted/definitive therapy may be mono- or combination, but is not intended to be broad-spectrum.</td>
</tr>
<tr>
<td><strong>Broad-spectrum therapy</strong></td>
<td>The use of one or more antimicrobial agents with the specific intent of broadening the range of potential pathogens covered, usually during empiric therapy (e.g., piperacillin/tazobactam, vancomycin, and amikacin with each used to cover different groups of pathogens). Broad-spectrum therapy is typically empiric since its usual purpose is to ensure antimicrobial coverage with at least one drug when there is uncertainty about the possible pathogens. On occasion, broad-spectrum therapy may be continued into the targeted/definitive therapy phase if multiple pathogens are isolated.</td>
</tr>
<tr>
<td><strong>Multidrug therapy</strong></td>
<td>Therapy with multiple antimicrobials to deliver broad-spectrum therapy (i.e., to broaden coverage) for empiric therapy (i.e., where pathogen is unknown) or to potentially accelerate pathogen clearance (combination therapy) with respect to a specific pathogen(s) where the pathogen(s) is known or suspected (i.e., for both targeted or empiric therapy). This term therefore includes combination therapy.</td>
</tr>
<tr>
<td><strong>Combination therapy</strong></td>
<td>The use of multiple antibiotics (usually of different mechanistic classes) with the specific intent of covering the known or suspected pathogen(s) with more than one antibiotic (e.g., piperacillin/tazobactam and an aminoglycoside or fluoroquinolones for gram-negative pathogens) to accelerate pathogen clearance rather than to broaden antimicrobial coverage. Other proposed applications of combination therapy include inhibition of bacterial toxin production (e.g., clindamycin with β-lactams for streptococcal toxic shock) or potential immune modulatory effects (macrolides with a β-lactam for pseuoeopncal responses).</td>
</tr>
</tbody>
</table>


Crit Care Med. 2017; 45(3):486-552
Outlining IDSA’s Concerns Regarding SSCG

- 1-hour bundle applies to both sepsis and septic shock
- 1-hour bundle may lead to unintended consequences
  - Lack of standard “time to antibiotics” definition
- Indiscriminate use of “multidrug”, “combination” therapy
- Lack of specific guidance regarding use of procalcitonin
- Lack of specific guidance regarding optimization of abx PK/PD
- Doesn’t recommend against antibiotics for inflammatory disease of non-infectious origin
  - Recommendation against “sustained” antibiotic prophylaxis in these conditions - not strong enough
- Oversimplified recommendation for antibiotic treatment duration
  - 7-10 days for most patients

CID 2018;66(10):1631–5

Lemonade from Lemons: Stewardship Opportunities

- Overlying theme: sepsis criteria are overly sensitive and not overly specific – tend to over-diagnose (and treat)
- Provide recommendations on antibiotic selection and appropriate dosing
  - Develop sepsis guidelines
    - Sepsis, unknown origin
    - Source-specific
  - Create order sets to help reinforce institutional guidelines, recommendations
- Promote good culturing practices!
  - Remember, only blood cultures are necessary to meet measure
    - Minimize contamination; optimize process (timing, location)
  - Pan-culturing on ALL patients should be discouraged
- Encourage prompt antibiotic de-escalation (antibiotic time out)
- Define appropriate durations of therapy
Example of Sepsis Order Sets

- IV Fluids:
  - lactated ringers (1lottas) IV bolus 2,000 ml.
    2,000 ml (rounded from 1,182 ml = 20 ml/kg per does > 59.4 kg, Intravenous, ORCE, 1 dose today at EMS
  - normal saline 3.5 % IV
  - bolus IV, Intravenous, CONTRAINDICATED, Starting Today at EMS

- Labs:
  - Sepsis Arrival Labs - Basic Infection Work-Up
  - Sepsis Arrival Labs - Organ Dysfunction

- Imaging

- Diagnostic Tests - Studies
  - Cardiac Studies

- Medications:
  - Antibiotics - Undifferentiated Sepsis
    - Antibiotics - Pneumonia - CAP
    - Antibiotics - Pneumonia - Severe, MRS
    - Antibiotics - Skin/Soft Tissue
    - Antibiotics - Neutropenic Fiever
    - Antibiotics - Intrabdominal
    - Antibiotics - C. diff coverage
    - Antibiotics - Neutropenic Fiever
    - Antibiotics - Meningitis Coverage
    - Fever/Flu

- IV Infusions:
  - Vasactive Infusions

Antibiotics for sepsis of unknown origin
Source-specific antibiotic selection

Order Sets: Antibiotic Selection

- Collaboration between stewardship, sepsis workgroups important
- Provide limited selection of appropriate broad-spectrum antibiotics based on institutional antibiogram
  - Provide guidance on selection of one regimen over another
  - Can provide option for combination Gram-negative therapy
- Include optimized dosing
Order Sets Used to Guide Cultures, Diagnostics

- Consider use of PCT but provide guidance on how to interpret!

- Don’t auto-select urine cultures

UM Example of PCT Guidance in Order Result

Procalcitonin

Collected: 10/19/19 0518
Resulting lab: MICHIGAN MEDICINE PATHOLOGY AND CLINICAL LABORATORIES
Reference range: 0.00 - 0.25 ng/mL
Value: 0.23

Comment: Please see full Michigan Medicine Adult Procalcitonin Usage Guidelines at https://tinyurl.com/yek6kucv. In all scenarios, procalcitonin should be evaluated in context with all findings and the total clinical status and not in isolation.

a. For SUSPECTED Lower Respiratory Tract Infections, antibiotics are strongly discouraged in patients with procalcitonin (PCT) levels of 0.1 ng/mL, and are discouraged in patients with PCT levels of 0.1-0.25 ng/mL. If the initial PCT level is low and no antibiotics are started, a repeat PCT measurement may be considered if clinical suspicion for infection persists.

b. In patients ADMITTED to the ICU with Undifferentiated Sepsis without a confirmed source of infection, if the initial PCT level is <0.50 ng/mL or if the PCT value decreases by >50% compared to the highest observed previous concentration.

*Additional information available - comment
Duration of therapy

- SSCG recommend 7-10 days, but longer is not necessarily (ever?) better!
  - Pneumonia: 5-7 days sufficient in many patients
  - Intra-abdominal: 4 days with source control
  - Gram-negative BSI: consider 7 days in some populations (eg urinary source)

Sepsis: Unanswered Questions

- Optimal timing of antibiotic initiation
  - Same for sepsis vs septic shock?
  - 1 hour vs 3 hours?
  - When do you start the clock?
  - How to best capture these data for reporting?

- Most effective empiric active antibiotic
  - Monotherapy vs combination therapy
  - Utility of clinical prediction scores

- Duration of therapy for culture-negative sepsis

- More effective use of rapid diagnostics and biomarkers for antibiotic use and duration
  - POC testing, rapid diagnostics
Febrile Neutropenia (FN)

Mortality in Patients with Febrile Neutropenia

Year

Mortality Rate

Empiric Therapy


Slide courtesy of Anthony Perissinotti
NCCN and IDSA Guideline Recommendations

**Fever (≥ 38.3°C) + Neutropenia (≤ 500 cells/mm³)**

*In high risk patients*

- Initiation of IV anti-PSA antibiotics
- Anti-MRSA if line or skin source suspected

*Clinically stable*

- Continue empiric regimen until ANC > 500 cells/mm³

2018 NCCN update: consider de-escalation to prophy abx; or continue empiric abx if afebrile, still neutropenic

Leads to LONG durations of antibiotics (often >14 days)


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**Early De-Escalation data in Pediatric Patients with FN, Low-Risk for Infection**

- Children with cancer, fever, and neutropenia (ANC ≤ 500/mm³)
- Randomized on day 3 to:
  - Group A: antibiotics stopped
  - Group B: antibiotic therapy continued until resolution of FN

Defined as no need for restarting, adjusting abx

Table 3. Outcome of 75 episodes of severe neutropenia and fever in 68 children with cancer according to study group.

<table>
<thead>
<tr>
<th>Outcome*</th>
<th>Group A: antibiotic therapy stopped (n = 36)</th>
<th>Group B: antibiotic therapy continued (n = 39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable outcome</td>
<td>34</td>
<td>36</td>
</tr>
<tr>
<td>Diversioned bacterial infection</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Probable bacterial infection</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Early Antibiotic De-escalation - Adults

- Hematologic malignancies or stem-cell transplant recipients
- Open-label, RCT
  - Experimental group: abx discontinued after > 72h of being afebrile, irrespective of counts
  - Control group: abx until count recovery WBC > 0.5 x 10^9 cells/L
- Similar outcomes
- Modest decrease in abx in experimental group

<table>
<thead>
<tr>
<th>Intention-to-treat population</th>
<th>Experimental group (n=190)</th>
<th>Control group (n=730)</th>
<th>Between-group absolute difference (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>72 (39%)</td>
<td>24 (33%)</td>
<td>-2.4 (-8.0 to -3.5)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Efficacy variable</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Exit fever days</td>
<td>16.9 (9.6)</td>
<td>13.8 (7.7)</td>
<td>2.3 (1.0 to 4.6)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Safety variables</th>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Exit fever days</td>
<td>17.5 (10.4)</td>
<td>13.3 (7.0)</td>
<td>4.3 (2.9 to 5.7)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

De-escalation in Allogenic HSCT

- Retrospective; adult patients with allo-HSCT, developed FN
  - Cohort 1: early de-escalation prior to engraftment (anti-PSA ± anti-MRSA to prophylaxis)
  - Cohort 2: anti-PSA ± anti-MRSA until engraftment
- Clinical outcomes similar; moderate decrease in abx, Cohort 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cohort 1 (n = 48)</th>
<th>Cohort 2 (n = 35)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to first NPF</td>
<td>10 (1–16)</td>
<td>10 (1–14)</td>
<td>.335</td>
</tr>
<tr>
<td>Duration of NPF</td>
<td>2 (1–10)</td>
<td>2 (1–7)</td>
<td>.002</td>
</tr>
<tr>
<td>Time to neutrophil engraftment</td>
<td>18 (13–28)</td>
<td>15 (11–23)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Acute assessment score</td>
<td>0.304 (0–2.1)</td>
<td>0.324 (0–2.0)</td>
<td>.937</td>
</tr>
<tr>
<td>Hospitalization course</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resistant fever within 72-hour time frame, n (%)d</td>
<td>7 (15)</td>
<td>14 (19)</td>
<td>.025</td>
</tr>
<tr>
<td>Length of stay, d</td>
<td>20 (15–35)</td>
<td>20 (14–40)</td>
<td>.688</td>
</tr>
<tr>
<td>Among survivors</td>
<td>20 (15–35)</td>
<td>20 (14–40)</td>
<td>.549</td>
</tr>
<tr>
<td>ICU admission, n (%)</td>
<td>6 (10)</td>
<td>8 (6)</td>
<td>.623</td>
</tr>
<tr>
<td>C. difficile-associated infections, n (%)e</td>
<td>2 (4)</td>
<td>1 (1)</td>
<td>.558</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td>0 (0)</td>
<td>3 (4)</td>
<td>.266</td>
</tr>
</tbody>
</table>

Early Antibiotic Discontinuation in FN

- The ANTIBIOSTOP study: prospective observational study; patients with hematological malignancies
  - 1st phase: antibiotics were stopped after 48h of being afebrile (irrespective of ANC)
  - 2nd phase: antibiotics were stopped no later than day 5 (irrespective of temperature or ANC)

- Clinical outcomes similar

<table>
<thead>
<tr>
<th>Outcome</th>
<th>1st phase</th>
<th>2nd phase</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of empiric antibiotics, median [IQR]</td>
<td>7 [5-12]</td>
<td>5 [4-5.5]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Primary composite*</td>
<td>10 (22.2%)</td>
<td>12 (32.4%)</td>
<td>0.11</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>1 (2.2%)</td>
<td>2 (5.4%)</td>
<td>0.80</td>
</tr>
<tr>
<td>ICU admission</td>
<td>1 (2.2%)</td>
<td>5 (13.5%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Relapse of fever ≤48h after DC of abx</td>
<td>9 (20%)</td>
<td>8 (21.6%)</td>
<td>0.82</td>
</tr>
</tbody>
</table>

*defined as in-hospital mortality, ICU admission, relapse of fever, or documented new infection

Infect Dis (Lond) 2018; 50(7):539-549.

Targeted Therapy: NCCN, IDSA Guideline Recommendations

- In setting of documented infection both societies recommend targeting therapy based on micro results

- Unclear how aggressively to de-escalate anti-pseudomonal coverage

- Unclear what optimal treatment is

- Practice varies across institutions

UM Antibiotic De-escalation Algorithm

Appendix A: Antibiotic De-escalation in Clinically Stable and Asymptomatic Adult AML Patients

Initial Presentation of Febrile Neutropenia in AML Patients

Choose Therapy
- Start broad spectrum I&I and initiate pyridostigmine, dexamethasone, and probenecid as appropriate for current infections.

Evaluate for De-escalation at Day 7

Low Risk for Bacterial Infection
- All bacterial cultures are negative
- No suggestion of bacterial infection on imaging studies or physical exam

Severe Risk for Bacterial Infection
- All bacterial cultures are negative
- Imaging studies or physical exam suggest possible bacterial infection

Documented Bacterial Infection
- Positive bacterial cultures, plus imaging or physical exam findings consistent with infection

Treatment Recommendations:
- For patients at low risk, consider an outpatient approach.
- For patients at severe risk, consider hospitalization.
- For patients with documented bacterial infection, consider empirical antibiotic therapy.

Daily monitoring for signs and symptoms of infection

If infection persists, consider readmission or re-escalation of treatment.

Avoid: (1) inpatient admission and (2) IV antibiotics

FN Management in Outpatient Setting?

Identification of candidates for outpatient management

Assess level of risk for serious medical complications associated with febrile neutropenia, using clinical judgment criteria (Table 1), or a validated risk assessment tool (Tables 2-4).

High risk: presence of clinical judgment criteria (Table 1) or MASCC score ≥21 (Table 2) or Talcott’s groups 1-3 (Table 3)

Low risk: absence of clinical judgment criteria or MASCC score ≤21 (or Talcott’s group 4)

Consider outpatient management or C3INE tool (Table 4) for low-risk patients with solid tumors who have undergone mild-to-moderate-intensity chemotherapy and appear to be clinically stable.

Avoid: (1) inpatient admission and (2) IV antibiotics

Candidates for outpatient management:
- Administer the first dose of empiric therapy in the clinic, emergency department, or hospital department.
- Oral empiric therapy with a fluoroquinolone (ie, ciprofloxacin or levofloxacin) plus amoxicillin/ clavulinate or plus clarithromycin for those with a penicillin allergy is recommended.
- Patients should be observed for ≥4 hours before discharge.

FN Stewardship Research Opportunities

- Early discontinuation of antibiotics or de-escalation to antibiotic prophylaxis in setting of negative cultures
  - Patient criteria: clinical stability, duration of afebrile period, underlying malignancy
  - Antibiotic re-initiation in setting of recurrent fevers
- De-escalation of antibiotic therapy in setting of documented infections
  - Targeted antibiotic therapy and early discontinuation of anti-PSA therapy
- Use of diagnostics to distinguish fever from infection vs fever from disease
  - Procalcitonin kinetics
  - May be different in this population; often excluded from RCTs

Questions?

- Thanks to Twisha Patel PharmD for her assistance with slides!