FLASCO
Rapid Integration

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Associate Professor, USF MCOM
FLASCO Rapid Integrations

• Audience: educational initiative for clinicians new to the area of hematology/oncology

• Topic: Infectious Disease for the Hem/Onc Practitioner

• Time: 2:45-3:30 pm

Learning Objectives

- Identify up and coming anti-infective options for oncologic patients
- Recognize techniques on how to risk stratify infections in patients with cancer
# NCCN Recommendations for Antimicrobial Prophylaxis

<table>
<thead>
<tr>
<th>Overall Infection Risk in Patients with Cancer</th>
<th>Syndrome / Disease / Chemotherapy Examples</th>
<th>Antimicrobial Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>NP &lt; 7d&lt;br&gt;Majority of solid tumor chemotherapy regimens</td>
<td>None except if history of VZV then consider antiviral</td>
</tr>
<tr>
<td>Intermediate</td>
<td>7d &lt; NP &lt; 10d&lt;br&gt;Lymphoma&lt;br&gt;Multiple myeloma&lt;br&gt;Purine analog therapy (fludarabine)&lt;br&gt;CAR T</td>
<td>Bacterial: consider FQ while NP&lt;br&gt;Fungal: consider antifungal while NP&lt;br&gt;Viral: consider while NP and longer if needed&lt;br&gt;PJP: consider depending on the Rx</td>
</tr>
<tr>
<td>High</td>
<td>NP &gt; 10d&lt;br&gt;Induction AML / consolidation&lt;br&gt;Alemtuzumab therapy&lt;br&gt;Allogeneic transplant&lt;br&gt;GVHD</td>
<td>Bacterial: consider FQ while NP&lt;br&gt;Fungal: consider antifungal while NP&lt;br&gt;Viral: consider while NP and longer if needed&lt;br&gt;PJP: consider depending on the Rx</td>
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### NCCN Recommendations for Immune and Targeted Treatments

<table>
<thead>
<tr>
<th>Mechanism of Action</th>
<th>Agents</th>
<th>Major Uses</th>
<th>Infection Concerns</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD 20</td>
<td>Obinutuzumab</td>
<td>CLL, FL CLL, NHL, ALL</td>
<td>HBV (high risk) HCV HSV / VZV PML</td>
<td>Screen for infections at baseline. Treat as needed per international guidelines. Consider prophy for HSV / VZV / PJP. Monitor for drug induced NP / lymphocytopenia / hypogammaglobulinemia</td>
</tr>
<tr>
<td></td>
<td>Ofatumumab</td>
<td>CLL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rituximab</td>
<td>CLL, ALL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 33</td>
<td>Gemtuzumab ozogamicin</td>
<td>AML</td>
<td>Bacterial infxn OI PJP</td>
<td>Monitor for drug-induced VOD / hepatotoxicity Monitor for NP enterocolitis and interstitial pneumonitis</td>
</tr>
<tr>
<td>CD 38</td>
<td>Daratumumab Isatuximab</td>
<td>MM ALL (T-cell)</td>
<td>Listeria HBV HSV / VZV CMV PJP Cryptococcus</td>
<td>Recommend HSV / VZV prophylaxis Consider PJP prophylaxis Monitor for drug-induced NP</td>
</tr>
</tbody>
</table>

AML Case

Work Up
- EKG
- 2D Echo
- Weight
- CT sinus without contrast
- CT chest without contrast
- Any special medical history

Prophylaxis
- Fluroquinolone > Cefdinir
- Micafungin then Triazole
- Acyclovir
AML Case

**Neutropenic fever**
- Persistent temperature of 100.4°F > 1 hr
- Or
- Single temperature of 101°F

**Pan culture**
- All lumens that are accessed + peripheral blood culture
- Urinalysis +/- urine culture (if with symptoms)
- Lactic acid
- NP fever can present with or without sepsis
- Respiratory PCR panel
- Radiology
## AML Case

<table>
<thead>
<tr>
<th></th>
<th>Gram Negative Coverage (esp anti-Pseudomonas)</th>
<th>Enterococcus Coverage</th>
<th>Gram Positive Coverage</th>
<th>Anaerobic Coverage</th>
<th>Extended Spectrum Beta Lactamase Producing (ESBL) Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cefepime</strong></td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pip-tazo</strong></td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Meropenem</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Allogeneic Transplant Patients and CMV Prophylaxis

• Letermovir
  • Inhibitor of CMV terminase complex
  • No activity on other herpes viruses (so the pt also needs to take acyclovir)
  • NOT approved for treatment of CMV
  • Can be taken by mouth or by IV

• Letermovir prophylaxis for CMV in HSCT (Marty et al, NEJM 2017)
  • From approx. day 5 to day 100
  • Phase 3, double blind trial for CMV seropositive recipients
  • Results: lower rates of clinically significant CMV infection over placebo

• Among the transplant programs in the US, this is now the standard of care.
Antifungal Pipeline

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Fig. 1  Mechanism of action of novel antifungal drugs discussed in this review. DHODH dihydroorotate dehydrogenase

The Antifungal Pipeline: Fosmanogepix, Ibrexafungerp, Olorofim ..., Hoenigl et al, Drugs 2021
### The Antifungal Pipeline

<table>
<thead>
<tr>
<th>Drug</th>
<th>Against What</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosmanogepix</td>
<td>Invasive candidiasis Aspergillosis Scedosporiosis</td>
<td>There might be synergy with liposomal amphotericin B</td>
</tr>
<tr>
<td></td>
<td>Fusariasis Mucormycosis Cryptococcosis Coccioidymycosis</td>
<td></td>
</tr>
<tr>
<td>Ibrexafungerp</td>
<td>Invasive candidiasis INCLUDING <em>C. auris</em> and <em>C. glabrata</em> Aspergillosis</td>
<td>Potential for an oral step-down therapy</td>
</tr>
<tr>
<td>Olorofim</td>
<td>MDR molds</td>
<td></td>
</tr>
<tr>
<td>Rezafungin</td>
<td><em>Candida</em> sp, <em>Aspergillus</em> sp, PJP</td>
<td>Echinocandin with long half life (qwk)</td>
</tr>
</tbody>
</table>

The Antifungal Pipeline: Fosmanogepix, Ibrexafungerp, Olorofim ..., Hoenigl et al, Drugs 2021
Antimicrobial Stewardship in a Cancer Center

It does not increase rates of:
- Sepsis
- Death related to infections
- Resistance issues

Look for opportunities to de-escalate:
- Post transplant cyclophosphamide \(\rightarrow\) high rates of CRS \(\rightarrow\) 24hrs later \(\rightarrow\) de-escalate
- If cultures neg x 5d, pt is AF and stable \(\rightarrow\) de-escalate

De-escalation is different than narrowing therapy:
- Narrowing therapy is based on a positive culture with sensitivities
Diagnostics

Speak to your local lab

- How long do blood cultures get held → 5 days
- How often do CMV PCRs get done per week → 4x per week
- How often do EBV PCRs get done per week → 3x per week
- Which items get sent out to a reference lab? Which reference lab? → ARUP

Multiplex PCRs

- BioFire® (as an example)
  - Respiratory panels
  - Blood culture panels
  - GI PCR panels
  - Meningitis encephalitis panels

MALDITOF

- They have bacterial, fungal and AFB libraries
Diagnostics

• Microbial cell free DNA (cfDNA) test for microbes
  • Karius® (currently the only example company available in the US)
    • CLIA certified for inpatient use
      • Approximately 30 hours for door-to-door turnaround time
    • Depending on the number of samples your hospital orders, the price shifts
      • Approx $2,000 / lab at Moffitt at this juncture

• Helps the multidisciplinary team make unusual diagnoses

• Example
  • Pt status post alloHSCT (approx. 25d) had fevers x 7d
  • Blood cxs / ucx / imaging: negative
  • #1 Karius®: toxoplasmosis at the amount of 54,000
  • #2 Karius® (after about 4 wks of high dose TMP SMX): toxoplasmosis at the amount of 89
  • Added benefit of a quantitative amount to show improvement in the infection
Goals and Objectives

Key Topics for Heme / Onc

- NCCN Recommendations for Antimicrobial Prophylaxis
- NCCN Recommendations for Immune and Targeted Treatments
- AML Case
  - Neutropenic Prophylaxis
  - Neutropenic Fever
- Allogeneic Transplant Patients and CMV Prophylaxis
- Antifungal Pipeline

Antimicrobials Stewardship in a Cancer Center

Diagnostics
Questions?

Welcome to our multidisciplinary Antimicrobial Stewardship Team at Moffitt Cancer Center.

We are clinical infectious diseases providers, clinical infectious diseases / ASP pharmacists, microbiology, infection prevention and staff.

We meet quarterly to help Moffitt Cancer Center give the best care possible to its patients.