Reduction of invasive fungal infections in patients with acute myeloid leukemia undergoing induction or re-induction chemotherapy

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University of Virginia Health System
26 January 2017
Institutional Overview

• 585 bed academic medical center in Charlottesville, VA

• Emily Couric Clinical Cancer Center
  – National Cancer Institute (NCI)-designated cancer center

• Treats 50-70 patients/year for acute myeloid leukemia
Team Members

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American Society of Clinical Oncology
21.7% of patients with AML undergoing induction or re-induction chemotherapy at UVA medical center had a proven/probable invasive fungal infection (IFI) leading to increased morbidity as evidenced by increased number of medical emergency team (MET) calls.
Baseline Data

- Inconsistent use of antifungal prophylaxis in acute leukemia patients

- Without antifungal prophylaxis, rate of IFI over 20% during induction chemotherapy for AML
  - National average 8-10%

- Increased # of MET calls in patients with proven/probable versus possible/none IFI
  - (0.14/day vs. 0.06/day)
Patients with acute leukemia admitted for chemotherapy → Neutropenia develops → Fever/Clinical signs of infections → Work-up

- IFI?
  - Yes → Antifungal treatment
  - No → No antifungal treatment; broaden antibiotics to meropenem and/or add vancomycin to current antibacterial

(No antifungal treatment; broaden antibiotics to meropenem and/or add vancomycin to current antibacterial) → Antifungal treatment
**Cause & Effect Diagram**

**Induction/Re-induction protocol**
- Use of fungal prophylaxis
- Safe environment

**Work-up**
- Blood cultures
- Serologic Studies
- Imaging Studies
- Physical Exam
- Subspecialist Involvement
- Lack of staff

**Education**
- Neutropenia Definition
- Fever Definition
- Clinical Signs/Sxs of Infections
- Sign-out
- Notification of Attending
- Anti-fungal Use

**Treatment**
- Appropriate anti-fungal
- Appropriate dosing/formulation chosen
- Length of therapy
- Follow-up to ensure completion of therapy and resolution

**Proven/Probable IFI**
Diagnostic Data

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th># Patients with prob/proven IFI</th>
<th># Patients who develop prob/proven IFI with risk factor</th>
<th>Cumulative Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Fungal Prophylaxis</td>
<td>27</td>
<td>36%</td>
<td>36%</td>
</tr>
<tr>
<td>No CT Chest within 24 hours of fever</td>
<td>22</td>
<td>65%</td>
<td>101%</td>
</tr>
<tr>
<td>No ID consult within 5 days of fever</td>
<td>18</td>
<td>89%</td>
<td>189%</td>
</tr>
<tr>
<td>No fungitell obtained</td>
<td>4</td>
<td>95%</td>
<td>284%</td>
</tr>
<tr>
<td>No aspergillus antigen obtained</td>
<td>4</td>
<td>100%</td>
<td>384%</td>
</tr>
</tbody>
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Aim Statement

Reduce the percentage of proven/probable IFI in patients with acute myeloid leukemia undergoing induction or re-induction chemotherapy at the University of Virginia Health System to 10% or less by January 2017.
Primary outcome: Proven or probable IFI incidence

Patient population
• Patients with acute myeloid leukemia undergoing induction or reinduction chemotherapy
  o Exclusions: Patients with prior IFI, patients who cannot receive antifungal prophylaxis, patients who survive less than 90 days after induction

Calculation methodology
• % IFI = # patients with proven or probable IFI / # induction encounters

Data Source
• EPIC Beacon treatment plans, EMR

Data collection frequency
• Monthly
# PDSA Plan (Test of Change)

<table>
<thead>
<tr>
<th>Date of PDSA Cycle</th>
<th>Intervention</th>
<th>Results</th>
<th>Action Steps</th>
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| July 31, 2014 – July 31, 2016 | • No planned intervention  
• Attending specific fluconazole prophylaxis given to leukemic patients | • Anecdotal decrease in IFI rates, but used inappropriately in many patients | • Institute antifungal prophylaxis guideline for patients with AML during induction |
| August 1, 2016 – December 31, 2016 | • Guideline implementation  
• Resident education | • Decreased rates of IFI  
• “Missed” previous IFI in patient with reinduction | • Evaluation process for previous IFI  
• Revise pharmacist documentation (iVent) |

**IFI** stands for *invasive fungal infection*.
Antifungal Prophylaxis Guideline

- Antifungal prophylaxis guideline
  - Patients undergoing induction or reinduction chemotherapy for AML
  - Posaconazole po (alternatives if contraindicated)
  - Continue until count recovery
Clinical Pathway for Refractory Fevers

• Clinical pathway for refractory neutropenic fever and/or clinical signs of invasive fungal infection

AML patient on posaconazole prophylaxis and any of the following:
- Persistent fevers (febrile for 3-5 days despite appropriate antibiotics and negative cultures)
- Recurrent fever (febrile episode after remaining afebrile for 48 hours on appropriate antibiotics)
  - Hemodynamic instability
  - Clinical signs and/or suspicion of invasive fungal infection

Immediate, mandatory Infectious Disease consult (PIC 1205)

Recommended investigation:
- Cultures: Blood (all patients), urine, sputum, other sites (as clinically indicated)
- Imaging: CT chest, sinus, abdomen, other sites (as clinically indicated)
- Skin exam (all patients)
- Serum aspergillus antigen [Galactomannan] and β-D-Glucan [Fungitell] (all patients)
- Bronchoscopy with biopsy (as clinically indicated)
- Posaconazole drug levels (as clinically indicated)

Consider empiric antifungal therapy in consultation with ID:
- Liposomal amphotericin B
  - 5 mg/kg IV q24 hours
Beacon Treatment Plan Update

Antifungal prophylaxis incorporated in Beacon Treatment plans
- Attending or fellow ordering
- Heme/onc clinical pharmacist review
i-Vent and Cheat Sheet

- Resident “cheat sheet”
  - Rotation on/off service weekly

- Standardized pharmacist i-Vent
  - Previous IFI
  - Posaconazole trough level
Invasive Fungal Infection Rates in Patients with Acute Myeloid Leukemia (p-chart, 3 sigma)

Baseline mean
% IFI
Upper Control Limit
Lower Control Limit

PDSA Cycle 1
PDSA Cycle 2
Conclusions

- Proven/Probable IFI rate at goal of ≤ 10%
- Better working relationship with infectious disease
- Positive for stem cell transplant program
Next Steps/Plan for Sustainability

• On-going evaluation of any resistant fungal organisms

• Continued discussion with infectious disease regarding therapy and appropriate workup for refractory or recurrent fevers

• Potential roll out of protocol to stem cell transplant service

• Poster presentation – ASCO Quality Symposium
Thank You

• ASCO QTP faculty and staff, especially Amy Guthrie
• Michael Keng
  – Medical director of 8West and our quality champion/guru
• 8West nurses, pharmacists, and residents
• Hematologists
• Infectious disease service
• IT support

• Our patients!
Patients with acute myeloid leukemia

Treat?

Y

Induction/re-induction chemotherapy?

Y

Allergy?

N

Supportive Care

Y

Supportive Care vs palliative chemotherapy

N

Induction/re-induction chemotherapy initiated with antifungal prophylaxis

Neutropenia develops
Fevers/Signs of sepsis

Case-guided work-up and antibiotics initiated

IFI?

Y

Initiate anti-fungal treatment

N

No anti-fungal agent

Persistent fevers?

Y

Initiate ID consultation, serologic and imaging studies

N

Continue current therapy
Anti-fungal Prophylaxis – p chart

Fraction Patients receiving fungal prophylaxis

- Mean fraction patients receiving fungal prophylaxis
- Actual fraction patients receiving fungal prophylaxis
- Lower Control Limit
- Upper Control Limit