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

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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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Problem Statement

- 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/note 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
Diagnostic Data

- No Fungal Prophylaxis
- No CT Chest within 24 hours of fever
- No ID consult within 5 days of fever
- No fungitell obtained
- No aspergillus antigen obtained

# patients with prob/proven IFI

- 27
- 22
- 18
- 4
- 4

Cumulative Percentage

- 36%
- 65%
- 89%
- 95%
- 100%

# patients who develop prob/proven IFI with risk factor
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
  ○ 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
Priority Matrix

High Impact
- Mandatory anti-fungal prophylaxis for patients with AML undergoing induction or re-induction chemotherapy
- ID department waiving mandatory consult for antifungal use other than fluconazole
- Education materials for refractory fever work-up
- Pharmacy follow antifungal levels

Low Impact
- Beacon plans amended to include antifungal prophylaxis
- All patients get baseline CT chests
- ED hospital best practice alert

Easy
- Patient Education

Difficult
- Creating an EPIC Fungal Best practice alert
- Daily detailed dermatologic exams after 1st neutropenic fever
- Have more patient isolation rooms
- Standardized work-up for refractory fevers
- Make fungal serologic studies on-site instead of send-out
# 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)                                                          |
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 $\leq 10\%$

• 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

1. Treat? [Y/N]
   - Y: Induction/re-induction chemotherapy?
     - Y: Allergy? [Y/N]
       - Y: Induction/Re-induction chemotherapy initiated with antifungal prophylaxis
       - N: Neutropenia develops
     - N: Supportive Care vs palliative chemotherapy
   - N: Supportive Care
Ideal Process Map

1. Fevers/Signs of sepsis
2. Case-guided work-up and antibiotics initiated
3. IFI?
   - Y: Initiate anti-fungal treatment
   - N: No anti-fungal agent
4. Persistent fevers?
   - Y: Initiate ID consultation, serologic and imaging studies
   - N: Continue current therapy
Anti-fungal Prophylaxis – p chart

Fraction Patients receiving fungal prophylaxis

PDSA Cycle 1

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

Timeframe:
- May-Aug 2011
- Sept-Dec 2011
- Jan-April 2012
- May-Aug 2012
- Sept-Dec 2012
- Jan-April 2013
- May-Aug 2013
- Sept-Dec 2013
- Jan-April 2014
- May-Aug 2014
- Sept-Dec 2014
- Jan-April 2015
- May-Aug 2015
- Sept-Dec 2015
- Jan-April 2016
- May-Aug 2016