Management of fungal infections in immunocompromised hosts

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# Disclosures

## Janos Sinko

<table>
<thead>
<tr>
<th>Company name</th>
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<th>Stockholder</th>
<th>Speakers bureau</th>
<th>Advisory board</th>
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</table>
INFECTION Prevention

Environment

State of immuno-suppression

History

Epidemiology
HSCT, AML, SOT, GVHD, prolonged neutropenia, congenital immuno-deficiency, prolonged corticosteroids, MAB-s, ATG, nucleosid analogues, HIV, TNF-alpha blocking agents, ICU patients, hepatic failure, COPD, post-operative patients, burn injuries, near-drowning, metabolic abnormalities, extremes of age, extremes of nutritional state, etc
Invasive aspergillosis (IA) still prevalent in the hemato/HSCT setting.

Pathology and Infectious Disease; 73 (2012) 293–300
Survival of IA patients in HSCT

FHCC data

Clinical Infectious Diseases 2007; 44:531–40
Why results are suboptimal?

- Increasing proportion of high-risk patients and procedures
- Long-term survival = prolonged immuno-suppression
- Early diagnosis still challenging
- No further influx of new drugs
- Limited/shrinking resources – differences in availability
Looking for the highway to bliss
Real-life roadwork
Basic points in antifungal management

- Patient factors (risk)
- Environment
- Epidemiology (methodology, incidence, spectrum, resistance)
- Preventive measures applied
- Diagnostic tools (available, trusted)
- Therapeutic options (available, tolerable, affordable)
- Monitoring efficacy, toxicity
- Alternative/salvage treatment options
- Personality issues
Risk of IA in immunocompromised patient groups

58 y/o female
MM relapse
post auto HSCT
salvage therapy

GM positive IMD
BAL: *Penicillium* spp
Voriconazole therapy
Recovered
Environment
Environment
Importance of post-mortem data

Demographics
Number of patients included: 607
  AlloHSCT: 242
  AutoHSCT: 365.
Follow-up time: 113 (1 – 891) days
Overall mortality: 77/607 patients.
  AlloHSCT: 61/242
  AutoHSCT: 16/365 patients

Mortality due to infection: 36/607 patients
  AlloHSCT: 33/242 patients
    (54 % of fatalities)
  AutoHSCT: 3/363
    (19 % of fatalities)
Mortality by pathogen type:
  AlloHSCT: Mold:15, bacterial:9, viral:7, protozoal:1, viral+mold:1
  AutoHSCT: Mold:2, bacterial: 1

Sinko J et al P472
EBMT 2012 Geneva Switzerland
Preventive measures

Hygiene + infection control

- HEPA filtered air
- No HEPA filter

Mould-active prophylaxis
Mould-inactive prophylaxis
No prophylaxis

based on J Antimicrob Chemother 2011; 66 Suppl 1: i45–53
Diagnostic activity

- Mould-active prophylaxis
- Mould-inactive prophylaxis
- No prophylaxis

BIOMARKERS

IMAGING

BAL

TISSUE?
<table>
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<tr>
<th>Therapy</th>
<th>Fever driven</th>
<th>Diagnostic driven</th>
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<tbody>
<tr>
<td>IFD incidence</td>
<td>high</td>
<td>average/low</td>
</tr>
<tr>
<td>Patient factors</td>
<td>suggest risk</td>
<td>unremarkable</td>
</tr>
<tr>
<td>Diagnostic tools</td>
<td>out of reach</td>
<td>available, reliable</td>
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<tr>
<td>Mould-active prophylaxis</td>
<td>not used</td>
<td>used</td>
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<tr>
<td>Environment</td>
<td>additional risk</td>
<td>protective</td>
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<tr>
<td>What next?</td>
<td>do not stop diagnostic activity</td>
<td>try to upgrade</td>
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Starting guns for early therapy

• **Galactomannan (+CT):**
  - No aspergillosis missed
  - Picking up afebrile cases
  - Reducing antifungal use by 78%

• **PCR**
  - 20.4 % more patients on antifungals
  - 4.8 % better mortality while monitored
  - No difference at day 100

• **Imaging**
  - Reducing antifungal use by 68%
  - In CT negative cases no IFD until day 100
  - No IFD left untreated (in 9% clinical treatment indications)

Clin Infect Dis 2005; 41:1242–50
Bone Marrow Transplant (2009) 43, 553–561
Bone Marrow Transplant (2009) 44, 51–56
Monitoring response

- **Clinical changes**: of primary importance
- **Imaging**: OK, but
  - Immunoreconstruction?
  - Radiation exposure
  - Appropriate at decision points
- **Biomarkers**
  - GM: may have prognostic significance
- **Long term follow-up**
  - Recovery of immune functions?
Treatment of breakthrough IFD
- the “azole-following-azole” paradoxon-

• Can patients on azole prophylaxis or therapy with breakthrough IFD be switched to a salvage treatment with another azole?

• **Fluco to vori:** yes, except resistant *Candida (C. glabrata)*

• **Posa to vori:**
  – PK issues suspected: probably yes
  – Absorption proven: switch class
Risk-seeking or risk-avoiding
Risk-seeking or risk-avoiding

COMFORTABLE WITH
• Stable patient
• NPV of diagnostic tests for IA

WORRIED ABOUT
• Candidemia
• Non-aspergillus moulds
• Diffdx of pulmonary complications
Conclusions

Given the complexity of influencing factors no single best antifungal strategy fitting for everyone

Diagnostics are key

Institutional approach, however, should be clearly defined and re-evaluated regularly

Some patients deviate from the average justifying a more tailored approach