Micafungin Versus Posaconazole Prophylaxis in Patients With Acute Leukemia or Myelodysplastic Syndrome: A Randomized, Open-label Study

David J. Epstein1,*, Susan K. Seo1,3, Yao-Ting Huang1, Jay H. Park2,3, Virginia M. Klimek2,3, Martin S. Tallman3,4, Mark G. Frattini2,3, Genovefa A. Papanicolaou1,3.

1Infectious Disease Service and 2Leukemia Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York. 3Department of Medicine, Weill Cornell Medical College, New York, New York.

*Current affiliation: Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University School of Medicine

Rationale

- Posaconazole suspension is effective for antifungal prophylaxis in patients with neutropenia from intensive chemotherapy (ICT).
- Administration of posaconazole may not be feasible due to severe mucositis or drug interactions.
- Micafungin is an appealing alternative due to antifungal activity, intravenous administration, and minimal drug interactions.

Objectives

Compare micafungin versus posaconazole suspension as antifungal prophylaxis:
- Primary outcome: Prophylaxis failure (premature prophylaxis discontinuation due to antifungal therapy, intolerance, adverse event, or death)
- Secondary outcomes: Time to prophylaxis failure, reasons for failure, invasive fungal infections (IFI)

Methods

- From 2011-2016, patients admitted to Memorial Sloan Kettering Cancer Center with AL or MDS receiving ICT were randomized (1:1) to open-label micafungin 100 mg IV daily or posaconazole suspension 400 mg PO bid during neutropenia for up to 28 days.
- Patients suspected of developing IFIs underwent routine diagnostic workup and prophylaxis was changed to antifungal therapy. Patients were followed for 12 weeks after the first study dose.

Baseline characteristics

<table>
<thead>
<tr>
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<th>Micafungin (N = 58)</th>
<th>Posaconazole (N = 55)</th>
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</thead>
<tbody>
<tr>
<td>Age, y, median (range)</td>
<td>61 (32-75)</td>
<td>59 (26-74)</td>
</tr>
<tr>
<td>Male, N (%)</td>
<td>33 (56.9)</td>
<td>29 (52.7)</td>
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<td>Treatment-naïve, N (%)</td>
<td>42 (72.4)</td>
<td>40 (72.7)</td>
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<tr>
<td>AML, N (%)</td>
<td>51 (87.9)</td>
<td>55 (81.8)</td>
</tr>
<tr>
<td>T+5 regimen, N (%)</td>
<td>42 (72.4)</td>
<td>40 (72.7)</td>
</tr>
<tr>
<td>Days neutropenic, median (IQR)</td>
<td>18 (15-26)</td>
<td>21 (16-28)</td>
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</tbody>
</table>

No significant differences between groups

IFI incidence

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<tr>
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<th>Micafungin (N = 20)</th>
<th>Posaconazole (N = 29)</th>
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</table>

Antifungal therapy | 19 (95%) | 12 (41.4) |
Possible IFI | 6 | 3 |
Probable IFI | 1 | 0 |
Other concern for IFI | 12 | 9 |
GI intolerance | 0 | 13 (44.8) |
Adverse event | 0 | 4 (13.8) |
Death | 1 (5%) | 0 |

IFI etiologies

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Aspergillus species | 2† | 1* |
Candida species | 2† | 1† |
Cryptococcus species | 1* | 0 |
Trichosporon asahii | 0 | 1† |

* IFI(s) occurred during prophylaxis phase of study
† IFI(s) occurred during follow-up phase after study drug completed
‡ One IFI occurred during each phase

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Contact: Genovefa Papanicolaou, MD
Email: Papanicg@mskcc.org

Conclusions

- Micafungin was associated with lower rates of prophylaxis failure than posaconazole suspension, driver largely by less GI intolerance and adverse events.
- IFI rates were low and similar in both arms, supporting that both strategies provided effective prophylaxis.
- Our data support the use of micafungin as an alternative to posaconazole for antifungal prophylaxis in patients with AL or MDS undergoing ICT.