**Clinical Outcomes of the Oral Suspension versus Delayed-Release Tablet Formulations of Posaconazole for Prophylaxis of Invasive Fungal Infections**

Gregory B. Tallman, PharmD, MS1; Jon P. Furuno, Ph.D.; Brie N. Noble, BS1; Joseph S. Bubalo, PharmD2; Graeme N. Forrest, MBBS2; James S. Lewis II, PharmD2; Ana F. Bienvenida, BS1,2; Courtney A. Holmes, BS1; Bo R. Weber BS1,2; Jessica C. McGregor, PhD1

1. Oregon State University/Oregon Health & Science University College of Pharmacy, 2. Oregon Health & Science University Hospitals and Clinics, 3. Veterans Affairs Portland Healthcare System

**Background**

- Posaconazole is associated with excess morbidity, mortality, and cost.
- Immunocompromised patients are at increased risk of IFI.
- Posaconazole prophylaxis is recommended for high-risk IFI and decrease morbidity in high-risk patient populations.
- Posaconazole is an extended-spectrum antifungal with activity against aspergillus and multiple Candida species.

**Absorption of Posaconazole oral suspension is poor and may limit effectiveness of prophylaxis**.

Table 1: The release of Posaconazole tablet was approved in 2013 and has improved bioavailability.

**Objectives**

1. To identify and compare frequency and rationale of discontinuation of posaconazole between patients receiving the different formulations.
2. To evaluate differences in target trough levels.

**Methods**

- **Intervention**: A single practice for patients with ARS or MDS with neutropenia: (a) Oral suspension without alitmin or meprobamate (b) Oral suspension with clear enteral or tube administration (throughout the duration of neutropia and day +90) (c) Oral suspension after granulocyte recover occurring high-dose corticosteroid therapy.
- **Prophylaxis** used for prophylaxis starting in 2008.

**Results**

- **Primary Objective**: No difference between suspension and tablet (75% vs. 79%, p=0.17)
- **Secondary Objective**: No difference between suspension and tablet formulations in the primary prophylaxis study period (unadjusted): 1.07 (0.84 to 1.35, 0.37).
- **Table 1: Characteristics of Posaconazole Patients by Posaconazole Formulation**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Suspension</th>
<th>Tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.5 (15.8)</td>
<td>60.5 (15.8)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>65.8%</td>
<td>65.8%</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.7 (5.5)</td>
<td>27.7 (5.5)</td>
</tr>
<tr>
<td>Neutrophil count</td>
<td>55 (15)</td>
<td>55 (15)</td>
</tr>
<tr>
<td>Platelet count</td>
<td>150 (110)</td>
<td>150 (110)</td>
</tr>
<tr>
<td>WBC (x10⁹/L)</td>
<td>8 (5)</td>
<td>8 (5)</td>
</tr>
<tr>
<td>Hemoglobin level</td>
<td>13.4 (1.2)</td>
<td>13.4 (1.2)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>65.8%</td>
<td>65.8%</td>
</tr>
<tr>
<td>Cancer type</td>
<td>547 (12.3)</td>
<td>547 (12.3)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

- **Incidence of proven or probable IFI** and did not differ between suspension and tablet formulations.
- **No association with formulation and tablet** after adjusting for confounding.
- **For patients with available data, failure to achieve trough levels ≥ 0.7 mcg/mL associated with** greater mortality and IFI.
- **Improved long-term alignment with tablet consistent with previous literature**.
- **Discontinuation frequency decreased in low-tolerant azole, QT prolongation and drug discontinuation** was rare.

**STRENGTHS**

- Large study comparing IFI between suspension and tablet formulations.
- Treatment groups were similar in baseline, adjusted for confounding with penalized Cox model.
- The majority of patients were at high risk of IFI (EORTC/MSG criteria for prophylaxis).
- Breakthrough IFI identified by expert panel using consensus definitions.

**LIMITATIONS**

- Low incidence of IFI similar to previous clinical trials of prophylaxis, but limits power.
- Determination of IFI and early discontinuation reliant on documentation in medical record.
- **Single center design limits generalizability of results.**

**CONCLUSIONS**

- **Incidence of IFI** was low and did not differ between suspension formulations.
- **Reasons for discontinuation of prophylaxis** were similar for both suspension and tablet formulations.

**REFERENCES**