

Does Metabolite Matter? Defining Target Itraconazole and Hydroxy-itraconazole Serum Levels for Blastomycosis

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BACKGROUND

- Itraconazole is first-line for mild-moderate & consolidation of moderate-severe blastomycosis
- Itraconazole is metabolized to 3 metabolites, including the active metabolite hydroxy-itraconazole
- Guideline target for blastomycosis is combined itraconazole plus hydroxy-itraconazole levels >1.0 mcg/mL however, parent compound alone >1.0 mcg/mL is targeted at our institution

OBJECTIVE

Compare outcomes of blastomycosis by itraconazole serum level

METHODS

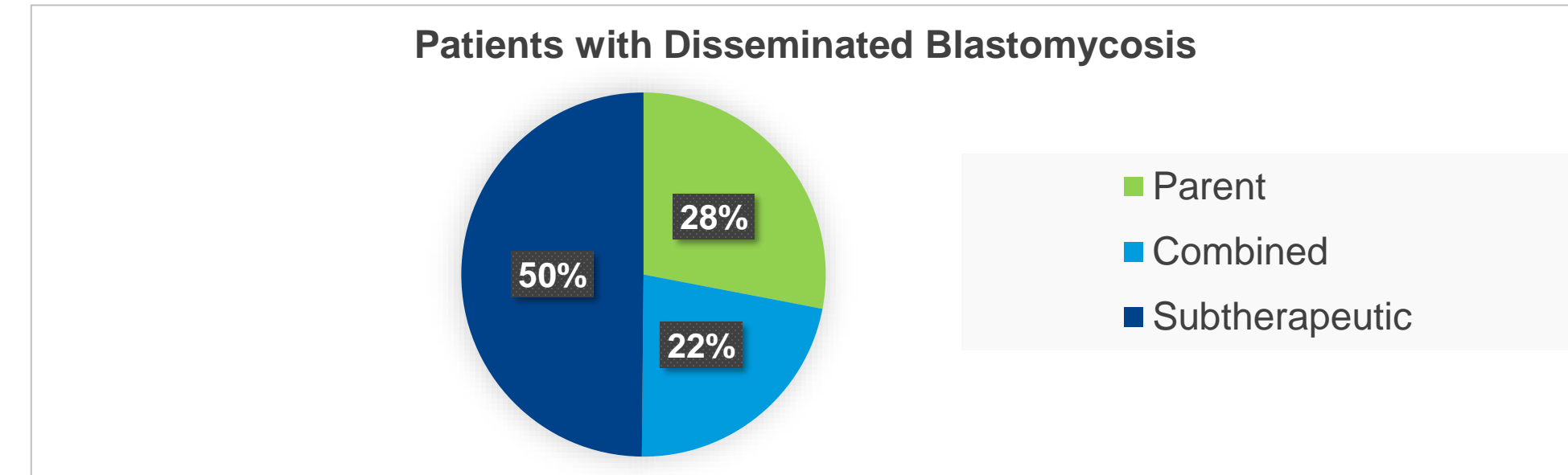
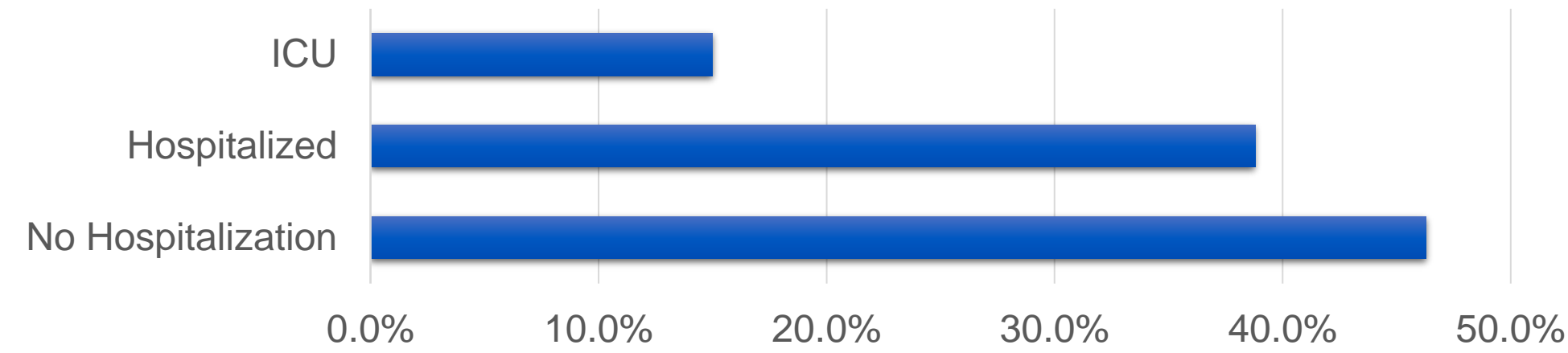
- Design:** Single-center, retrospective chart review
- Time:** January 1, 2004 – June 30, 2021
- Population:** ≥18 years with probable or proven *Blastomyces* infection with at least 1 documented serum itraconazole level
- Outcomes:**
 - Clinical Cure and Adverse Drug Events**
 - Partial Cure**=clinical improvement and >50% improvement in radiographic abnormalities
 - Complete Cure**=resolution of all attributable signs, symptoms, radiographic abnormalities

| Study Groups | Definition* |
|----------------|--|
| Parent | Itraconazole parent compound >1.0 mcg/mL |
| Combined | Itraconazole parent compound <1.0 mcg/mL, but a combined itraconazole and hydroxy-itraconazole level >1.0 mcg/mL |
| Subtherapeutic | Failure to achieve a combined itraconazole and hydroxy-itraconazole serum level >1.0 mcg/mL |

*for at least 75% of the total treatment course
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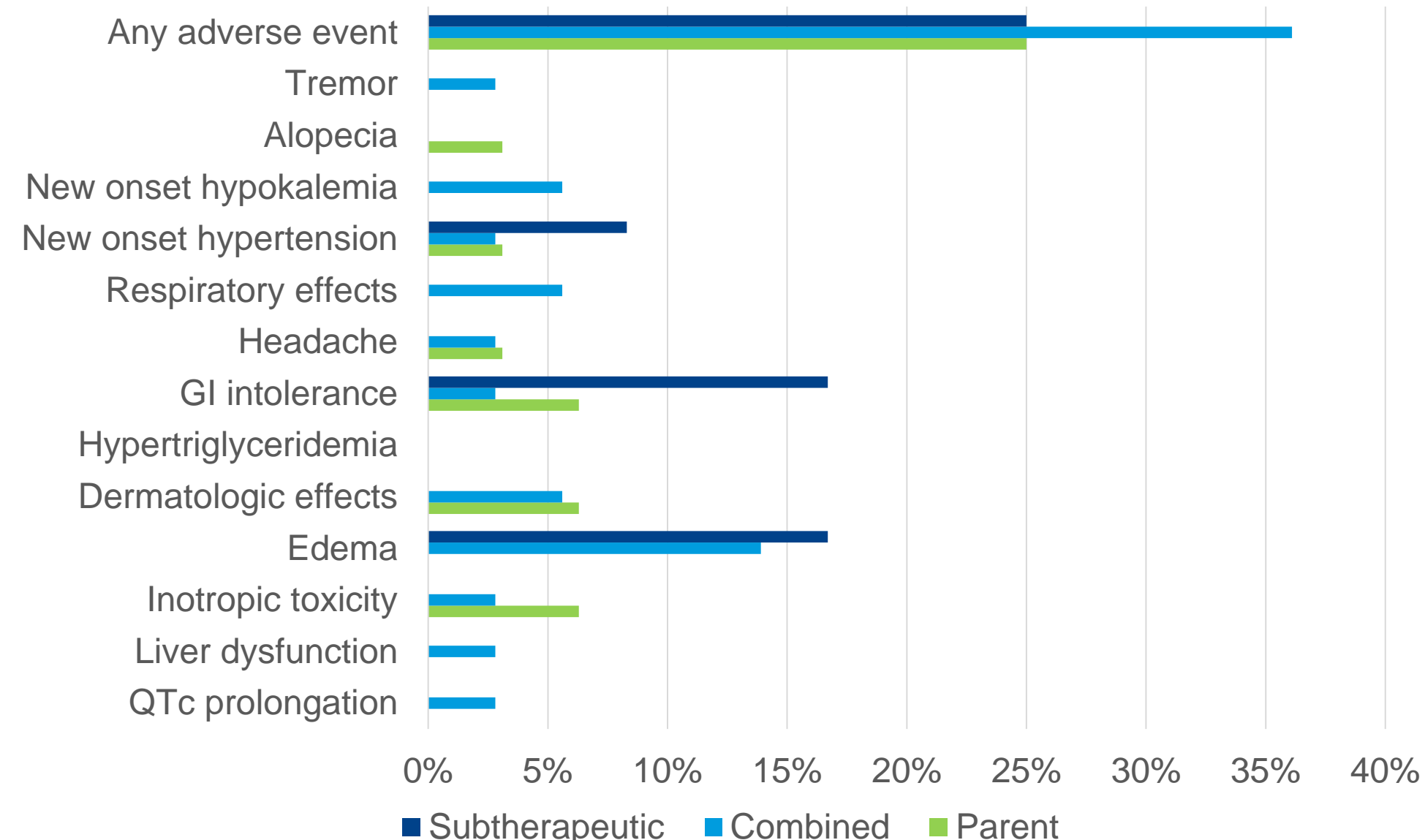
RESULTS

Figure 1: Severity of Disease by Percentage of Care Setting Across Treatment Groups



*1 patient with CNS involvement in parent group

Figure 3: Adverse Drug Event Percentage Observed Across Treatment Groups



*No statistically significant difference in ADEs between groups apart from edema (p=0.042)

Figure 2: Percent of Partial or Complete Treatment Responses Across Treatment Groups

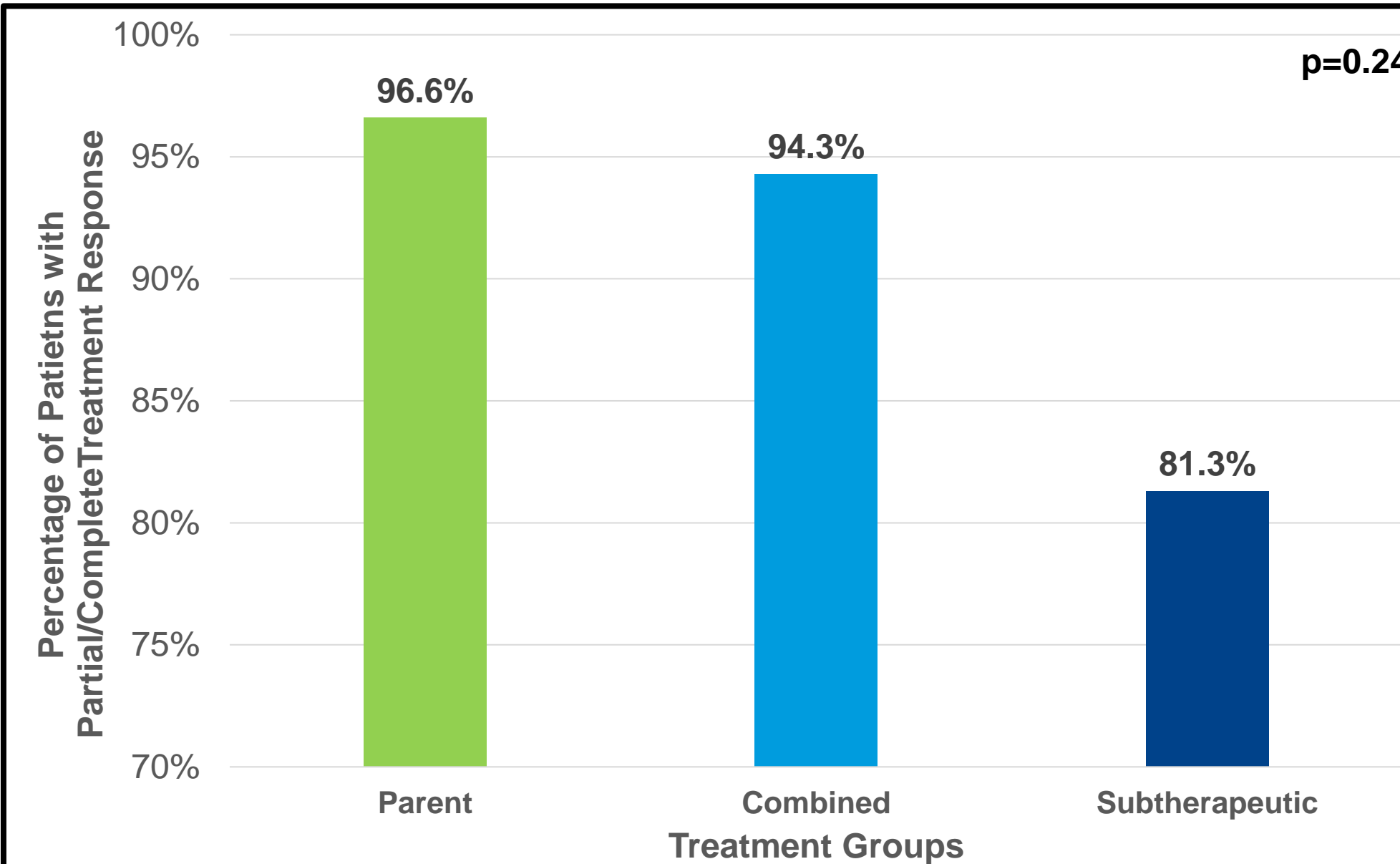
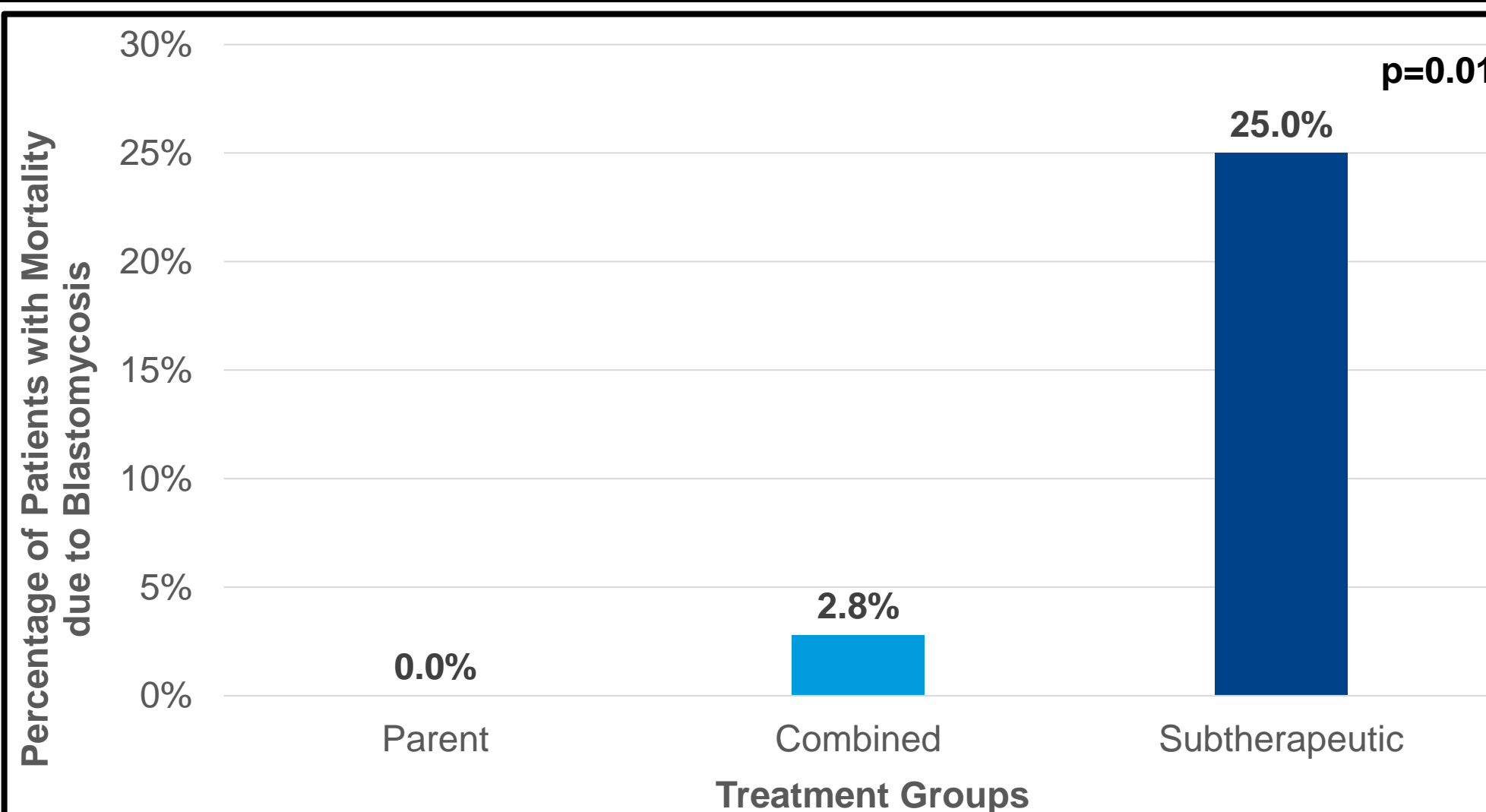
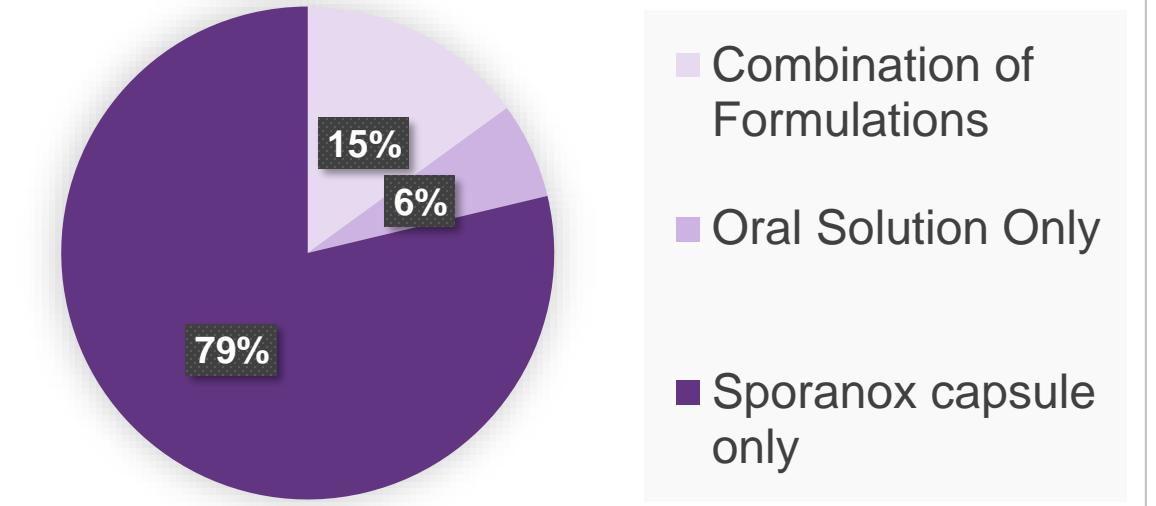


Figure 4: Percent Mortality from Blastomycosis Across Treatment Groups



ITRACONAZOLE DOSING



Median of Average Total Daily Dose = 400 mg
Median Length of Therapy = 7 months
Median Number of TDM Levels = 2

CONCLUSIONS

- It is imperative to target itraconazole + hydroxyitraconazole >1.0 mcg/mL given the worse outcomes seen in those with levels <1.0 mcg/mL
- Target combination of itraconazole + hydroxy-itraconazole >1.0 mcg/mL in the treatment of blastomycosis is supported

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