CIDARA THERAPEUTICS

Lessons Learned: Final Considerations for Antifungal Drug Development

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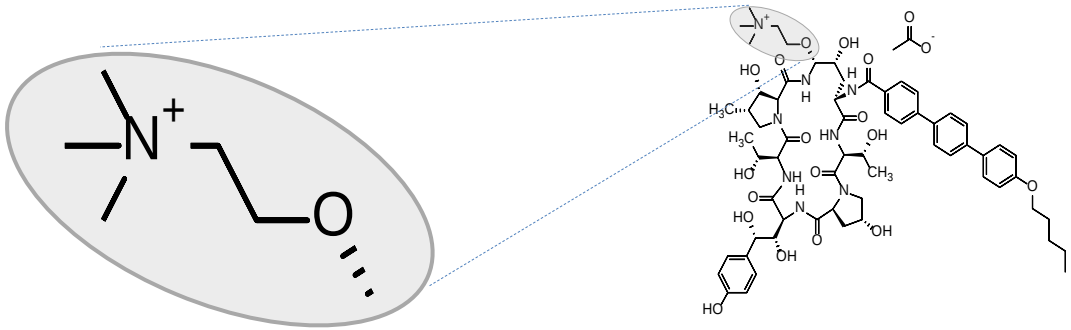
Rezafungin: A novel echinocandin in Phase 3 for treatment and prevention



Structural modification from anidulafungin is designed to yield distinct chemical & biological properties

- Prolonged PK ---once weekly dosing
- High, front-loaded exposures ---potential for improved efficacy
- Absence of hepatotoxicity in preclinical models
- No DDIs ---compatible with other medications

Development Program

- Studies
  - Completed Phase 2 trial in Treatment of Candidemia/ Invasive Candidiasis (n=207)
  - Ongoing Phase 3 trial in Treatment of Candidemia/ Invasive Candidiasis
  - Ongoing Phase 3 trial in Prophylaxis of Invasive Fungal Disease (*Candida* spp, *Aspergillus* spp, *Pneumocystis*) in Allogeneic Blood and Marrow Transplant
- Proposed Indications
  - Treatment of Candidemia/ Invasive Candidiasis
  - Prophylaxis of Invasive Fungal Disease in Allogeneic Blood and Marrow Transplant

Lessons Learned- Summary

Our goal: to enable approval of safe and effective drugs so that doctors can have antifungal options to improve patient outcomes.

Changing Environment

- Epidemics of COVID and *C. auris* have alerted all of us to unknown future needs and challenges

Enrollment Challenges

- Enrollment in candidemia/IC and IA studies is far more difficult than in past pivotal studies (<0.2 pts/site/month) with challenges multiplied when a single *Candida* species (e.g. *Candida auris*) is targeted
- COVID has increased the complexity with fewer sites available for clinical research and increased risk of missed visits due to COVID threatening study visits for immunosuppressed population

Exclusion Criteria

- Largest reasons for pre-screen failures are >96 hours from randomization for slow-growing *Candida* cultures and >48-hour empiric antifungal therapy when early, directed therapy is known to improve mortality

Unanswered Questions

Feasibility

- Have we reached the point where large scale Phase 3 studies for antifungal agents are no longer feasible?

Substantial Evidence

- Given recent advances in PK/PD target attainment, can more emphasis be placed on PK/PD in lieu of a Phase 3 clinical trial powered for inferential statistics.
- Given the described challenges, what can be considered ‘substantial evidence of effectiveness’ for a full candidemia/IC, single species development program, or for a salvage therapy study?

Exclusion Criteria

- Can there be some leniency in the key exclusion criteria that prevent enrollment in order to increase patient experience with candidate drugs?