

Phase 2 STRIVE Clinical Trial of Rezafungin for the Treatment of Candidemia and/or Invasive Candidiasis: Consistent Pharmacokinetics Across a Diverse Patient Population

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BACKGROUND

- Rezafungin is a novel echinocandin antifungal in development for the treatment and prevention (prophylaxis) of invasive fungal infections
- Rezafungin exhibits an exceptionally long half-life (~133 h) which enables the administration of once-weekly dosing regimens [1]
- STRIVE (NCT02734862) is a global, randomized, double-blind, placebo-controlled, Phase 2 trial that evaluated the safety and efficacy of IV rezafungin once weekly (QWk) in the treatment of candidemia and/or invasive candidiasis compared with standard-of-care (IV caspofungin once daily with optional oral stepdown)
- A population pharmacokinetic (PK) model has been developed which robustly describes the PK of rezafungin; although statistically significant covariates were identified, none appeared clinically relevant [2]
- Here we report a sub-analysis of PK results from Part A of the STRIVE trial and exploratory analysis of rezafungin trough (C_{min}) results versus patient demographics at baseline to evaluate potential trends

METHODS

Rezafungin C_{min} concentrations, following administration of 400 mg on Day 1 and collected within 30 minutes prior to the start of infusion on Day 8, were summarized categorically by:

- Race (black or white)
- Sex (male or female)
- Geographic region (North America [NA], or Europe [EU])

And were plotted versus continuous variables:

- Age
- Body weight, body mass index (BMI)
- Body surface area (BSA)

All samples were quantifiable and results were analyzed without imputation following exclusion of 16 (of 69) samples that were outside of collection time window. Additionally, 3 subjects were excluded based on race (non-black, non-white).

RESULTS

- Small differences were noted in mean rezafungin C_{min} values between the groups compared by race, sex, or geographic region (Table 1), but there was a great deal of overlap and the differences are not clinically meaningful (Figure 1)

Table 1. Rezafungin C_{min} ($\mu\text{g/mL}$) Summary by Categorical Group

| Variable | Group | N | Mean | SD |
|-------------------|----------------|----|------|------|
| Race | Black | 8 | 1.79 | 0.68 |
| | White | 42 | 2.30 | 1.18 |
| Sex | Female | 23 | 2.55 | 1.20 |
| | Male | 30 | 1.91 | 0.96 |
| Geographic Region | North America | 20 | 1.85 | 0.61 |
| | European Union | 33 | 2.39 | 1.29 |

- Similarly, no trends in C_{min} values were observed across a range of ages (20-80 years), weights (~40-155 kg), BMI (~15-65 kg/m²), and BSA (~1.4-2.4 m²) (Figure 2)

Figure 2. Individual Rezafungin C_{min} ($\mu\text{g/mL}$) Across Various Continuous Variables

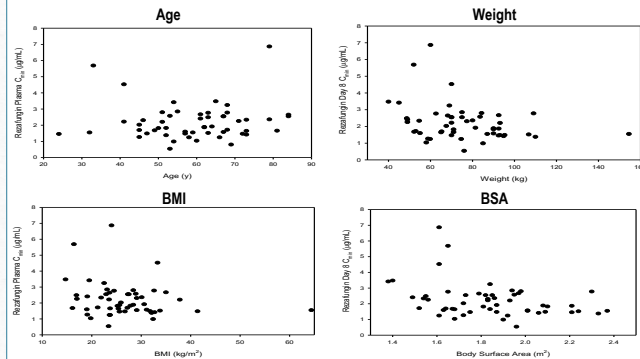
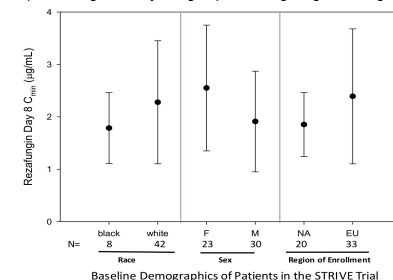


Figure 1. Mean (\pm SD) Rezafungin C_{min} by Subgroup Following Single 400-mg Dose (1 Week Post Dose)



CONCLUSIONS

- No meaningful differences in rezafungin C_{min} values were observed in patients grouped by sex, race, or geographic region, or across a wide range of patient factors including age and body size
- Consistent with conclusions from population PK analyses, this analysis suggests that rezafungin can be expected to provide consistent PK for most patients

REFERENCES

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