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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).

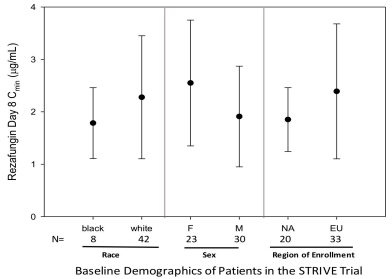
RESULTS

- 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} (µg/mL) Summary by Categorical Group

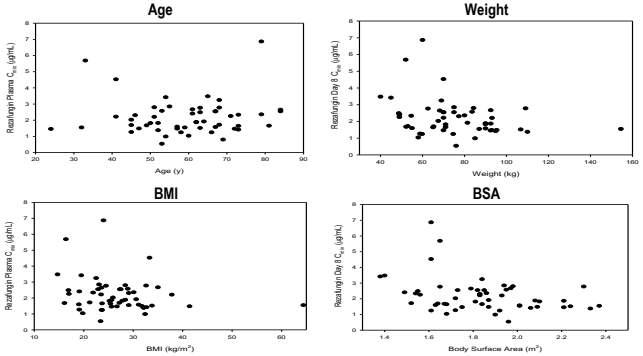
Variable	Group	N	Mean	SD
Race	Black	8	1.79	0.68
	White	42	2.30	1.18
Sex	Female	23	2.55	1.20
	Male	30	1.91	0.96
Geographic Region	North America	20	1.85	0.61
	European Union	33	2.39	1.29

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



- 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 m^2) (**Figure 2**)

Figure 2. Individual Rezafungin C_{min} (µg/mL) Across Various Continuous Variables



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

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