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

- 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
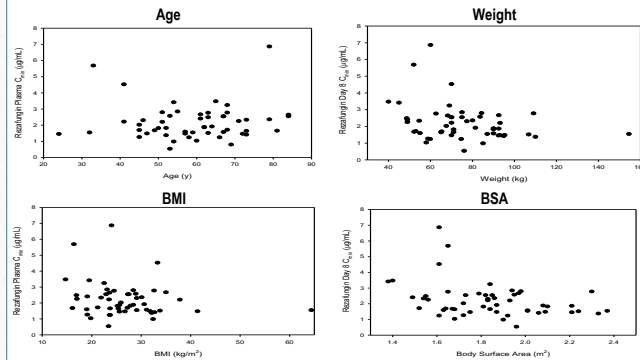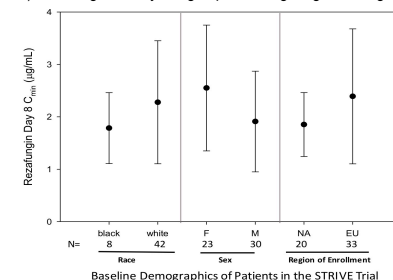

Figure 1. Mean ($\pm$SD) Rezafungin C_{min} by Subgroup Following Single 400-mg Dose (1 Week Post Dose)

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

1. Sandison T, Ong V, Lee J, Thye D. Safety and Pharmacokinetics of CD101 IV, a Novel Echinocandin, in Healthy Adults. *Antimicrob Agents Chemother*. 2017;61:e01627-16.
2. Lakota EA, Rubino CM, Ong V, et al. Population Pharmacokinetic and Pharmacokinetic-Pharmacodynamic Target Attainment Analyses for Rezafungin for Treatment of *Candida* Infections. Presented at ASM Microbe 2019; June 20-24, 2019; San Francisco, CA. Poster AAR-736.

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