Outcomes by BMI in the STRIVE Phase 2 Trial of Once-Weekly Rezafungin for Treatment of Candidemia and Invasive Candidiasis Compared with Caspofungin

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INTRODUCTION

- Body size is an important variable of drug exposure
- Pharmacokinetic (PK) models suggest size-based adjustments to achieve target drug exposure
- Rezafungin is a novel echinocandin with a distinctive PK profile (long half-life, extensive tissue distribution, and front-loaded drug exposure) that allow for once-weekly dosing and efficacy[2,3]
- Rezafungin is currently in Phase 3 development for treatment of candidemia and invasive candidiasis (IC) [ReSTORE; NCT03667690] and for prevention of invasive fungal disease caused by *Candida*, *Aspergillus*, and *Pneumocystis* in blood and marrow transplant recipients [ReSPECT; NCT04368559]

OBJECTIVES

To evaluate outcomes based on patient body mass index (BMI) in a subanalysis of the Phase 2 STRIVE trial of rezafungin in the treatment of candidemia and/or IC [NCT02734862] compared with caspofungin (Fig. 1)[4,5]

Figure 1. Treatment Groups of the Phase 2 STRIVE Trial

Group	Dose Regimen	Dose Schedule
RZF Group 1	IV RZF 400 mg QWk	On Days 1 and 8
RZF Group 2	IV RZF 400 mg on Week 1, followed by 200 mg QWk[a]	Optional dose(s) on Day 15 (and on Day 22 for IC)
CAS	IV CAS 70 mg on Day 1, followed by 50 mg QD (with optional step-down to oral fluconazole)	QD for up to 21 days for candidemia or 28 days for IC ± candidemia

[a]Rezafungin dosing regimen in Phase 3.
CAS=caspofungin; RZF-rezafungin; QD=once daily; QWk=once weekly

METHODS

Data were stratified by BMI categories (<30 kg/m^2 and ≥30 kg/m^2) and assessed for

- **Safety**: treatment-emergent adverse events [TEAEs]
- **Efficacy**: overall response [resolution of clinical signs of infection and mycological eradication], mycological response, and investigator assessment of clinical response
- **PK**: area under the curve [AUC] from RZF-treated patients in the first part of the trial with PK data available for analysis

RESULTS

Mean BMI Values

- Rezafungin Group 1, 26.9 kg/m^2; rezafungin Group 2 and caspofungin arms, 26.8 kg/m^2

Safety

- TEAEs rates showed no concerning trends (Table 1)

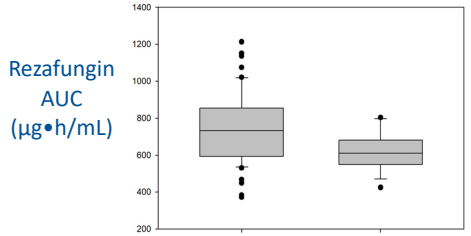
Efficacy

- Outcomes by BMI categories were similar (Table 2)

PK

- AUC ranges by BMI overlapped (Fig. 2). Mean ± SD AUC was ~20% lower for the higher BMI category (615 ± 104 vs 741 ± 194 µg•h/mL, respectively)

Figure 2. Rezafungin AUC Following 400-mg Dose at Week 1



BMI category	<30 kg/m^2	≥30 kg/m^2
N	51	17
Mean ± SD BMI, kg/m^2	23.1 ± 4.2	35.9 ± 8.4

Table 1. TEAEs by BMI Category

TEAE	n (%) [Safety Population]					
	BMI <30 kg/m^2			BMI ≥30 kg/m^2		
	RZF Grp 1 N=59	RZF Grp 2 N=37	CAS N=51	RZF Grp 1 N=21	RZF Grp 2 N=15	CAS N=17
At least 1 TEAE	51 (86.4)	33 (89.2)	42 (82.4)	19 (90.5)	15 (100)	13 (76.5)
Study drug–related TEAE	4 (6.8)	5 (13.5)	6 (11.8)	3 (14.3)	1 (6.7)	3 (17.6)
TEAE leading to study drug discontinuation	4 (6.8)	1 (2.7)	4 (7.8)	2 (9.5)	0	0

Table 2. Efficacy Outcomes by BMI Category

Outcomes at Day 14	n (%) [mITT Population]					
	BMI <30 kg/m^2			BMI ≥30 kg/m^2		
	RZF Grp 1 N=57	RZF Grp 2 N=34	CAS N=48	RZF Grp 1 N=18	RZF Grp 2 N=11	CAS N=13
Overall Response	34 (59.6)	26 (76.5)	32 (66.7)	11 (61.1)	8 (72.7)	9 (69.2)
Mycological Response	37 (64.9)	26 (76.5)	33 (68.8)	12 (66.7)	8 (72.7)	9 (69.2)
Investigator Assessment of Clinical Cure	40 (70.2)	28 (82.4)	33 (68.8)	12 (66.7)	8 (72.7)	10 (76.9)

CONCLUSIONS

- Rezafungin safety, efficacy, and PK in STRIVE was consistent across BMI categories
- These results suggest that rezafungin dose adjustments in obese patients are not necessary
- These findings contribute to the evaluation of rezafungin in a range of patient populations and its further development

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