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Outcomes by Body Mass Index (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

- A 'silent epidemic' of antifungal underdosing in the treatment of invasive disease in the critically ill may also affect special populations, such as the obese[1]
- Body size is an important variable affecting drug exposure
- Pharmacokinetic (PK) models of antifungal dosing suggest size-based adjustments to achieve target drug exposure
- Rezafungin is a novel echinocandin distinguished by a PK profile that includes long half-life, extensive tissue distribution, and front-loaded drug exposure, lending to once-weekly (QWk) dosing and antifungal 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]
- A sub-analysis of results from the Phase 2 STRIVE trial of rezafungin QWk in the treatment of candidemia and/or IC [NCT02734862] compared with caspofungin once daily (**Figure 1**) was conducted to evaluate outcomes based on patient BMI

Figure 1. Treatment Groups of the Phase 2 STRIVE Trial

Group	Dose Regimen	Dose Schedule
RZF Group 1	IV rezafungin 400 mg QWk	On Days 1 and 8
RZF Group 2	IV rezafungin 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 caspofungin 70 mg on Day 1, followed by 50 mg QD (with optional step-down to oral fluconazole)	Once daily 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

- For this subanalysis, data were stratified by BMI categories (<30 kg/m^2 and ≥30 kg/m^2) and assessed for:
- Safety
  - Treatment-emergent adverse events [TEAEs] by treatment group
- Efficacy
  - Overall response (resolution of clinical signs of infection and mycological eradication)
  - Mycological response
  - Investigator assessment of clinical response
- PK
  - Area under the curve (AUC) from RZF-treated patients in the first part of the trial

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 were generally similar between categories (**Table 1**), with no concerning safety trends

Table 1. Summary of TEAEs by BMI Category (<30 mg/kg^2 vs ≥30 mg/kg^2) from the STRIVE Trial (Safety Population)

TEAE	n (%)					
	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

RESULTS (cont'd)

Efficacy

- Efficacy outcomes at Day 14 were similar between BMI categories (**Table 2**)

Table 2. Efficacy Outcomes by BMI Category (<30 kg/m^2 vs ≥30 kg/m^2) in STRIVE (mITT Population)

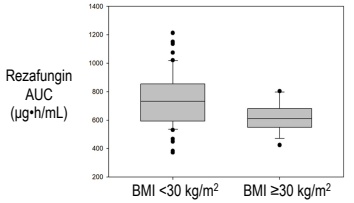
Outcomes at Day 14	n (%)					
	BMI <30 kg/m^2			BMI ≥30 kg/m^2		
	RZF Grp 1 N=57	RZF Grp 2 N=34	CAS N=48	RZF Grp 1 N=18	RZF Grp 2 N=11	CAS N=13
Overall Response	34 (59.6)	26 (76.5)	32 (66.7)	11 (61.1)	8 (72.7)	9 (69.2)
Mycological Response	37 (64.9)	26 (76.5)	33 (68.8)	12 (66.7)	8 (72.7)	9 (69.2)
Investigator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

RESULTS (cont'd)

PK

- Following one dose of rezafungin 400 mg (Week 1), AUC ranges by BMI category overlapped (**Figure 2**)
- AUC values for BMI ≥30 kg/m^2 group were ~20% lower vs in the <30 kg/m^2 group (mean [SD] AUC: 615 [104] µg•h/mL vs 741 [194] µg•h/mL, respectively)

Figure 2. Rezafungin AUC Following One 400-mg Dose at Week 1 by BMI Category (<30 kg/m^2 vs ≥30 kg/m^2)



	BMI <30 kg/m^2	BMI ≥30 kg/m^2
N[a]	51	17
Mean (SD) BMI, kg/m^2	23.1 (4.2)	35.9 (8.4)

[a]AUC data shown for patients with PK data available for this analysis.

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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