Analysis of the STRIVE Phase 2 Trial of Once-Weekly Rezafungin for Treatment of Candidemia and Invasive Candidiasis Compared with Caspofungin: Outcomes by ICU Status and APACHE II Score

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INTRODUCTION

- Invasive fungal disease (IFD) caused by *Candida* spp. is associated with longer hospital duration and higher mortality rates for the critically ill[1-3]
- For such patients, echinocandin treatment is recommended first-line therapy[4]
- Rezafungin (RZF) is a novel, next-generation echinocandin in Phase 3 development for treatment of candidemia and invasive candidiasis (IC) (NCT03667690) and for prevention of IFD caused by *Candida*, *Aspergillus*, and *Pneumocystis* in blood and marrow transplantation (NCT04368559)

OBJECTIVES

To evaluate outcomes of the Phase 2 STRIVE trial (NCT02734862)[5] of RZF once-weekly (QWk) for treatment of candidemia and/or IC compared with caspofungin (CAS) once-daily (QD) (Fig. 1), based on ICU status and Acute Physiology and Chronic Health Evaluation (APACHE II) scores

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.

METHODS

Data were stratified by ICU status (no ICU or ICU admission within Days 1–4) and by APACHE II score category (<10, 10-19, and ≥20) and assessed for

- **Efficacy**: overall response [resolution of clinical signs of infection and mycological eradication], mycological response, and investigator assessment of clinical response at Day 14; and 30-day all-cause mortality
- **Safety**: treatment-emergent adverse events [TEAEs]

Patients with time in ICU outside of Days 1–4 were not included in the analysis.

RESULTS

Efficacy

- Efficacy outcomes in RZF-treated patients were similar across ICU status and APACHE II scores (Tables 1 and 2). CAS-treated patients had lower efficacy rates in the ICU cohort (vs non-ICU; Table 1) and at higher APACHE II scores (Table 2)

Table 1. Outcomes by ICU Status – STRIVE mITT Population – number of patients (%)

	No ICU Admission[a]		ICU Admission (Days 1-4)	
	RZF Pooled N=61	CAS N=25	RZF Pooled N=40	CAS N=24
Overall Success	37 (60.7)	20 (80.0)	30 (75.0)	14 (58.3)
Mycological Success	39 (63.9)	20 (80.0)	32 (80.0)	14 (58.3)
Investigator-Assessed Clinical Cure	43 (70.5)	21 (84.0)	32 (80.0)	14 (58.3)
30-d All-Cause Mortality	4 (6.6)	2 (8.0)	7 (17.5)	5 (20.8)

mITT=Microbiological ITT (any amount of study drug and documented *Candida* infection)

Table 2. Outcomes by APACHE II Score – STRIVE mITT Population – number of patients (%)

	APACHE II Score					
	<10		10–19		≥20	
	RZF Pooled N=36	CAS N=16	RZF Pooled N=58	CAS N=33	RZF Pooled N=25	CAS N=9
Overall Success	21 (58.3)	12 (75.0)	43 (74.1)	20 (60.6)	16 (64.0)	6 (66.7)
Mycological Success	22 (61.1)	13 (81.3)	45 (77.6)	20 (60.6)	17 (68.0)	6 (66.7)
Investigator-Assessed Clinical Cure	24 (66.7)	13 (81.3)	47 (81.0)	21 (63.6)	18 (72.0)	6 (66.7)
30-d All-Cause Mortality	2 (5.6)	0	4 (6.9)	5 (15.2)	8 (32.0)	3 (33.3)

[a]APACHE II data not available for efficacy outcomes from 6 patients (N=3 each, RZF Pooled and CAS)

Safety

- No concerning trends or differences were seen between RZF and CAS. Not surprisingly, SAEs were higher in patients with ICU admission (Table 3) and with APACHE II scores ≥20 (vs scores <20) (data not shown)

Table 3. Safety by ICU Status – STRIVE Safety Population – number of patients (%)

	No ICU Admission[a]		ICU Admission (Days 1-4)	
	RZF Pooled N=65	CAS N=30	RZF Pooled N=47	CAS N=25
SAE	28 (43.1)	11 (36.7)	25 (53.2)	14 (56.0)
SAE leading to death	7 (7.7)	7 (23.3)	12 (25.5)	7 (28.0)

CONCLUSIONS

- RZF demonstrated efficacy in patients in the ICU and across APACHE II scores
- RZF safety in these subpopulations was comparable to that of caspofungin
- The high numbers of indeterminate outcomes (i.e., missing data and lost to follow-up) among lower acuity patients affects interpretation of outcomes
- These findings contribute to the evidence of RZF safety and efficacy in a broad range of patients and support the ongoing Phase 3 development of RZF for the treatment of candidemia and IC

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