Poster #P13

Rezafungin Treatment of Candidemia and Invasive Candidiasis: Outcomes Stratified by Baseline Renal Function – Analysis of the Phase 2 + Phase 3 Trials

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INTRODUCTION

- Rezafungin is a next-generation echinocandin in development for the treatment of candidemia and invasive candidiasis (IC) and for the prevention of invasive fungal disease caused by *Candida*, *Aspergillus*, and *Pneumocystis* spp. in patients undergoing bone and marrow transplantation
- Rezafungin once weekly (QWk) was compared with caspofungin once daily (QD) in two double-blind, randomized, controlled trials of treatment of candidemia and/or IC: STRIVE (Phase 2, NCT02734862; primary endpoint: overall cure [defined as resolution of clinical signs of candidemia/IC and mycological eradication] at Day 14)[1] and ReSTORE (Phase 3, NCT03667690; primary endpoint: US – all-cause mortality at Day 30; EU – global cure [defined as clinical and radiological cure and mycological eradication] at Day 14)[2,3]
- In a previous analysis from the STRIVE study, the pharmacokinetics of rezafungin were unchanged by renal function (creatinine clearance rate [CrCL] <60 mL/min vs. ≥60 mL/min)[4]
- Here we report the patient-level meta-analyses of efficacy and safety data from both STRIVE and ReSTORE in which outcomes were stratified by renal function at baseline

METHODS

- STRIVE and ReSTORE methods were previously described.[1-3,5] This analysis of data from both trials compared patients who received rezafungin QWk (400 mg on Week 1, then 200 mg) with those who received caspofungin QD (70 mg on Day 1 followed by 50 mg with optional step-down to oral fluconazole) for ≥14 days (up to 4 weeks)
- Data were stratified by renal function at baseline according to CrCl ≥60 mL/min (normal/mild impairment) and CrCl <60 mL/min (moderate/severe impairment)
- Outcomes included in the integrated analysis were mycological eradication at Day 5 and Day 14, 30-day all-cause mortality and incidence of treatment-emergent adverse events (TEAEs). Differences were evaluated between the CrCl categories and treatment groups

RESULTS

Patient Demographics

- Demographics and baseline characteristics were comparable in the rezafungin (N=139) and caspofungin (N=155) groups in the pooled analysis (**Table 1**)
- The proportions of patients with normal/mild and moderate/severe renal function were comparable between treatment groups (**Table 1**)

Table 1. Demographics and Baseline Characteristics (mITT population[a])

Characteristic	Rezafungin (N=139)	Caspofungin (N=155)
Age, mean years ± SD, (range)	59.8 ± 15.7 (19, 91)	60.8 ± 15.0 (20, 93)
Female, n (%)	49 (35.3)	65 (41.9)
Diagnosis, n (%)		
Candidemia only	100 (71.9)	115 (74.2)
Invasive candidiasis	39 (28.1)	40 (25.8)
Baseline renal function		
Normal/mild (CrCl ≥60 mL/min)	75 (54.0)	83 (53.5)
Moderate/severe (CrCl <60 mL/min)	54 (38.8)	59 (38.1)

[a]All patients who received any amount of study drug and with documented *Candida* infection. mITT=modified intent-to-treat.

Mycological Eradication

- The proportion of patients achieving mycological eradication with rezafungin was comparable in patients with normal/mild vs. moderate/severe renal impairment at Day 5 and Day 14 (**Figure 1**)
- Eradication rates with rezafungin vs. caspofungin were comparable in patients with normal/mild renal impairment but were higher with rezafungin in the moderate/severe category

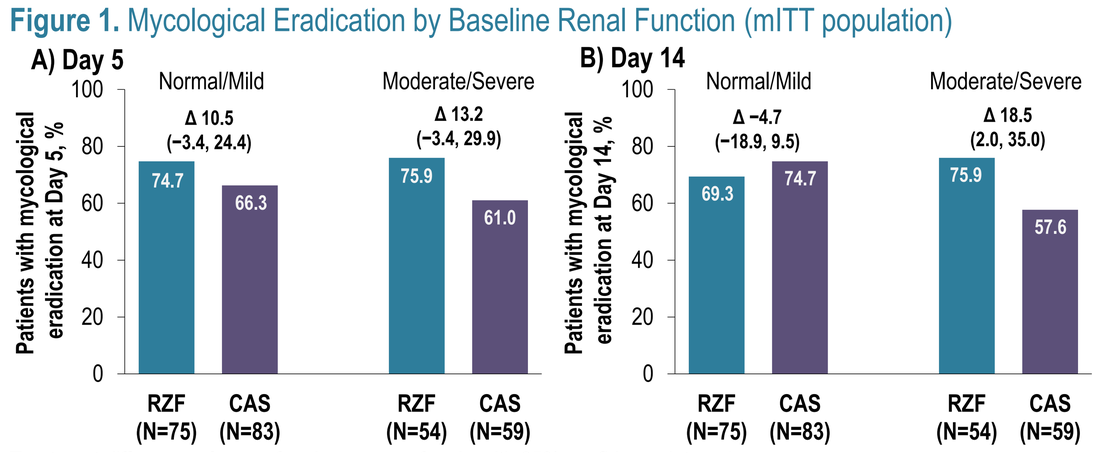
All-Cause Mortality at Day 30

- All-cause mortality at Day 30 in rezafungin-treated patients was lower in those with moderate/severe compared with normal/mild renal impairment (**Figure 2**)
- Conversely, for the caspofungin treatment group, all-cause mortality was higher for moderate/severe vs. normal/mild impairment
- All-cause mortality was lower for rezafungin vs. caspofungin in patients with moderate/severe renal impairment

Adverse Events

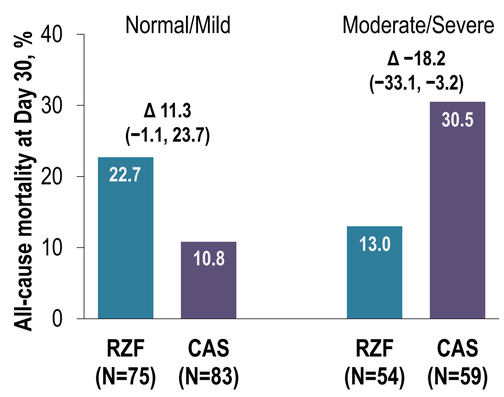
- Rates of TEAEs were generally higher for patients with moderate/severe vs. normal/mild renal impairment; these differences were observed for both rezafungin and caspofungin (**Table 2**)

Figure 1. Mycological Eradication by Baseline Renal Function (mITT population)



Treatment differences for rezafungin vs. caspofungin with 95% confidence intervals.
CAS=caspofungin; mITT=modified intent-to-treat; RZF=rezafungin.

Figure 2. All-Cause Mortality[a] at Day 30 by Baseline Renal Function (mITT population[a])



Treatment differences for rezafungin vs. caspofungin with 95% confidence intervals.
[a]Patients who died on or before Day 30, or with unknown survival status.
CAS=caspofungin; mITT=modified intent-to-treat; RZF=rezafungin.

Table 2. Summary of TEAEs by Baseline Renal Function (Safety Population[a])

	Normal/mild		Moderate/severe	
Incidence of patients, n (%)	RZF (N=81)	CAS (N=90)	RZF (N=59)	CAS (N=63)
with ≥1 TEAE	72 (88.9)	69 (76.7)	55 (93.2)	56 (88.9)
≥1 SAE	41 (50.6)	35 (38.9)	36 (61.0)	38 (60.3)
≥1 TEAE leading to d/c of study drug	8 (9.9)	7 (7.8)	5 (8.5)	8 (12.7)
≥1 TEAE leading to study d/c	12 (14.8)	13 (14.4)	10 (16.9)	17 (27.0)

[a]All patients who received any amount of study drug. CAS=caspofungin; d/c=discontinuation; RZF=rezafungin; SAE=serious adverse event; TEAE=treatment-emergent adverse event.

CONCLUSIONS

- The efficacy of rezafungin was comparable in patients with normal/mild vs. moderate/severe impairment in baseline renal function
- In patients with moderate/severe renal impairment who received rezafungin, mycological eradication was higher, and 30-day all-cause mortality was lower, compared with caspofungin-treated patients with moderate/severe renal impairment
- Further analyses are needed to evaluate the observed differences between treatment groups

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DISCLOSURES AND ACKNOWLEDGMENTS

T.S. is an employee and shareholder of Cidara Therapeutics. STRIVE was funded by Cidara Therapeutics. ReSTORE was funded by Cidara Therapeutics and Mundipharma. Editorial support was provided by Thomas Owens (Aspire Scientific Ltd., Bollington, UK) and funded by Cidara Therapeutics.