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

Thompson GR III,[1] Horcajada JP,[2] Locke JB,[3] Viani R,[3] Pappas P,[4] Ghannoum M,[5] Sandison T,[3] Soriano A[6]

[1]Univ of California Davis Medical Center, Sacramento, CA, USA; [2]Hospital del Mar-IMIM, Barcelona, Spain; [3]Cidara Therapeutics, Inc., San Diego, CA, USA; [4]Univ of Alabama at Birmingham, Birmingham, AL, USA; [5]Center for Medical Mycology, Case Western Reserve Univ and Univ Hospitals Cleveland Medical Center, Cleveland, OH, USA; [6]Hospital Clínic de Barcelona, IDIBAPS, Univ of Barcelona, Spain

George R. Thompson III, MD
grthompson@ucdavis.edu
916-734-5644

INTRODUCTION

- Rezafungin is a novel echinocandin 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]
- Rezafungin demonstrates a long half-life, extensive tissue distribution, and front-loaded drug exposure, which allow for rezafungin's once-weekly (QWk) dosing and are determinants of antifungal efficacy [1,2]
- In this analysis of the Phase 2 STRIVE trial (NCT02734862) of rezafungin treatment of candidemia and IC, outcomes based on baseline pathogen species and susceptibility were evaluated

METHODS

- In STRIVE, adults (≥18 y) with systemic signs and mycological evidence of candidemia and/or IC were randomized to either rezafungin once weekly or caspofungin once daily for ≥14 days (**Figure 1**)

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

- The primary efficacy endpoint was Overall Response (resolution of clinical signs of infection + mycological eradication) at Day 14 in the microbiological intent-to-treat (mITT) population
- For this analysis, outcomes by treatment group were stratified by *Candida* species and in vitro susceptibility (CLSI broth microdilution MIC values; M27-Ed4)

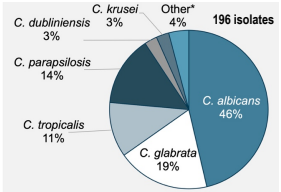
RESULTS

- Of 196 *Candida* isolates recovered from 183 patients across all treatment groups, *C. albicans* was the most common species; non-*albicans Candida* comprised 54% of all baseline isolates (**Figure 2**).

RESULTS (cont'd)

- Rezafungin MIC distribution and ranges were generally lower than or comparable to those for CAS (Table 1)
- Based on MICs, all isolates exhibited a wild-type in vitro susceptibility profile
- Outcomes by species did not appear to be affected by MIC distribution for either treatment (Table 1)

Figure 2. *Candida* spp. Distribution (mITT)



*Other: *C. fermentati*, *C. intermedia*, *C. kefyr*, *C. metapsilosis*, *C. rugosa*, *C. utilis* (n=1 each), and *C. guilliermondii* (n=2)

Table 1. Overall Response (%) by Species and MIC Distribution (mITT)

Organism Study Grp (n)	Rate of Overall Response, n/N[a] (%) by MIC (µg/mL)								
	≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2
C. albicans									
RZF Group 1 (38)	1/3 (33.3)	6/15 (40)	2/7 (28.6)	6/8 (75.0)	1/2 (50)				
RZF Group 2 (19)	3/3 (100)	8/9 (88.9)	2/3 (66.7)	0/2 (0)	1/2 (50)				
CAS (33)			0/1 (0)	6/6 (100)	12/20 (60)	4/4 (100)	2/2 (100)		
C. glabrata									
RZF Group 1 (13)				6/6 (100)	5/6 (83.3)	1/1 (100)			
RZF Group 2 (14)				5/7 (71.4)	5/5 (100)	1/2 (50)			
CAS (10)					1/1 (100)	4/6 (66.7)	2/3 (66.7)		
C. parapsilosis									
RZF Group 1 (10)							2/3 (66.7)	1/2 (50)	3/5 (60)
RZF Group 2 (7)							1/1 (100)	2/2 (100)	3/4 (75)
CAS (11)				0/1 (0)			1/1 (100)	3/9 (33.3)	
C. tropicalis									
RZF Group 1 (9)		1/1 (100)	1/3 (33.3)	1/2 (50)	1/1 (100)	0/2 (0)			
RZF Group 2 (7)			3/3 (100)	2/3 (66.7)	0/1 (0)				
CAS (6)					1/1 (100)	3/4 (75)	1/1 (100)		

[a]Numerator: the number of patients who demonstrated overall response; denominator: the number of patients whose isolate(s) had the MIC value (µg/mL) indicated by column header. Not all isolates had MIC data.

RESULTS (cont'd)

- Outcomes by study group showed no clear correlations with MIC values (Table 2)

Table 2. Overall Response (%) for Most Frequently Isolated *Candida* spp. by Study Group (mITT)

***Candida* species** MIC, µg/mL (no. isolates[a])	Overall Response, n/N (%)		
	Rezafungin 400 mg/400 mg QWk[b]	**Rezafungin 400 mg/200 mg QWk**	**Caspofungin 70 mg/50 mg QD**
C. albicans	19/38 (50)	14/19 (73.7)	25/34 (73.5)
MIC_{90} (89[c])	0.06		0.25
Range	≤0.008–0.25		0.03–0.5
C. glabrata	12/13 (92.3)	11/14 (78.6)	7/10 (70)
MIC_{90} (37)	0.25		0.5
Range	0.03–0.25		0.12–1
C. parapsilosis	6/10 (60)	6/7 (85.7)	4/11 (36.4)
MIC_{90} (28)	2		1
Range	0.5–2		0.06–1
C. tropicalis	4/9 (44.4)	5/7 (71.4)	5/6 (83.3)
MIC_{90} (22)	0.12		0.5
Range	0.016–0.25		0.03–0.5

[a]Not all isolates had MIC data.
[b]Values for Group 1 were affected by a high number of indeterminates (n=10)
[c]MIC_{90} of rezafungin against *C. albicans* based on 87 isolates.

CONCLUSIONS

- In this Phase 2 study, outcomes in rezafungin Group 2 were similar to or better than outcomes with caspofungin
- Rezafungin Group 2 received the dose regimen being studied in Phase 3
- Group 1 results were confounded by high number of indeterminate outcomes
- These Phase 2 findings and results from the ongoing Phase 3 treatment trial (ReSTORE) will further understanding of the relationships between MIC values and clinical outcomes in patients with candidemia or IC

REFERENCES

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ACKNOWLEDGMENTS

Cidara Therapeutics sponsored and funded the STRIVE trial and had a role in the trial design, data collection, and analysis, and in the decision to submit these data for presentation. Medical writing assistance was provided by T. Chung (Scribant Medical) with funding from Cidara.