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Outcomes by Baseline Pathogen and Susceptibility in the ReSTORE Phase 3 Trial of Rezafungin Once Weekly Compared With Caspofungin Once Daily in Patients With Candidemia and/or Invasive Candidiasis

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INTRODUCTION

- Rezafungin is a next-generation, once-weekly (QWk) echinocandin in development for the treatment of candidemia and invasive candidiasis (IC), and for the prevention of invasive fungal diseases caused by *Candida*, *Aspergillus*, and *Pneumocystis* spp. in patients undergoing blood and marrow transplantation¹
- ReSTORE (NCT03667690) was a Phase 3, global, double-blind, double-dummy, 1:1 randomized, noninferiority trial that evaluated the efficacy and safety of rezafungin QWk versus caspofungin once daily (QD) in patients with candidemia and/or IC¹
- Here, we report a subanalysis of the ReSTORE outcomes stratified by baseline pathogen and susceptibility

METHODS

- Patients:** Adults (≥18 years old) with systemic signs and mycological confirmation of candidemia and/or IC¹
- Treatment:** Rezafungin QWk (400 mg Week 1, then 200 mg QWk) or 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)¹
- Endpoints assessed in this analysis:**
 - Global cure (defined as clinical and radiological cure and mycological eradication) at Day 14 (primary endpoint [EMA]¹)
 - Mycological eradication at Day 14 (secondary endpoint¹)
- Analysis:** Endpoints were analyzed by *Candida* spp. and *in vitro* susceptibility at baseline (Clinical and Laboratory Standards Institute [CLSI] broth microdilution minimum inhibitory concentration [MIC] values; M27Ed4²) in the modified intent-to-treat population (n = 93 rezafungin; n = 94 caspofungin)

RESULTS

Figure 1. *Candida* spp. Distribution of Baseline Isolates Across Both Treatment Arms^a

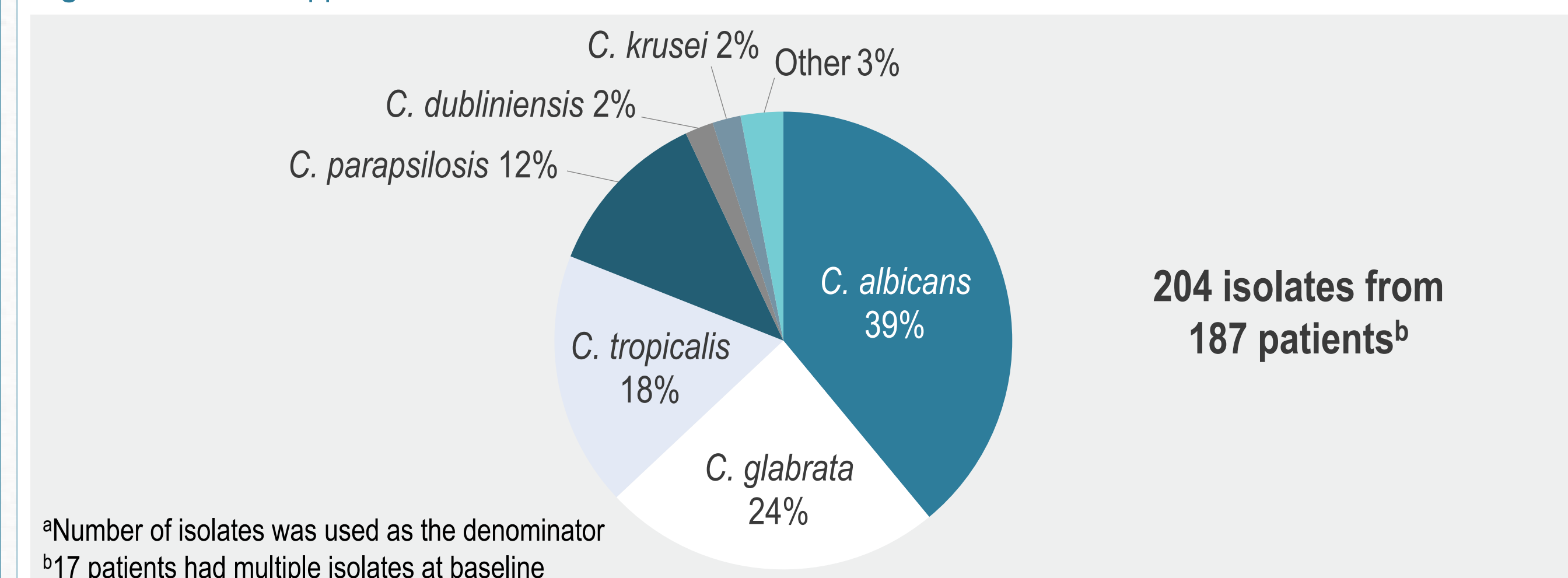


Table 1. Global Cure and Mycological Eradication at Day 14 by Most Frequently Isolated *Candida* spp. at Baseline

<i>Candida</i> spp.		Rezafungin	Caspofungin
<i>C. albicans</i>	Global cure, n/N ^a (%)	21/39 (53.8)	23/40 (57.5)
	Mycological eradication, n/N ^a (%)	23/39 (59.0)	24/40 (60.0)
	MIC ₉₀ ^b (MIC range), µg/mL	0.06 (0.008–0.12)	0.06 (0.008–0.12)
	n ^c	39	39
<i>C. glabrata</i>	Global cure, n/N ^a (%)	16/24 (66.7)	14/25 (56.0)
	Mycological eradication, n/N ^a (%)	20/24 (83.3)	15/25 (60.0)
	MIC ₉₀ ^b (MIC range), µg/mL	0.12 (0.03–0.5)	0.06 (0.03–0.12)
	n ^c	24	25
<i>C. tropicalis</i>	Global cure, n/N ^a (%)	14/20 (70.0)	10/17 (58.8)
	Mycological eradication, n/N ^a (%)	15/20 (75.0)	10/17 (58.8)
	MIC ₉₀ ^b (MIC range), µg/mL	0.06 (0.015–0.12)	0.06 (0.015–0.12)
	n ^c	20	16
<i>C. parapsilosis</i>	Global cure, n/N ^a (%)	6/8 (75.0)	11/17 (64.7)
	Mycological eradication, n/N ^a (%)	6/8 (75.0)	14/17 (82.4)
	MIC ₉₀ ^b (MIC range), µg/mL	-- (0.5–2)	0.5 (0.25–0.5)
	n ^c	8	16

^an/N indicates number of patients with listed response at Day 14/number of patients with the corresponding *Candida* pathogen at baseline; ^bFor pathogens isolated ≥10 times in a treatment group; ^cNumber of patients with baseline pathogens and susceptibility data available

RESULTS (cont'd)

Table 2. Outcomes at Day 14 by Baseline *Candida* spp. by Rezafungin and Caspofungin CLSI MIC Values

<i>Candida</i> spp.	Treatment [isolates ^b]	n/N ^a (%) by treatment-specific MIC value, µg/mL								
		0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2
<i>C. albicans</i>										
Rezafungin [39]										
	Global cure	4/7 (57)	11/20 (55)	4/6 (67)	1/4 (25)	1/2 (50)				
	Mycological eradication	5/7 (71)	11/20 (55)	5/6 (83)	1/4 (25)	1/2 (50)				
Caspofungin [39]										
	Global cure	1/2 (50)	5/9 (56)	11/21 (52)	5/6 (83)	0/1 (0)				
	Mycological eradication	1/2 (50)	5/9 (56)	12/21 (57)	5/6 (83)	0/1 (0)				
<i>C. glabrata</i>										
Rezafungin [24]										
	Global cure			6/8 (75)	4/6 (67)	6/9 (67)		0/1 (0)		
	Mycological eradication			7/8 (88)	6/6 (100)	6/9 (67)		1/1 (100)		
Caspofungin [25]										
	Global cure			2/5 (40)	11/19 (58)	1/1 (100)				
	Mycological eradication			2/5 (40)	12/19 (63)	1/1 (100)				
<i>C. tropicalis</i>										
Rezafungin [20]										
	Global cure		3/3 (100)	5/8 (63)	5/7 (71)	1/2 (50)				
	Mycological eradication		3/3 (100)	5/8 (63)	5/7 (71)	2/2 (100)				
Caspofungin [16]										
	Global cure		1/1 (100)	3/7 (43)	4/7 (57)	1/1 (100)				
	Mycological eradication		0/1 (0)	4/7 (57)	4/7 (57)	1/1 (100)				
<i>C. parapsilosis</i>										
Rezafungin [8]										
	Global cure							1/1 (100)	2/4 (50)	3/3 (100)
	Mycological eradication							1/1 (100)	2/4 (50)	3/3 (100)
Caspofungin [16]										
	Global cure						5/8 (63)	6/8 (75)		
	Mycological eradication						5/8 (63)	8/8 (100)		

^an/N indicates number of patients with listed response at Day 14/number of patients with the corresponding *Candida* pathogen and MIC value at baseline. Not all isolates had MIC data; ^bNumber of isolates. All baseline isolates in this table were susceptible to rezafungin³

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CONCLUSIONS

- The ReSTORE trial demonstrated the noninferiority of rezafungin to caspofungin for global cure at Day 14 and all-cause mortality at Day 30 in patients with candidemia and/or IC¹
- In this analysis, rezafungin demonstrated efficacy for global cure and mycological eradication regardless of baseline *Candida* spp.
- Efficacy outcomes across *Candida* spp. did not appear to be impacted by MIC values for either rezafungin or caspofungin; assessment of other clinical factors (e.g., catheter removal) may be warranted