Rezafungin and caspofungin treatment response in candidaemia/invasive candidiasis by baseline *Candida* species: Analysis of pooled Phase 2 and Phase 3 results

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INTRODUCTION AND OBJECTIVES

- Candidemia and invasive candidiasis remain significant causes of morbidity and mortality.[1,2]
- Rezafungin is a next-generation once-weekly echinocandin antifungal for intravenous injection currently in development for the treatment of *Candida* infections and prevention of *Candida*, *Aspergillus*, and *Pneumocystis* infections in allogeneic blood and marrow transplantation.[3–7] Rezafungin offers prolonged half-life (approximately 133 hours) and high front-loaded plasma exposures.[3–5]
- The current analysis examined pooled data regarding mycological response by *Candida* species and *in vitro* susceptibility at baseline from the rezafungin STRIVE (Phase 2: NCT02734862) and ReSTORE (Phase 3: NCT03667690) trials.[6,7]

METHODS

- STRIVE and ReSTORE were international, double-blind, randomised, controlled trials.
- Adults with candidaemia and/or invasive candidiasis, diagnosed by systemic manifestations of active infection and mycological confirmation, received intravenous rezafungin once-weekly (QWk; Week 1: 400 mg; Weeks 2–4: 200 mg) or caspofungin once daily (QD; Day 1: 70 mg; Days 2–28: 50 mg) for ≥14 days (≤4 weeks).
- The current analysis used pooled STRIVE and ReSTORE data to examine mycological response rates at Days 5 and 14 by *Candida* species and *in vitro* susceptibility at baseline according to the European Committee for Antimicrobial Susceptibility Testing (EUCAST) broth microdilution minimum inhibitory concentration (MIC) values.

RESULTS

Baseline demographics and characteristics

- The analysis included 294 subjects; 139 patients treated with rezafungin and 155 receiving caspofungin. Treatment groups were balanced regarding patient characteristics and *Candida* species at baseline (Table 1).
- The majority of subjects had candidemia (73.1%). The most common species identified at baseline were *C. albicans* (43.2%), *C. glabrata* (24.8%), *C. tropicalis* (16.7%) and *C. parapsilosis* complex (13.9%).

Table 1. Baseline demographics and characteristics (mITT population)

	Rezafungin (400/200 mg) (N=139)	Caspofungin (70/50 mg) (N=155)	Total (N=294)
Age, mean ± SD (range), years	59.8 ± 15.7 (19, 91)	60.8 ± 15.0 (20, 93)	
Age <65 years, n (%)	82 (59.0)	92 (59.4)	174 (59.2)
Age ≥65 years, n (%)	57 (41.0)	63 (40.6)	120 (40.8)
Female, n (%)	49 (35.3)	65 (41.9)	114 (38.8)
Diagnosis, n (%)			
Candidaemia	100 (71.9)	115 (74.2)	215 (73.1)
Invasive candidiasis	39 (28.1)	40 (25.8)	79 (26.9)
Candida species diagnosed at baseline, n (%)			
Candida albicans	58 (41.7)	69 (44.5)	127 (43.2)
Candida glabrata	38 (27.3)	35 (22.6)	73 (24.8)
Candida tropicalis	27 (19.4)	22 (14.2)	49 (16.7)
Candida parapsilosis complex	14 (10.1)	27 (17.4)	41 (13.9)
Candida krusei	5 (3.6)	3 (1.9)	8 (2.7)
Candida metapsilosis	3 (2.2)	0	3 (1.0)
Candida dubliniensis	3 (2.2)	2 (1.3)	5 (1.7)
Candida guilliermondii	2 (1.4)	0	2 (0.7)
Candida kefyr	0	1 (0.6)	1 (0.3)
Candida lusitaniae	1 (0.7)	1 (0.6)	2 (0.7)
Candida nivariensis	0	1 (0.6)	1 (0.3)

All analyses were conducted using the mITT population comprising all STRIVE/ReSTORE subjects with a mycological diagnosis of candidaemia and/or invasive candidiasis within 96 hours of randomisation who received ≥1 dose of study drug.
Abbreviations: mITT, modified intention to treat; SD, standard deviation.

Mycological response rates by *Candida* species

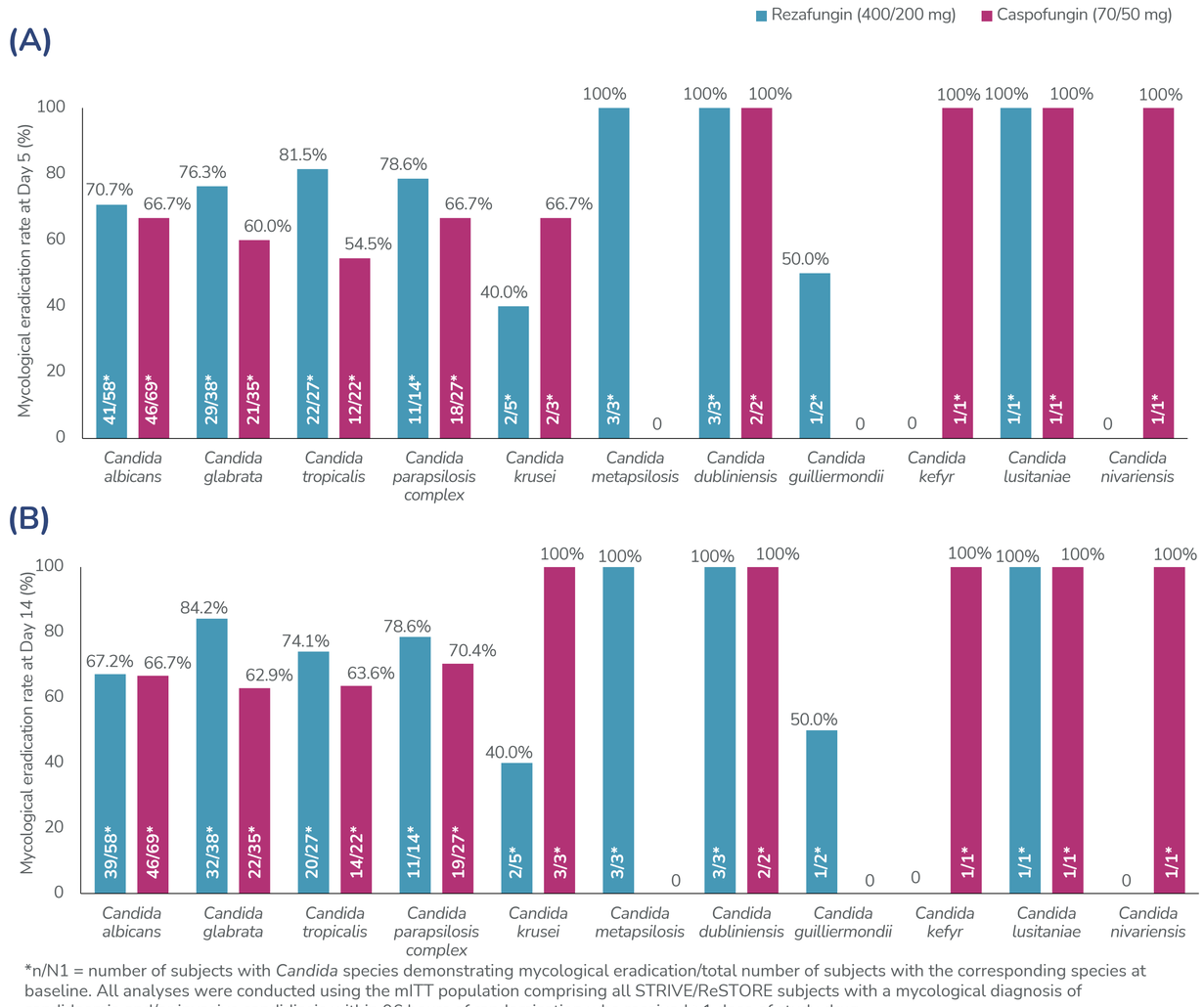
- Mycological eradication rates at Day 5 were, 70.7% (*C. albicans*), 76.3% (*C. glabrata*), 81.5% (*C. tropicalis*) and 78.6% (*C. parapsilosis* complex) with rezafungin and 66.7%, (*C. albicans*) 60.0% (*C. glabrata*), 54.5% (*C. tropicalis*) and 66.7% (*C. parapsilosis* complex) with caspofungin (Figure 1).
- Day 14 mycological eradication rates were 67.2% (*C. albicans*), 84.2% (*C. glabrata*), 74.1% (*C. tropicalis*) and 78.6% (*C. parapsilosis* complex) with rezafungin and 66.7%, (*C. albicans*) 62.9% (*C. glabrata*), 63.6% (*C. tropicalis*) and 70.4% (*C. parapsilosis* complex) with caspofungin.

Mycological response rates according to baseline MIC value

- Mycological response with rezafungin and caspofungin according to *Candida* species at Days 5 and 14 did not appear to be affected by baseline MIC values (Table 2).

RESULTS (CONTINUED)

Figure 1. Mycological response with rezafungin (400 mg/200 mg) and caspofungin (70 mg/50 mg) treatment according to baseline *Candida* species. (A) Day 5 response (B) Day 14 response (mITT population)



*n/N1 = number of subjects with *Candida* species demonstrating mycological eradication/total number of subjects with the corresponding species at baseline. All analyses were conducted using the mITT population comprising all STRIVE/ReSTORE subjects with a mycological diagnosis of candidaemia and/or invasive candidiasis within 96 hours of randomisation who received ≥1 dose of study drug.
Abbreviations: mITT, modified intention to treat.

Table 2. Mycological response at Day 5 and Day 14 with rezafungin (400 mg/200 mg) and caspofungin (70 mg/50 mg) by MIC at baseline (mITT population)

	Day 5 mycological response		Day 14 mycological response	
Candida species MIC value (µg/mL)	Rezafungin (400/200 mg) (N=139), n/N1 (%)	Caspofungin (70/50 mg) (N=155) n/N1 (%)	Rezafungin (400/200 mg) (N=139) n/N1 (%)	Caspofungin (70/50 mg) (N=155) n/N1 (%)
Candida albicans				
0.008	4/7 (57.1)	4/6 (66.7)	5/7 (71.4)	3/6 (50.0)
0.015	13/20 (65.0)	6/9 (66.7)	11/20 (55.0)	5/9 (55.6)
0.03	7/11 (63.6)	20/34 (58.8)	8/11 (72.7)	24/34 (70.6)
0.06	10/12 (83.3)	15/18 (83.3)	8/12 (66.7)	14/18 (77.8)
0.12	7/8 (87.5)	1/2 (50.0)	7/8 (87.5)	0/2 (0)
Candida glabrata				
0.03	8/10 (80.0)	3/6 (50.0)	9/10 (90.0)	3/6 (50.0)
0.06	16/17 (94.1)	18/27 (66.7)	15/17 (88.2)	18/27 (66.7)
0.12	5/10 (50.0)	0/2 (0)	7/10 (70.0)	1/2 (50.0)
0.5	0/1 (0)	0	1/1 (100.0)	0
Candida parapsilosis complex				
0.25	0	8/11 (72.7)	0	7/11 (63.6)
0.5	0/1 (0)	10/17 (58.8)	1/1 (100.0)	12/17 (70.6)
1	7/8 (87.5)	0	6/8 (75.0)	0
2	4/4 (100.0)	0	4/4 (100.0)	0
Candida tropicalis				
0.015	3/3 (100.0)	0/1 (0)	3/3 (100.0)	0/1 (0)
0.03	9/11 (81.8)	3/8 (37.5)	8/11 (72.7)	4/8 (50.0)
0.06	7/10 (70.0)	8/11 (72.7)	6/10 (60.0)	8/11 (72.7)
0.12	3/3 (100.0)	1/2 (50.0)	3/3 (100.0)	2/2 (100.0)
Candida krusei				
0.03	1/2 (50.0)	0	1/2 (50.0)	0
0.06	1/3 (33.3)	0	1/3 (33.3)	0
0.12	0	1/2 (50.0)	0	2/2 (100.0)
0.25	0	1/1 (100.0)	0	1/1 (100.0)

n = number of subjects with *Candida* species demonstrating mycological eradication. N1= total number of subjects with the corresponding species at baseline. All analyses were conducted using the mITT population comprising all STRIVE/ReSTORE subjects with a mycological diagnosis of candidaemia and/or invasive candidiasis within 96 hours of randomisation who received ≥1 dose of study drug.
Abbreviations: MIC, minimum inhibitory concentration; mITT, modified intention to treat.

CONCLUSION

- Pooled analysis of data from the STRIVE and ReSTORE trials revealed comparable mycological response rates with rezafungin and caspofungin at Day 5 and Day 14 against most *Candida* species.
- Outcome response with rezafungin and caspofungin was generally unaffected by EUCAST MIC values.

Disclosures

GR Thompson: grants and consulting fees from Amplyx, Astellas, Cidara, F2G, and Manye; grants from Merck; and data safety monitoring board membership for Pfizer, outside of the submitted work. **OA Cornely:** reports grants or contracts from Amplyx, Basilea, Bundesministerium für Bildung und Forschung, Cidara, German Center for Infection Research, European Union Directorate-General for Research and Innovation (101037867), F2G, Gilead, Matinas, MedPace, MSD, Mundipharma, Octapharma, Pfizer, and Scynexis; consulting fees from AbbVie, Amplyx, Biocon, Biosys, Cidara, Da Volterra, Gilead, IQVIA, Janssen, Matinas, MedPace, Menarini, Molecular Partners, Noxxon, Octapharma, Pardes, Pfizer, Pharma Support America, Scynexis, and Seres; honoraria from Abbott, AbbVie, Al-Jazeera Pharmaceuticals, Astellas, Gilead, Grupo Biotoscana/ United Medical/Knight, Hikma, MedScape, MedUpdate, Merck/MSD, Mylan, Noscendo, Pfizer, and Shionogi; payment for expert testimony from Cidara; data safety monitoring board or advisory board membership for Actelion, Allecra, Cidara, Entasis, IQVIA, Janssen, MedPace, Paratek, Pharma Support America, Pulmocide, Shionogi, and The Prime Meridian Group; a patent at the German Patent and Trade Mark Office (DE 10 2021 113 007.7); stocks from CoRe Consulting; and is a board member of German Society for Haematology and Medical Oncology, Deutsche Gesellschaft für Information und Wissen, ECMM European Confederation of Medical Mycology, International Society for Human & Animal Mycology, Mycoses Study Group–Education and Research Consortium, and Wiley, outside of the submitted work. **A Soriano:** grant from Gilead Sciences; consulting fees and honoraria from Angelini, Gilead, Menarini, MSD, and Shionogi, outside of the submitted work; and grants, consulting fees, honoraria, and support attending meetings from Pfizer, outside of the submitted work. **BJ Kullberg:** independent data review committee membership for Cidara. GRT reports grants and consulting fees from Amplyx, Astellas, Cidara, F2G, and Manye; grants from Merck; and data safety monitoring board membership for Pfizer, outside of the submitted work. **M Kollef:** grants from Barnes-Jewish Hospital Foundation and consulting fees from Merck, Pfizer, and Shionogi, outside of the submitted work. **J Vazquez:** consulting fees from and membership of data safety monitoring board or advisory board for F2G and consulting fees from Cidara and Scynexis, outside of the submitted work. **M Bassetti:** honoraria from and membership of data safety monitoring board or advisory board for Angelini, Cidara, Gilead, Menarini, MSD, Pfizer, and Shionogi, outside of the submitted work. **AF Das:** consulting fees from Cidara. **PG Pappas:** grants from and data review committee membership for Cidara; grants from Astellas, Scynexis, and Merck; and advisory board membership for F2G, outside of the submitted work. **T Sandison:** employee of and stocks in Cidara. All other authors declare no competing interests.

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