Clinical outcomes with rezafungin or caspofungin in adults with invasive infections due to non-*albicans Candida*: pooled analysis from STRIVE and ReSTORE trials (including extension phase data)

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INTRODUCTION AND OBJECTIVES

- Emergence of azole-resistant *Candida* species (particularly non-*albicans* species) represents an increasing burden.[1]
- The STRIVE (Phase 2: NCT02734862) and ReSTORE (Phase 3: NCT03667690) trials examined treatment outcomes with once-weekly rezafungin or daily caspofungin in candidaemia and/or invasive candidiasis (C/IC).[2,3]
- The current analysis reports pooled data from STRIVE and ReSTORE, including the ReSTORE extended phase in China.[2,3]

METHODS

- STRIVE and ReSTORE were multicentre, double-blind, randomised trials.
- Adults with C/IC received intravenous (IV) rezafungin once-weekly (Week 1: 400 mg; Weeks 2–4: 200 mg) or caspofungin once-daily (Day 1: 70 mg; Days 2–28: 50 mg) for at least 14 days and up to 4 weeks. A step down to oral therapy was allowed for patients who met relevant criteria after ≥3 doses of IV therapy (rezafungin arm: placebo; caspofungin arm: fluconazole).

Endpoints

- Efficacy endpoints examined the modified intention-to-treat (mITT) population with subanalysis according to the non-*albicans Candida* (NAC) species detected at baseline. The mITT comprised all patients with a documented *Candida* infection within 96 hours before randomisation (receiving ≥1 dose of study drug).
- The current analysis reports Day 30 all-cause mortality (ACM) and mycological response at Days 5 and 14 for the full mITT population and for each NAC species subgroup.
- Treatment-emergent adverse events (TEAEs) were reported for the safety population, comprising all randomised patients who received study drug.

RESULTS

Study population

- The analysis included 161 patients treated with rezafungin and 178 caspofungin recipients. The most common NAC species at baseline were *C. glabrata*, *C. tropicalis* and *C. parapsilosis* (**Table 1**).

Table 1. Pooled ReSTORE and STRIVE trial data (including extended phase in China): patient demographics, characteristics and *Candida* species detected at baseline (mITT population)

	Rezafungin 400/200 mg (n=161)	Caspofungin 70/50 mg (n=178)
Age, mean (SD), years	59.1 (16.37)	60.4 (14.96)
Aged ≥65 years, n (%)	66 (41.0)	71 (39.9)
Sex, n (%)		
Male	108 (67.1)	102 (57.3)
Female	53 (32.9)	76 (42.7)
Race , n (%)		
White	95 (59.0)	106 (59.6)
Asian	46 (28.6)	57 (32.0)
Black or African American	11 (6.8)	8 (4.5)
American Indian or Alaska Native	1 (0.6)	1 (0.6)
Other	3 (1.9)	2 (1.1)
Not reported	5 (3.1)	4 (2.2)
Diagnosis		
Candidaemia only	120 (74.5)	136 (76.4)
Invasive candidiasis	41 (25.5)	42 (23.6)
Modified APACHE II score ≥20	24 (14.9)	30 (16.9)
Baseline *Candida* species, n (%)		
C. albicans	64 (39.8)	76 (42.7)
C. glabrata	40 (24.8)	37 (20.8)
C. tropicalis	34 (21.1)	28 (15.7)
C. parapsilosis	18 (11.2)	33 (18.5)
C. krusei	5 (3.1)	3 (1.7)
C. dubliniensis	3 (1.9)	2 (1.1)
C. metapsilosis	3 (1.9)	0
C. guilliermondii	2 (1.2)	1 (0.6)
C. lusitaniae	1 (0.6)	1 (0.6)
C. guilliermondii var membranifaciens	0	1 (0.6)
C. kefyr	0	1 (0.6)
C. nivariensis	0	1 (0.6)

mITT population: all patients in the STRIVE/ReSTORE trials (plus China extended phase) with documented *Candida* infection within 96 hours who received ≥1 dose of study drug. Abbreviations: APACHE, acute physiology and chronic health evaluation; mITT, modified intention-to-treat; SD, standard deviation.

Efficacy endpoints

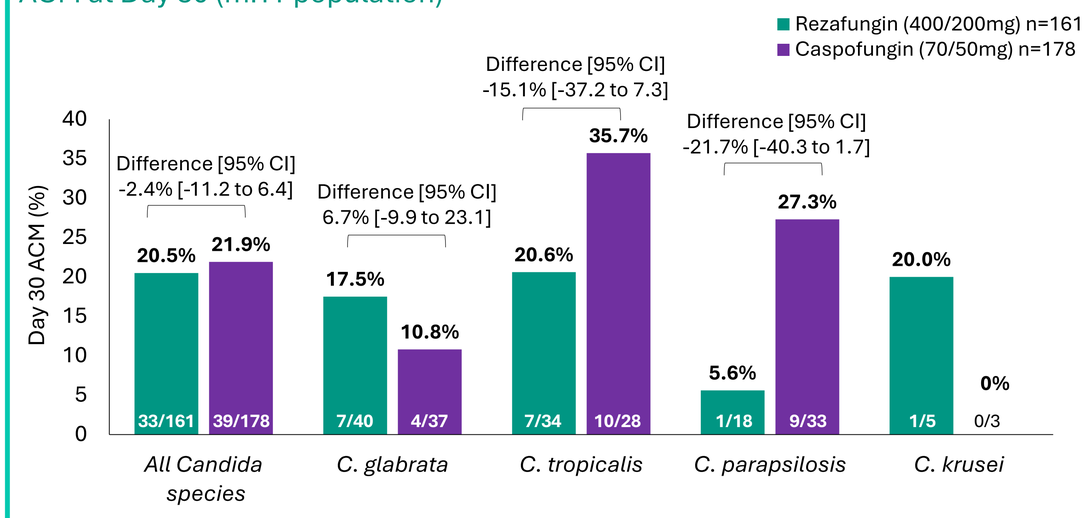
- Day 30 ACM in patients with NAC infections ranged between 5.6–20.6% with rezafungin and 0–35.7% with caspofungin (**Figure 1**).
- Range of mycological response for NAC infections (**Figure 2**):
  - Rezafungin arm: 40.0–77.8% (Day 5) and 40.0–82.5% (Day 14).
  - Caspofungin arm: 59.5–66.7% (Day 5) and 64.3–100% (Day 15).

Safety endpoints

- Treatment-related TEAEs were similar and reported in 27 (15.6%) rezafungin recipients and 24 (12.6%) caspofungin-treated patients (**Table 2**).

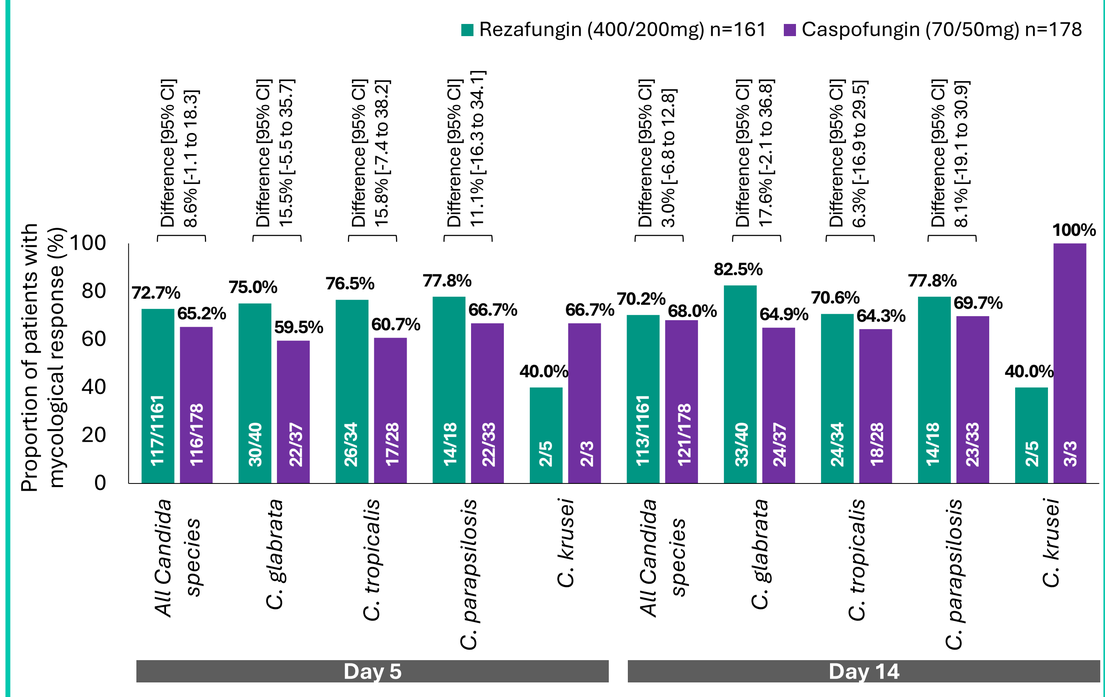
RESULTS CONTINUED

Figure 1. Pooled STRIVE and ReSTORE trial data (plus extended phase in China): ACM at Day 30 (mITT population)



mITT population: all patients in the STRIVE/ReSTORE trials (plus China extended phase) with documented *Candida* infection within 96 hours who received ≥1 dose of study drug. Calculations for 95% CIs used unstratified Miettinen and Nurminen methodology (completed for species observed in >10 patients). Abbreviations: ACM, all-cause mortality; CI, confidence interval; mITT, modified intention-to-treat.

Figure 2. Pooled STRIVE and ReSTORE trial data (plus extended phase in China): mycological response at Days 5 and 14 (mITT population)



mITT population: all patients in the STRIVE/ReSTORE trials (plus China extended phase) with documented *Candida* infection within 96 hours who received ≥1 dose of study drug. Calculations for 95% CIs used unstratified Miettinen and Nurminen methodology (completed for species observed in >10 patients). Abbreviations: CI, confidence interval; mITT, modified intention-to-treat.

Table 2. Pooled ReSTORE and STRIVE trial data (plus extended phase in China): TEAEs (Safety Population)

	Rezafungin 400/200 mg (n=173)	Caspofungin 70/50 mg (n=191)
Patients with ≥1 TEAE, n (%)	159 (91.9)	162 (84.8)
Patients with ≥1 TEAE leading to discontinuation, n (%)	15 (8.7)	16 (8.4)
Patients with ≥1 treatment-related TEAE, n (%)	27 (15.6)	24 (12.6)
Treatment-related TEAEs affecting ≥1%, n (%)		
Alanine aminotransferase increased	2 (1.2)	1 (0.5)
Blood bilirubin increased	1 (0.6)	2 (1.0)
Gamma-glutamyltransferase increased	0	2 (1.0)
Hypokalaemia	1 (0.6)	2 (1.0)
Nausea	2 (1.2)	0
Diarrhoea	1 (0.6)	5 (2.6)
Infusion related reaction	3 (1.7)	0
Patients with ≥1 SAE, n (%)	92 (53.2)	95 (49.7)
Patients with ≥1 treatment-related SAE, (n (%)	3 (1.7)	5 (2.6)
Atrioventricular block first degree	1 (0.6)	0
Ventricular tachycardia	0	1 (0.5)
Infusion related reaction	1 (0.6)	0
Urticaria	1 (0.6)	0
Hypertransaminasaemia	0	1 (0.5)
Liver injury	0	1 (0.5)
Rectal haemorrhage	0	1(0.5)
Anaphylactic shock	0	1 (0.5)

Safety population: all patients in the STRIVE/ReSTORE trials (plus China extended phase) who received ≥1 dose of study drug. Abbreviations: SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSION

- Subanalysis of pooled data from the STRIVE and ReSTORE trials (including the extension phase in China) showed that adults with C/IC treated with rezafungin and caspofungin demonstrated varying rates of Day 30 ACM according to baseline NAC species.
- Mycological response rates were high with both echinocandins from Day 5, although rezafungin recipients achieved numerically higher rates for *C. parapsilosis*, *C. glabrata* and *C. tropicalis* compared with caspofungin.
- Safety outcomes were similar across groups.

References

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Disclosures

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