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All-cause and attributable mortality in invasive candidiasis and/or candidaemia with rezafungin and caspofungin treatment: outcomes from the ReSTORE trial

06. Fungal infection & disease

6d. Antifungal drugs & treatment (incl. clinical trials)

Likely attendance

Onsite

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Background

ReSTORE (NCT03667690) was a global, randomised, double-blind, double-dummy, Phase 3 non-inferiority trial, evaluating the efficacy and safety of rezafungin and caspofungin in the treatment of candidaemia and/or invasive candidiasis (C/IC) (1).

Methods

The current analysis examined all-cause mortality (ACM) and therapeutic step-down data from the ReSTORE trial. Adults diagnosed with C/IC (by systemic manifestations and mycological confirmation) were randomised to receive rezafungin once-weekly intravenous (IV) infusion (Week 1: 400 mg; Weeks 2–4: 200 mg) or once daily caspofungin (Day 1: 70 mg; Days 2–28: 50 mg) for ≥14 days (≤4 weeks). Oral step-down treatment (caspofungin arm: fluconazole; rezafungin arm: placebo), was allowed from Day 4 for subjects with resolved/stable signs and symptoms of C/IC and negative blood cultures. The analysis examined Day 30 (-2 days) ACM (20% non-inferiority margin) in the modified intention-to-treat (mITT) population (randomised subjects receiving ≥1 study drug dose). Deaths attributable to C/IC (independent data review committee assessment) through Day 59,

duration of treatment exposure and the proportion receiving step-down therapy were also reported.

Results

The analysis included 93 subjects in the rezafungin arm and 94 in the caspofungin arm (mITT population; Table 1). Day 30 ACM rate was 23.7% (rezafungin arm) and 21.3% (caspofungin arm; Figure 1). Through Day 59, 5 (5.4%) deaths were attributable to C/IC in the rezafungin arm and 7 (7.4%) in the caspofungin arm. Median duration of IV therapy exposure was 14 days in both arms. A switch to oral therapy was implemented for 25.8% (24/93) of the rezafungin arm and 36.2% (34/94) of the caspofungin arm. Overall, 83.4% (20/24; rezafungin arm) and 61.8% (21/34; caspofungin arm) of patients receiving oral step-down treatment met the criteria for step down by Day 7–9.

Conclusions

Rezafungin treatment demonstrated non-inferiority, versus caspofungin, concerning Day 30 ACM. Mortality due to C/IC was low in both treatment groups during the study period. Median duration of IV therapy was similar in both arms, with >25% of patients meeting oral step-down criteria in each treatment group.

Table 1

Table 1. Baseline demographics and characteristics from the ReSTORE trial (mITT population)

	Rezafungin (400/200 mg) (N=93)	Caspofungin (70/50 mg) (N=94)
Age, mean ± SD (range), years	59.5 ± 15.8 (19–89)	61.9 ± 14.6 (20–91)
Age <65 years, n (%)	55 (59.1)	56 (59.6)
Age ≥65 years, n (%)	38 (40.9)	38 (40.4)
Sex, n (%)		
Male	62 (66.7)	56 (59.6)
Female	31 (33.3)	38 (40.4)
Race, n (%)		
Asian	23 (24.7)	31 (33.0)
Black or African American	5 (5.4)	4 (4.3)
White	59 (63.4)	55 (58.5)
Other/not reported	1 (1.1)	1 (1.1)
Final diagnosis		
Candidaemia-only, n (%)	64 (68.8)	67 (71.3)
Invasive candidiasis, n (%)[a]	29 (31.2)	27 (28.7)
Modified APACHE II score[b]		
Mean ± SD	12.3 ± 7.54	13.0 ± 7.18
≥20, n (%)	12 (12.9)	17 (18.21)
<20, n (%)	80 (86.0)	77 (81.9)
Mean BMI, kg/m^2 ± SD	25.5 ± 7.19	24.3 ± 6.64
ANC <500/µL, n (%)	7 (7.5)	5 (5.3)
Mechanically ventilated at baseline, n (%)	16 (17.2)	28 (29.8)

The mITT population included all subjects who had a documented *Candida* infection based on central laboratory evaluation of a blood culture or a culture from a normally sterile site obtained ≤4 days (96 hours) before randomisation and received ≥1 dose of study drug.

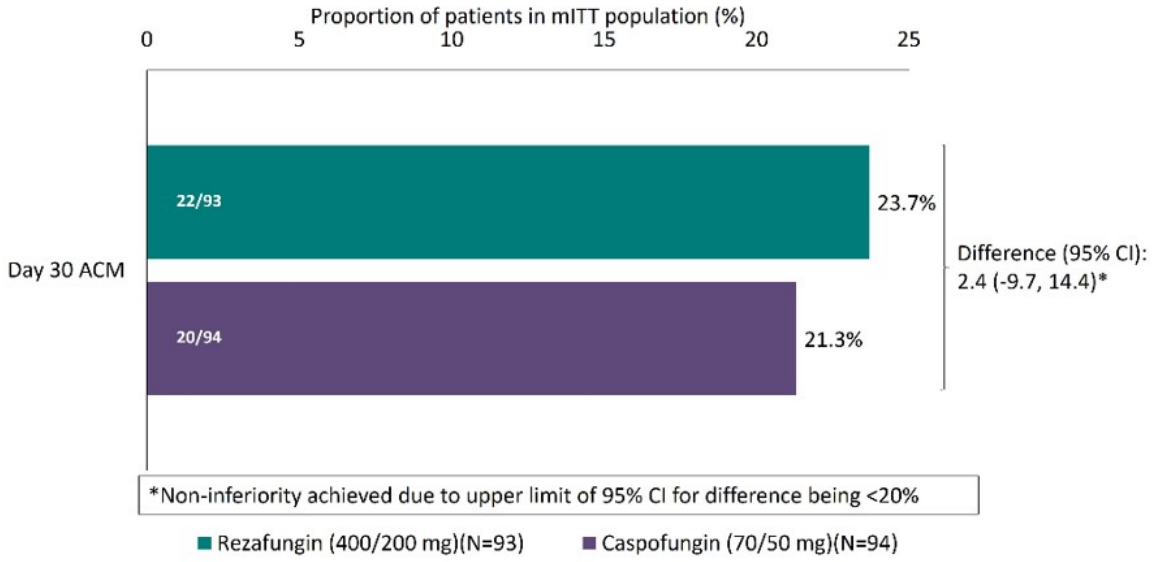
[a]Includes patients who progressed from candidaemia to invasive candidiasis based on radiological and/or tissue/fluid culture assessment through Day 14.

[b]Reported for patients with APACHE II score data available.

Abbreviations: ANC, absolute neutrophil count; APACHE, acute physiology and chronic health evaluation; BMI, body mass index; mITT, modified intention-to-treat; SD, standard deviation.

Figure 1

Figure 1. Day 30 all-cause mortality in the mITT population (US FDA primary endpoint)



All analyses were conducted using the mITT, comprising all subjects diagnosed with candidaemia/invasive candidiasis (based on systemic signs and mycological confirmation) who received ≥1 dose of study drug.
N = total number of subjects in the corresponding treatment group.
Abbreviations: ACM, all-cause mortality; CI, confidence interval; mITT, modified intention-to-treat; US FDA, United States Food and Drug Administration.

Keyword 1
Clinical trials
Keyword 2
Fungi and clinical mycology
Keyword 3
Rezafungin
References, word count: 30 words
1. Thompson GR, et al. Rezafungin versus caspofungin for treatment of candidaemia and invasive candidiasis (ReSTORE): a multicentre, double-blind, double-dummy, randomised phase 3 trial. Lancet. 2022 Nov 25:S0140-6736(22)02324-8.
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Conflicts of interest

Do you have any conflicts of interest to declare?
Yes
Honoraria or consultation fees
Personal grants/research supports
Institutional grants/research supports
I hold stock or stock options in companies in the medical field