# Treatment outcomes with rezafungin and caspofungin in people aged 65 years and above with candidaemia and/or invasive candidiasis: Integrated analysis of pooled Phase 2 and Phase 3 data

ePoster

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## INTRODUCTION AND OBJECTIVES

- Factors including frailty and multimorbidity can affect candidaemia and/or invasive candidiasis treatment in older people.[1]
- The current analysis explored data from candidaemia and/or invasive candidiasis patients aged ≥65 years who were treated with the novel, once-weekly echinocandin, rezafungin, or caspofungin in the STRIVE (Phase 2: NCT02734862) and ReSTORE (Phase 3: NCT03667690) clinical trials.[2,3]

## METHODS

- STRIVE was a Phase 2, randomised, double-blind, double-dummy trial conducted in 44 centres across 10 countries. ReSTORE comprised a randomised, double-blind, double-dummy, Phase 3 non-inferiority trial, conducted at 66 centres across 15 countries.
- In both studies, adults with candidaemia and/or invasive candidiasis, diagnosed by systemic signs and mycological confirmation, received rezafungin once-weekly (Week 1: 400 mg; Weeks 2–4: 200 mg) or once daily caspofungin (Day 1: 70 mg; Days 2–28: 50 mg) by intravenous injection for ≥14 days (≤4 weeks).
- Post hoc analysis examined pooled STRIVE/ReSTORE data for subjects aged ≥65 years.
- Day 30 all-cause mortality (ACM) and mycological response at Days 5 and 14 were examined for the modified intention-to-treat (mITT) population, comprising subjects with mycological candidaemia and/or invasive candidiasis diagnosis within 96 hours of randomisation who received ≥1 study drug dose.
- Safety outcomes included treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) in subjects who received ≥1 dose of study drug (safety population).

## RESULTS

### Study populations (aged ≥65 years)

- The mITT population included 120 patients: 57 subjects in the rezafungin treatment arm and 63 in the caspofungin arm. The safety population included 132 subjects: 64 patients in the rezafungin treatment arm and 68 in the caspofungin arm.
- Baseline demographic and characteristic data are shown in Table 1 for subjects in the mITT population (aged ≥65 years), along with the *Candida* species identified at baseline. The treatment arms were generally well balanced. The majority of each treatment group was male (68.4% rezafungin arm; 60.3% caspofungin arm) and diagnosed with candidaemia (75.4% rezafungin arm; 74.6% caspofungin arm). The most common *Candida* species identified at baseline were *C. albicans*, *C. glabrata*, *C. tropicalis and C. Parapsilosis* complex.

### Table 1. Baseline demographics and characteristics for subjects aged ≥65 years included in the pooled analysis of STRIVE (Phase 2) and ReSTORE (Phase 3) study data (mITT population)

| | Rezafungin (400/200 mg) (N=57) | Caspofungin (70/50 mg) (N=63) |
|---|---|---|
| Age, mean ± SD (range), years | 74.9 ± 7.23 (65–91) | 74.7 ± 6.71 (65–93) |
| Gender, n (%) | | |
| Male | 39 (68.4) | 38 (60.3) |
| Female | 18 (31.6) | 25 (39.7) |
| Race, n (%) | | |
| Black or African American | 2 (3.6) | 1 (1.6) |
| Asian | 9 (16.4) | 13 (20.6) |
| White | 43 (78.2) | 49 (77.8) |
| Other/not reported | 3 (5.2) | 0 |
| Final diagnosis, n (%) | | |
| Candidaemia | 43 (75.4) | 47 (74.6) |
| Invasive candidiasis[a] | 14 (24.6) | 16 (25.4) |
| Modified APACHE II score[b] | | |
| ≥20, n (%) | 8 (14.0) | 15 (23.8) |
| <20, n (%) | 49 (86.0) | 48 (76.2) |
| *Candida species* | | |
| *Candida albicans* | 28 (49.1) | 31 (49.2) |
| *Candida glabrata* | 16 (28.1) | 13 (20.6) |
| *Candida kefyr* | 0 | 1 (1.6) |
| *Candida krusei* | 2 (3.5) | 2 (3.2) |
| *Candida metapsilosis* | 1 (1.8) | 0 |
| *Candida parapsilosis* complex | 6 (10.5) | 10 (15.9) |
| *Candida tropicalis* | 9 (15.8) | 8 (12.7) |

[a]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.
The mITT population used in the current analysis included all subjects included in the STRIVE and ReSTORE trials (aged ≥65 years) with a mycological diagnosis of candidaemia and/or invasive candidiasis within 96 hours of randomisation who received ≥1 dose of study drug.
Abbreviations: APACHE, acute physiology and chronic health evaluation; SD, standard deviation.

### ACM and mycological response in patients aged ≥65 years (mITT population)

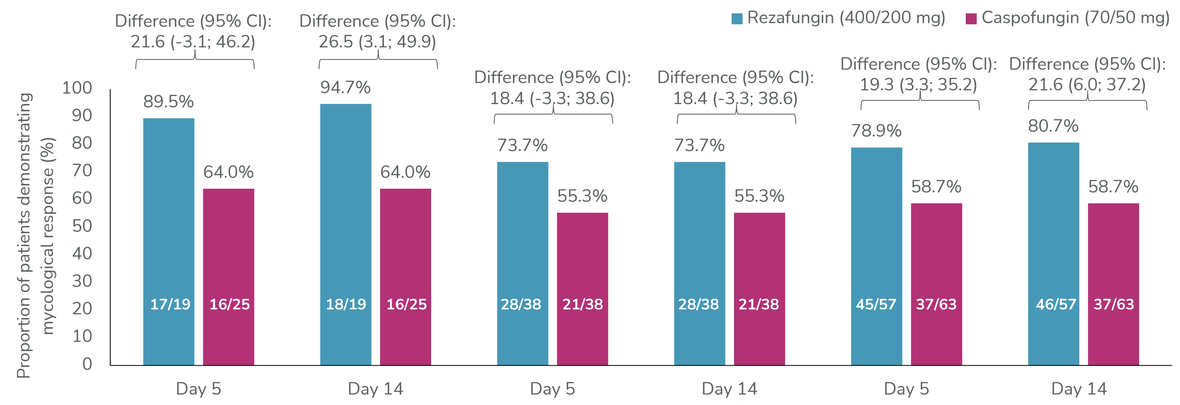
- Day 30 ACM rate was 14.0% (rezafungin arm) and 31.7% (caspofungin arm). The between-group difference (95% confidence interval [CI]) for Day 30 ACM was -17.6 (-32.5; -2.8).
- Day 5 mycological response was 78.9% (rezafungin arm) and 58.7% (caspofungin arm). The between-group difference (95% CI) at Day 5 was 19.3 (3.3; 35.2; Figure 1). Day 14 mycological response was 80.7% (rezafungin arm) and 58.7% (caspofungin arm). The between-group difference (95% CI) at Day 14 was 21.6 (6.0; 37.2).

### Time to negative blood culture (mITT population)

- Median time to negative blood culture was 20.5 hours (rezafungin arm) and 26.8 hours (caspofungin arm). The between group difference was statistically significant (*P*=0.006; Log Rank Test). Overall, 68.9% (rezafungin arm) and 47.8% (caspofungin arm) had negative blood cultures at 24 hours, while 82.2% (rezafungin arm) and 58.7% (caspofungin arm) had negative cultures at 48 hours.

## RESULTS (CONTINUED)

### Figure 1. Mycological response at Days 5 and 14 in candidaemia/invasive candidiasis patients aged ≥65 years: STRIVE, ReSTORE and pooled analysis (mITT population)




All analyses were conducted using the mITT population, which included all subjects with a mycological diagnosis of candidaemia and/or invasive candidiasis within 96 hours of randomisation who received ≥1 dose of study drug.
Abbreviations: CI, confidence interval; mITT, modified intention to treat.

### Pooled STRIVE/ReSTORE trial safety data for candidaemia/invasive candidiasis patients aged ≥65 years (safety population)

- The most common TEAEs with rezafungin were hypokalaemia, diarrhoea, vomiting and anaemia (Table 2). Eight subjects reported rezafungin-related TEAEs and 7 had caspofungin-related TEAEs. SAEs comprised one case each of first-degree atrioventricular block (rezafungin arm) and acute liver injury (caspofungin arm).

### Table 2. Pooled STRIVE/ReSTORE trial safety data for candidaemia/invasive candidiasis patients aged ≥65 years treated with rezafungin (400 mg/200 mg) or caspofungin (70 mg/50 mg; safety population)

| System Organ Class<br>Preferred Term | Rezafungin (400/200 mg) (N=64) | Caspofungin (70/50 mg) (N=68) |
|---|---|---|
| Subjects with ≥1 TEAE, n (%) | 59 (92.2) | 62 (91.2) |
| Subjects with TEAEs leading to study discontinuation, n (%) | 7 (10.9) | 19 (27.9) |
| TEAEs affecting ≥10% of safety population, n (%) | | |
| Blood and lymphatic system disorders | | |
| Anaemia | 7 (10.9) | 5 (7.4) |
| Gastrointestinal disorders | | |
| Diarrhoea | 10 (15.6) | 9 (13.2) |
| Vomiting | 8 (12.5) | 2 (2.9) |
| Metabolism and nutrition disorders | | |
| Hypokalaemia | 11 (17.2) | 7 (10.3) |
| Infections and infestations | | |
| Septic shock | 6 (9.4) | 8 (11.8) |
| Renal and urinary disorders | | |
| Acute kidney injury | 4 (6.3) | 8 (11.8) |
| Urinary tract infection | 1 (1.6) | 7 (10.3) |
| Subjects with ≥1 drug-related TEAE, n (%) | 8 (12.5) | 7 (10.3) |
| Cardiac disorders | | |
| Atrioventricular block (first degree) | 1 (1.6) | 0 |
| Gastrointestinal disorders | | |
| Diarrhoea | 1 (1.6) | 1 (1.5) |
| Administration site conditions | | |
| Catheter site discolouration | 0 | 1 (1.5) |
| Hepatobiliary disorders | | |
| Hepatocellular injury | 0 | 1 (1.5) |
| Hyperbilirubinemia | 1 (1.6) | 0 |
| Liver injury | 0 | 1 (1.5) |
| Infections and infestations | | |
| Sepsis | 1 (1.6) | 0 |
| Investigations | | |
| Blood bilirubin increased | 1 (1.6) | 0 |
| Electrocardiogram QT prolonged | 1 (1.6) | 1 (1.5) |
| Eosinophil count increased | 1 (1.6) | 0 |
| Hepatic enzyme increased | 1 (1.6) | 1 (1.5) |
| Metabolism and nutrition disorders | | |
| Hyponatraemia | 1 (1.6) | 0 |
| Nervous system disorders | | |
| Co-ordination abnormal | 0 | 1 (1.5) |
| Headache | 0 | 1 (1.5) |
| Nystagmus | 0 | 1 (1.5) |
| Tremor | 1 (1.6) | 0 |
| Subjects with ≥1 SAE, n (%) | 37 (57.8) | 38 (55.9) |
| Subjects with ≥1 drug-related SAE, n (%) | 1 (1.6) | 1 (1.5) |

The safety population included all subjects who had received ≥1 dose of study drug.
Abbreviations: SAE, serious adverse event; TEAE, treatment-emergent adverse event.

## CONCLUSION

- Subanalysis of ReSTORE study data for patients aged ≥65 years showed comparable efficacy with rezafungin and caspofungin therapy. Early outcomes of mycological response at Day 5 and time to negative blood culture were improved with rezafungin, suggesting a potential clinical effect associated with the front-loaded dosing.
- Incidence of drug-related TEAE and SAEs were similar between groups, indicating no impact of the front-loaded dose on safety outcomes for this specific and potentially frail patient population.
- Further analysis is required to understand underlying factors that may impact treatment outcomes.

**Disclosures**

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