Early outcomes and intensive care unit length of stay with rezafungin once-weekly echinocandin in invasive *Candida* disease

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INTRODUCTION/BACKGROUND

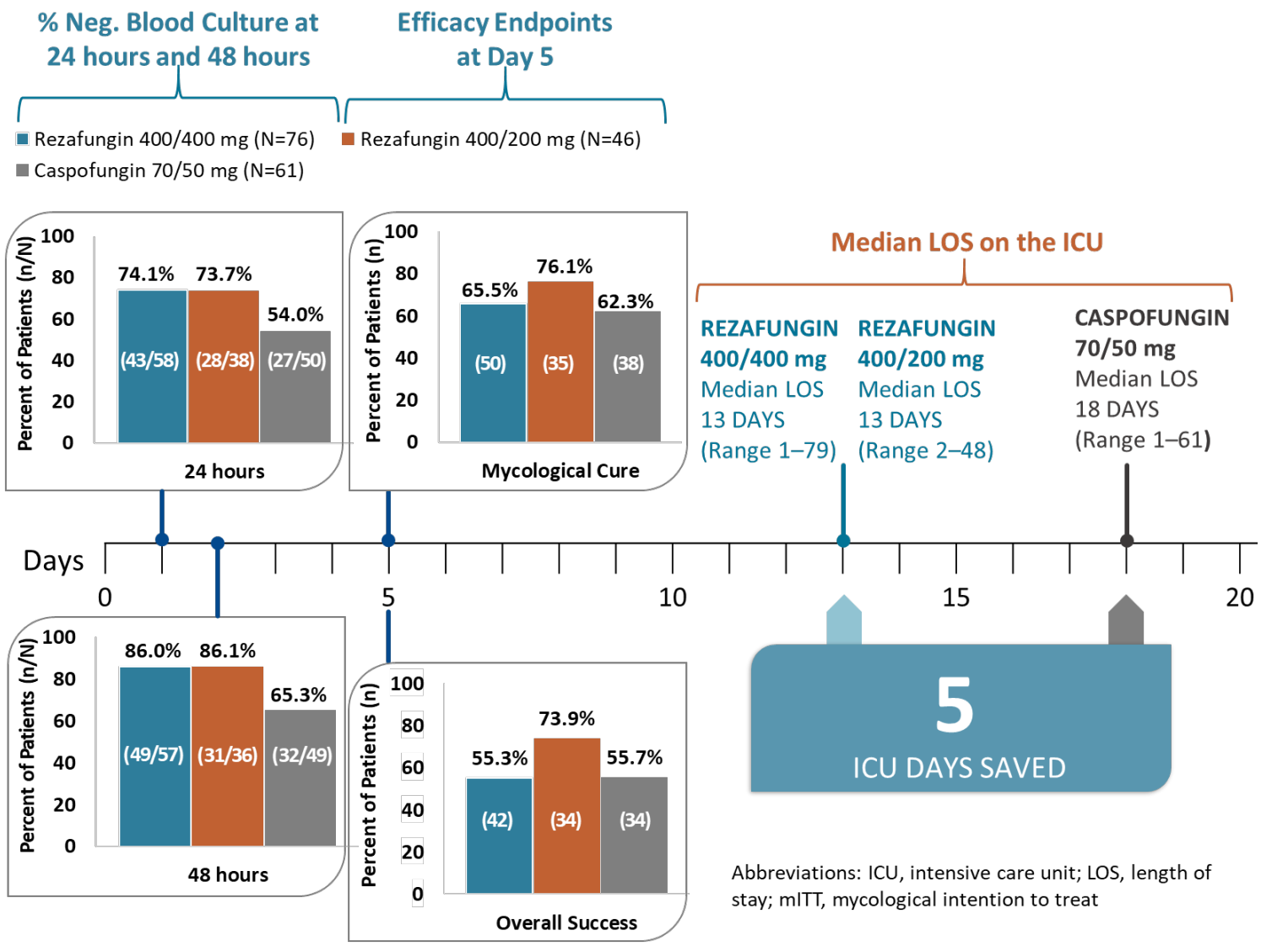
Rezafungin is a next generation, once-weekly echinocandin demonstrating a prolonged half-life (~133 hours) and high front-loaded plasma exposures.[1,2] The STRIVE trial was a Phase 2, double-blind, randomized study, which examined the efficacy and safety of once-weekly rezafungin intravenous (IV) infusion, compared with caspofungin once daily, in the treatment of candidaemia and invasive candidiasis (IC).[3] Early outcomes with *Candida* infection and the current analysis presents early treatment outcomes and length of stay (LOS) in the intensive care unit (ICU) for patients enrolled on the STRIVE trial.[4]

METHODS

Adults (≥18 years) with candidaemia and/or IC were randomised to receive rezafungin 400/400 mg (400 mg once weekly), rezafungin 400/200 mg (Week 1: 400 mg; 200 mg once-weekly thereafter), or caspofungin (Day 1:70 mg; 50 mg daily thereafter) for ≤4 weeks. The treatment groups were balanced concerning Acute Physiology and Chronic Health Evaluation (APACHE) II scores and the number of candidaemia and IC cases. Day 5 overall cure and mycological success rates were evaluated. The study was not powered for statistical analysis. Post-hoc analysis examined time to negative blood culture, blood culture clearance at 24 and 48 hours, and ICU LOS data (based on discharge from ICU excluding discharge due to death).

RESULTS

FIGURE 1. NEGATIVE BLOOD CULTURE DATA, DAY 5 EFFICACY OUTCOMES AND MEDIAN LOS ON THE ICU (mITT POPULATION)



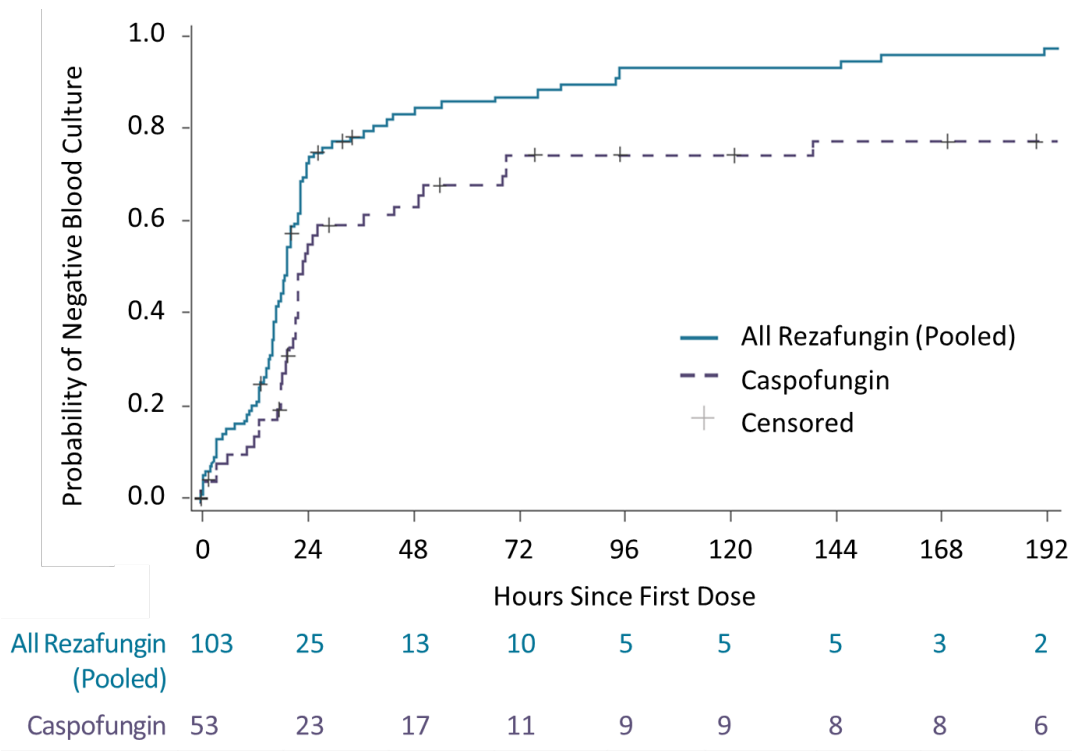
Abbreviations: ICU, intensive care unit; LOS, length of stay; mITT, mycological intention to treat

Numerical differences were shown between rezafungin and caspofungin treatment groups regarding the percentage of patients with negative blood cultures at both 24 and 48 hours and those demonstrating mycological cure and overall success at Day 5 (Figure 1).

At study enrolment, 44% (80/183) of subjects were in the ICU, with a further 6% (11/183) admitted during the trial. Median LOS (range) on the ICU was 13 (1–79), 13 (2–48) and 18.0 (1–61) days for those in the rezafungin 400/400 mg, rezafungin 400/200 mg and caspofungin groups, respectively (Figure 1). LOS on the ICU was therefore, on average, approximately 5 days shorter for those treated with rezafungin, compared with patients receiving caspofungin therapy.

Post-hoc analysis for pooled data for the rezafungin groups versus the caspofungin group showed a significant difference in the time to negative blood culture (p=0.0016 post-hoc log-rank test; Figure 2). In addition, of those with a central venous catheter fitted at screening, 33.3% (17/51), 35.7% (10/28) and 38.6% (17/44) underwent catheter removal within 48 hours in the rezafungin 400/400 mg, rezafungin 400/200 mg and caspofungin groups, respectively.

FIGURE 2. TIME TO NEGATIVE BLOOD CULTURE (mITT POPULATION)



Overall in the STRIVE trial, the most common treatment-emergent adverse events (TEAEs) in the rezafungin and caspofungin groups were hypokalaemia, diarrhoea, and vomiting (Table 1). No concerning safety trends were observed with rezafungin treatment.

TABLE 1. TREATMENT-EMERGENT ADVERSE EVENTS (≥10%, SAFETY POPULATION)

	Rezafungin 400 mg/400 mg Weekly N=81	Rezafungin 400 mg/200 mg Weekly N=53	Rezafungin (Pooled) N=134	Caspofungin 70 mg/50 mg Daily N=68
Treatment-emergent Adverse Event, n (%)				
Hypokalaemia	13 (16.0)	9 (17.0)	22 (16.4)	9 (13.2)
Diarrhoea	7 (8.6)	11 (20.8)	18 (13.4)	10 (14.7)
Vomiting	6 (7.4)	8 (15.1)	14 (10.4)	5 (7.4)
Pyrexia	9 (11.1)	4 (7.5)	13 (9.7)	6 (8.8)
Anaemia	6 (7.4)	7 (13.2)	13 (9.7)	4 (5.9)
Nausea	4 (4.9)	8 (15.1)	12 (9.0)	6 (8.8)
Abdominal Pain	5 (6.2)	6 (11.3)	11 (8.2)	5 (7.4)
Septic Shock	9 (11.1)	1 (1.9)	10 (7.5)	3 (4.4)

CONCLUSIONS

Early treatment efficacy was demonstrated with rezafungin by the outcomes of negative blood culture at 24 and 48 hours and Day 5 overall response rate. A shorter ICU median LOS was also observed in the rezafungin groups, compared with the caspofungin group. The efficacy shown early in the rezafungin treatment course support the high front-loaded plasma exposure as a pharmacometric determinant in patients with candidemia or IC in the ICU.

References
1. Lakota E, et al. Agents Chemother. 2017;61(11):e00758-17; 2. Sandison T, et al. Antimicrob Agents Chemother. 2017;61(2):e01627-16; 3. Thompson GR, et al. Clin Infect Dis. 2020:ciaa1380,; 4. Kollef M, et al. Clin Infect Dis. 2012;54(12):1739-46.

Disclosures
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