E0053

Resolution of clinical signs in adults with invasive candidiasis and/or candidaemia treated with rezafungin or caspofungin: ReSTORE and STRIVE trial pooled analysis

George R Thompson III[1], Alex Soriano[2,3], Matteo Bassetti[4], Patrick M Honore[5], Jose Vazquez[6], Sara Dickerson[7], Oliver A. Cornely[8–10]

[1]University of California Davis Medical Center, Davis, CA, USA; [2]Clinic Hospital of Barcelona, Barcelona, Spain; [3]Carlos III Health Institute-CIBERINFEC, Madrid, Spain; [4]University of Genoa, Genoa, Italy; [5]CHU UCL Namur Godinne, UCL, Louvain Medical school of Medicine, Godinne, Belgium; [6]Augusta University, Augusta, Georgia, USA; [7]Mundipharma Research Limited, Cambridge, UK; [8]University Hospital Cologne, Department I of Internal Medicine, Excellence Center for Medical Mycology (ECMM), Cologne, Germany; [9]University of Cologne, Institute of Translational Research, Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), Cologne, Germany; [10]German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Cologne, Germany

INTRODUCTION AND OBJECTIVES

- Rezafungin is a next-generation, once-weekly echinocandin approved for use in candidaemia and invasive candidiasis treatment in the United States, European Union and United Kingdom.[1,2]
- Efficacy and safety outcomes with rezafungin have been evaluated in the setting of candidaemia and invasive candidiasis in two prospective, randomised clinical trials: STRIVE (Phase 2; NCT02734862) and ReSTORE (Phase 3 NCT03667690).[3,4]
- The current analysis examined pooled data from the STRIVE and ReSTORE trials to investigate resolution of clinical signs and symptoms in patients treated with rezafungin or caspofungin.[5]

METHODS

- STRIVE and ReSTORE were multicentre, double-blind, double-dummy, randomised, controlled trials.
- Adults with candidaemia and/or invasive candidiasis, diagnosed by systemic signs of active infection and mycological confirmation, 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 (up to 4 weeks). The study protocols allowed a step down to oral therapy for patients who met relevant criteria after ≥3 doses of IV therapy (placebo for rezafungin recipients and fluconazole for caspofungin-treated participants).
- The analysis reported pooled data for the modified intention-to-treat (mITT) population, comprising all patients included in the STRIVE and ReSTORE trials who received ≥1 dose of study drug and had documented *Candida* infection within 96 hours before randomisation.

Efficacy endpoints

- Resolution of systemic signs and symptoms at Days 5 and 14.
- Resolution of signs and symptoms during follow-up (Days 52–59).

Statistical analysis

- Two-sided 95% confidence intervals (CIs) were calculated for observed treatment differences using stratified Miettinen and Nurminen methodology. *P* values were determined using Fisher's Exact Test.

RESULTS

Study population

- The mITT population included 139 patients treated with rezafungin and 155 caspofungin recipients. Patient demographics and baseline characteristics were well balanced across groups (Table 1).
- The majority of participants were diagnosed with candidaemia only; 72% in the rezafungin group and 74% in the caspofungin arm.
- Modified APACHE II score was typically <20 in both groups (>80%).

Efficacy endpoints

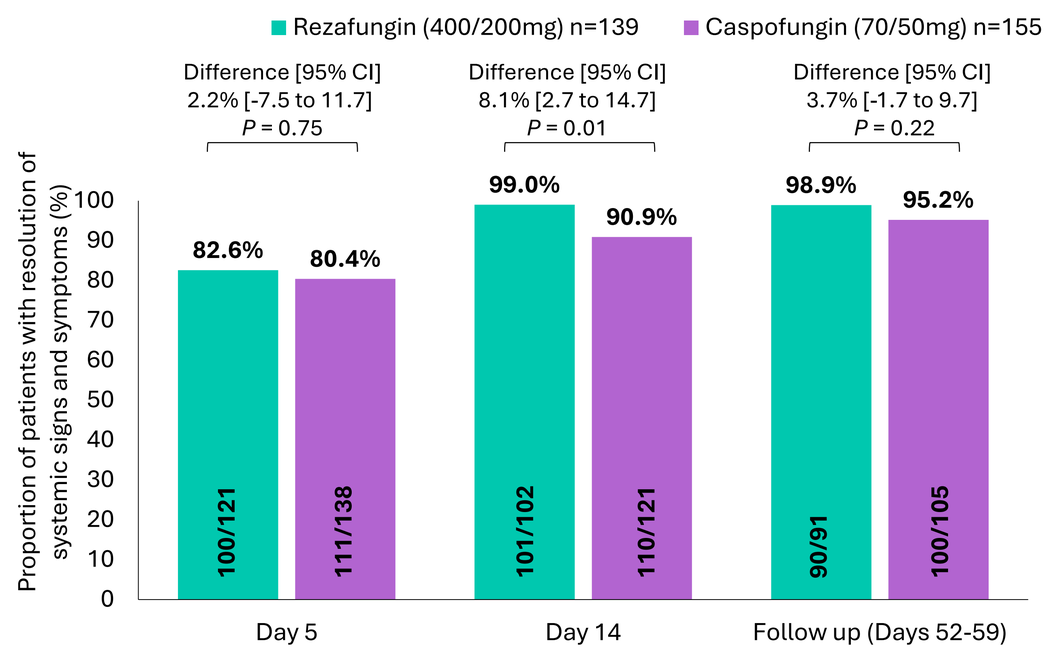
- The majority of participants in each group demonstrated resolution of systemic signs and symptoms from Day 5 through follow up (Figure 1):
  - Day 5: 82.6% (rezafungin) and 80.4% (caspofungin); treatment group difference [95% CI] 2.2% [-7.5 to 11.7] (*P* = 0.75)
  - Day 14: 99.0% (rezafungin) and 90.9% (caspofungin); treatment difference [95% CI] 8.1% [2.7 to 14.7] (*P* = 0.01)
  - Follow-up (Days 52–59): 98.9% (rezafungin) and 95.2% (caspofungin); treatment difference [95% CI] 3.7% [-1.7 to 9.7] (*P* = 0.22)

Table 1. Pooled ReSTORE and STRIVE trial data: baseline demographics and characteristics (modified mITT population)

	Rezafungin 400/200 mg (n=139)	Caspofungin 70/50 mg (n=155)
Age, years, median (IQR)	60 (49–71)	62 (52–71)
Gender, n (%)		
Male	90 (65)	90 (58)
Female	49 (35)	65 (42)
Race, n (%)		
White	95 (68)	106 (68)
Asian	24 (17)	34 (22)
Black/African American	11 (8)	8 (5)
American Indian or Alaska Native	1 (<1)	1 (<1)
Other	3 (2)	2 (1)
Not reported	5 (4)	4 (3)
Diagnosis*, n (%)		
Candidaemia only	100 (72)	115 (74)
Invasive candidiasis	39 (28)	40 (26)
Modified APACHE II score, n (%)		
≥20	21/137 (15)	26/152 (17)
<20	116/137 (84%)	126/152 (81%)

*For ReSTORE, determined based on the radiological or tissue culture assessment, or both, through Day 14; for STRIVE, the same as the baseline diagnosis. The mITT included all patients with a documented *Candida* infection within 96 hours before randomisation who received at least one dose of study drug.
Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; IQR, interquartile range; mITT, modified intention-to-treat.

Figure 1. Pooled ReSTORE (including extended phase from China) and STRIVE trial data: resolution of systemic signs and symptoms (mITT population)



Percentages were calculated as the number of subjects in whom all attributable systemic signs of candidaemia and/or invasive candidiasis present at screening had resolved, divided by the number of subjects with at least one attributable sign or symptom at screening and a non-missing systemic sign score at each visit.
The 95% CI was calculated using stratified (by study and, where applicable, study part) Miettinen and Nurminen methodology. *P* values were determined using Fisher's Exact Test.
Abbreviations: CI, confidence interval; mITT, modified intention-to-treat.

CONCLUSION

- Adults with candidaemia and/or invasive candidiasis included in the ReSTORE and STRIVE trials demonstrated high rates of resolution of systemic signs and symptoms by Day 5 with rezafungin and caspofungin treatment.
- The proportion of patients achieving resolution of systemic signs and symptoms at Day 14 was significantly greater with rezafungin compared with caspofungin.
- Resolution of signs and symptoms was maintained at a comparable rate throughout the follow-up (Days 52–59) in both groups.

References
1. Mundipharma GmbH. Rezzayo 200 mg. Summary of product characteristics. January 2024; 2. Melinta Therapeutics LLC. Rezzayo (rezafungin for injection), Prescribing information. March 2023; 3. Thompson GR, et al. Clin Infect Dis. 2021;73(11):e3647-e3655; 4. Thompson GR 3rd, et al. Lancet. 2023;401(10370):49-59; 5. Thompson GR 3rd, et al. Lancet Infect Dis. 2024;24(3):319-328.

Disclosures
George R Thompson III: Grants and consulting fees from Astellas, Cidara, F2G, Mayne, Mundipharma, and Scynexis; Alex Soriano: Fees for lectures and advisory boards from Pfizer, MSD, Shionogi, Novartis, Angelini and Gilead. Grants from Pfizer and Gilead; Matteo Bassetti: Honoraria from, and data safety monitoring board or advisory board membership for, Angelini, Astellas, Bayer, Biomerieux, Cidara, Gilead, Menarini, MSD, Nabriva, and Shionogi, outside of the submitted work; Oliver A. Cornely: Grants (paid to the University Hospital of Cologne) from BMBF, Cidara, DZIF, EU-DG RTD, F2G, Gilead, MedPace, MSD, Mundipharma, Octapharma, Pfizer, Scynexis; Consulting fees from Abbvie, AiCuris, Basilea, Biocon, Cidara, Seqirus, Gilead, GSK, IQVIA, Janssen, Matinas, MedPace, Menarini, Molecular Partners, MSG-ERC, Mundipharma, Noxxon, Octapharma, Pardes, Partner Therapeutics, Pfizer, PSI, Scynexis, Seres, Elion Therapeutics, Menarini, Melinta; Honoraria for lectures/presentations/speaker bureaus/educational activities from Abbott, Abbvie, Akademie für Infektionsmedizin, Al-Jazeera Pharmaceuticals/Hikma, amedes, AstraZeneca, Deutscher Ärzteverlag, Gilead, GSK, Grupo Biotoscana/ United Medical/Knight, Ipsen Pharma, Medscape/WebMD, MedUpdate, MSD, Moderna, Mundipharma, Noscendo, Paul-Martini-Stiftung, Pfizer, Sandoz, Seqirus, Shionogi, streamedup!, Touch Independent, Vitis; Expert testimony from Cidara; Data Safety Monitoring Board or Advisory Board from Boston Strategic Partners, Cidara, IQVIA, Janssen, MedPace, PSI, Pulmocide, Shionogi, The Prime Meridian Group, Vedanta Biosciences, AstraZeneca, Melinta; Sara Dickerson: Employee at Mundipharma Research Limited; Patrick M Honore: Grants or contracts from Baxter, Cytosorbents, and Pfizer; consulting fees from Baxter, Cytosorbents, and Pfizer; honoraria from Baxter, and Cytosorbents; and support for attending meetings from Mundipharma, and Pfizer, outside of the submitted work; Jose Vazquez: Speaker Bureau for Melinta; Consultant F2G, Scynexis. The study was funded by Mundipharma Research Limited.

April 2025