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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

06. Fungal infection & disease

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

Likely attendance

Onsite

Oliver A Cornely [1, 2, 3, 4], George R Thompson 3rd [5], Alex Soriano [6], Bart-Jan Kullberg [7], Marin Kollef [8], Jose Vazquez [9], Patrick M Honore [10], Matteo Bassetti [11], John Pullman [12], Cecilia Dignani [13], Anita F Das [14], Taylor Sandison [14], Peter G Pappas [15]

[1]University of Cologne, Faculty of Medicine and University Hospital Cologne, Department of Internal Medicine, Excellence Center for Medical Mycology (ECMM) - Cologne (Germany), [2]University of Cologne, Faculty of Medicine and University Hospital Cologne, Chair Translational Research, Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD) - Cologne (Germany), [3]University of Cologne, Faculty of Medicine and University Hospital Cologne, Clinical Trials Centre Cologne (ZKS Köln) - Cologne (Germany), [4]German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne - Cologne (Germany), [5]University of California Davis Medical Center - Sacramento, California (United States), [6]Hospital Clínic de Barcelona, IDIBAPS, University of Barcelona - Barcelona (Spain), [7]Radboud University Medical Center - Nijmegen (Netherlands), [8]Washington University - St. Louis, Missouri (United States), [9]Augusta University - Augusta, Georgia (United States), [10]Brugman University Hospital - Brussels (Belgium), [11]University of Genoa - Genoa (Italy), [12]Mercury Street Medical - Butte, Montana (United States), [13]PSI-CRO - Durham, North Carolina (United States), [14]Cidara Therapeutics, Inc. - San Diego, California (United States), [15]University of Alabama at Birmingham - Birmingham, Alabama (United States)

Background

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

Methods

STRIVE and ReSTORE were double-blind, randomised studies. Adults with C/IC, 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. Safety outcomes included treatment-

emergent adverse events (TEAEs) and serious adverse events (SAEs) in subjects who received ≥1 dose of study drug (safety population). Day 30 all-cause mortality (ACM) and mycological response at Days 5 and 14 were examined for the modified intention-to-treat (mITT) population (subjects with mycological C/IC diagnosis within 96 hours of randomisation who received ≥1 study drug dose).

Results

The safety population included 132 subjects (rezafungin arm: 64; caspofungin arm: 68). The mITT population included 120 subjects (rezafungin arm: 57; caspofungin arm: 63). The most common TEAEs with rezafungin were hypokalaemia, diarrhoea, vomiting and anaemia (Table 1). 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). Day 30 ACM rate was 14.0% (rezafungin arm) and 31.7% (caspofungin arm). The between-group difference (95% confidence interval [CI]) was -17.6 (-32.5, -2.8). Day 5 mycological response was 78.9% (rezafungin arm) and 58.7% (caspofungin arm; difference [95% CI]: 19.3 [3.3, 35.2]; Figure 1).

Conclusions

Integrated analysis of pooled STRIVE/ReSTORE study data revealed similar incidence of drug-related TEAEs and SAEs in patients aged ≥65 years treated with rezafungin or caspofungin. Further analyses are required to understand underlying factors influencing between-group differences regarding treatment outcomes.

Table 1

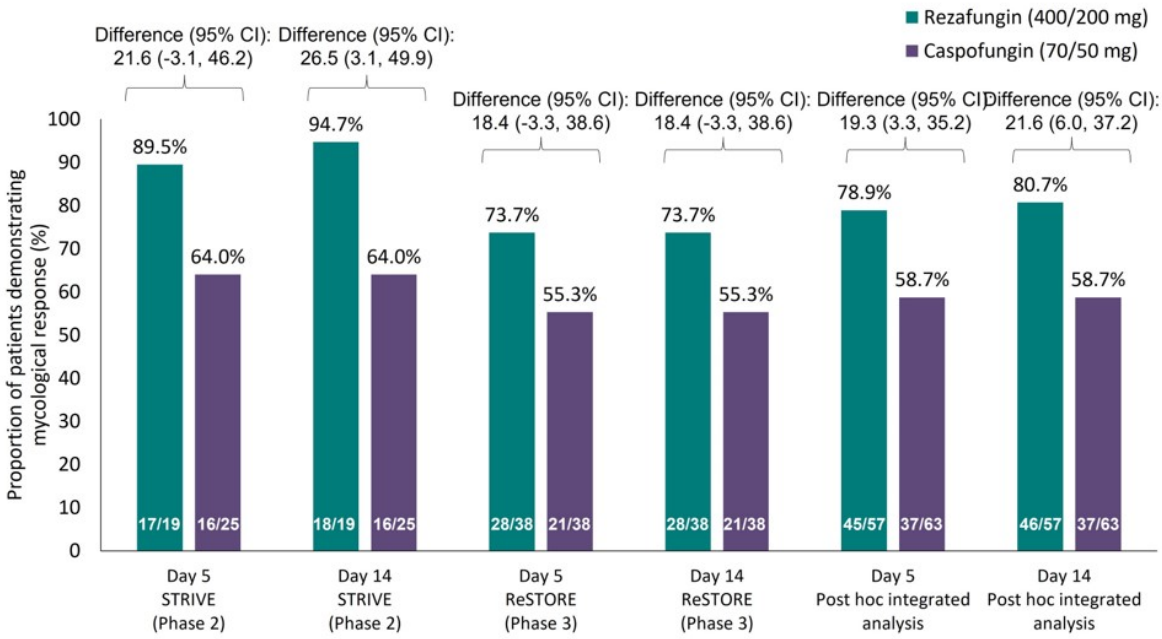
Table 1. Safety data for candidaemia/invasive candidiasis patients aged ≥65 years treated with rezafungin (400 mg/200 mg) or caspofungin (70 mg/50 mg) (safety population)

	Rezafungin (400/200 mg) (N=64)	Caspofungin (70/50 mg) (N=68)
Subjects with at least 1 TEAE, n (%)	59 (92.2)	62 (91.2)
Subjects with TEAEs leading to study discontinuation, n (%)	7 (10.9)	19 (27.9)
Subjects with at least 1 drug-related TEAE, n (%)	8 (12.5)	7 (10.3)
Subjects with at least 1 SAE, n (%)	37 (57.8)	38 (55.9)
Subjects with at least 1 drug-related SAE, n (%)	1 (1.6)	1 (1.6)
TEAEs affecting at least 10% of safety population		
Hypokalaemia	11 (17.2)	7 (10.3)
Diarrhoea	10 (15.6)	9 (13.2)
Vomiting	8 (12.5)	2 (2.9)
Anaemia	7 (10.9)	5 (7.4)
Septic shock	6 (9.4)	8 (11.8)
Acute kidney injury	4 (6.3)	8 (11.8)
Urinary tract infection	1 (1.6)	7 (10.3)

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

Figure 1

Figure 1. Analysis regarding mycological response at Days 5 and 14 in candidaemia/invasive candidiasis patients aged ≥65 years included in the STRIVE (Phase 2) and ReSTORE (Phase 3) clinical trials and integrated analysis of STRIVE/ReSTORE data (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.

Keyword 1
Clinical trials
Keyword 2
Fungi and clinical mycology
Keyword 3
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References, word count: 30 words

1. Dekkers BGJ, et al. Drugs Aging. 2018;35(9):781–789. 2. Thompson GR, et al. Clin Infect Dis. 2020 :ciaa1380. 3. Thompson GR, et al. Lancet. 2022 Nov 25:S0140-6736(22)02324-8.

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ReSTORE trial: co-funded by Cidara Therapeutics and Mundipharma. STRIVE study: Cidara Therapeutics were involved in trial design, execution, and data analysis. Cidara Therapeutics and Mundipharma were involved in trial reporting.

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