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Safety outcomes with rezafungin and caspofungin in the treatment of candidaemia and/or invasive candidiasis: Phase 3 data from the ReSTORE trial

06. Fungal infection & disease

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

Likely attendance

Onsite

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Background

The current analysis reports safety data from the ReSTORE trial (NCT03667690), examining treatment outcomes with rezafungin or caspofungin in people with candidaemia/invasive candidiasis (C/IC) (1).

Methods

ReSTORE comprised a global, randomised, double-blind, double-dummy, Phase 3 non-inferiority trial. Adults with C/IC, diagnosed by systemic manifestations and mycological confirmation, were randomised to receive intravenous (IV) once-weekly rezafungin (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). Vital signs data were collected throughout the study. Safety outcomes included reporting of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs). The analysis examined the safety population (all participants who received ≥1 dose of study drug).

Results

The safety population included 98 patients in each treatment arm. During the study period, 29.2% (rezafungin arm) and 26.3% (caspofungin arm) demonstrated reductions in systolic blood pressure ≥20 mmHg to a value of ≤90 mmHg. Heart rate was raised by ≥15 bpm to a value ≥120 bpm for 24.0% (rezafungin arm) and 26.0% (caspofungin arm). QTcF values increased by ≥30 msec in 12.0% (rezafungin arm) and 17.5% (caspofungin arm). Sixteen subjects reported treatment-related TEAEs with rezafungin (including 5 related to IV saline/placebo administration) and 9 with caspofungin (Table 1). Early treatment-related TEAEs occurred within the first 4 days (Figure 1). Adverse events (AEs) of special interest included Grade 1 tremors (2 rezafungin-treated subjects), which were resolved. Grade 2 peripheral neuropathy (1 subject) and polyneuropathy (1 subject) were reported in the caspofungin group. Both remained unresolved during the study period. Treatment-related SAEs included reactions related to IV placebo infusion (rezafungin arm; considered an AE of special interest) and anaphylactic shock (caspofungin arm).

Conclusions

Safety outcomes from the ReSTORE trial indicated that rezafungin had a similar safety profile to caspofungin and did not have any additional impact on safety outcomes. Treatment-related TEAEs and SAEs were uncommon in both treatment groups and changes relating to vital signs were similar across groups.

Table 1

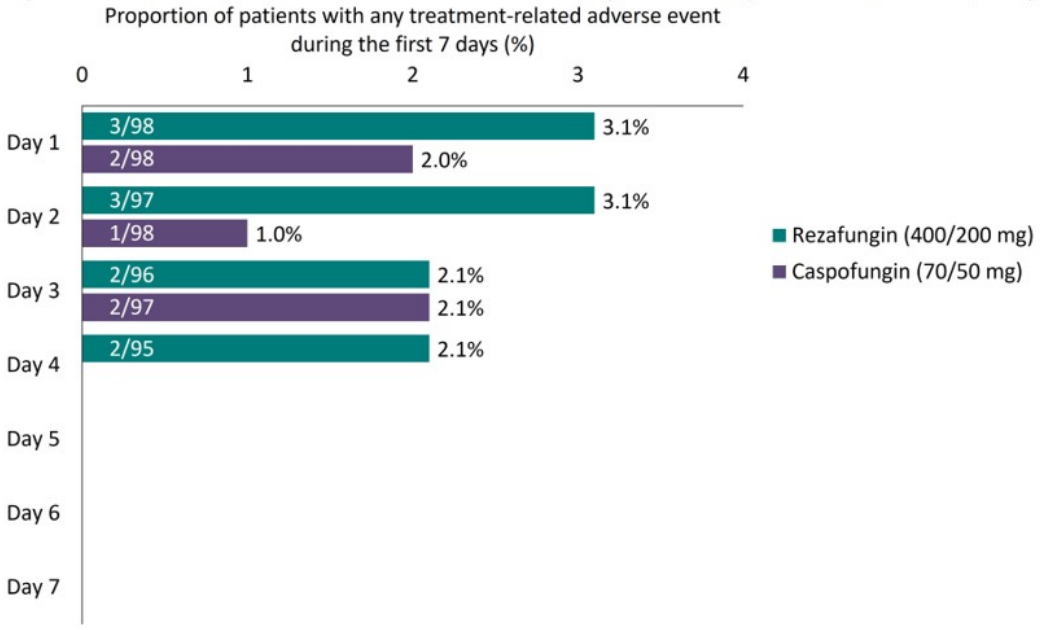
Table 1. ReSTORE trial treatment-related safety data (safety population)

	Rezafungin (400/200 mg) (N=98)	Caspofungin (70/50 mg) (N=98)
Subjects with ≥1 drug-related TEAE, n (%)*	16 (16.3)	9 (9.2)
TEAEs affecting ≥10% of Safety Population (preferred term)		
Pyrexia	14 (14.3)	5 (5.1)
Hypokalaemia	13 (13.3)	9 (9.2)
Pneumonia	10 (10.2)	3 (3.1)
Septic shock	10 (10.2)	9 (9.2)
Subjects with ≥1 SAE, n (%)	55 (56.1)	52 (53.1)
Subjects with ≥1 drug-related SAEs (preferred term), n (%)	2 (2.0)	3 (3.1)
Infusion-related reaction†	1 (1.0)	0
Urticaria	1 (1.0)	0
Elevated transaminase levels	0	1 (1.0)
Liver injury	0	1 (1.0)
Anaphylactic shock	0	1 (1.0)
Subjects with AEs of special interest (preferred term), n (%)	6 (6.1)	3 (3.1)
Adverse drug reaction	1 (1.0)	0
Hypersensitivity reaction†	1 (1.0)	0
Anaphylactic shock	0	1 (1.0)
Infusion-related reaction†	3 (3.1)	0
Tremor	2 (2.0)	0
Peripheral neuropathy	0	1 (1.0)
Polyneuropathy	0	1 (1.0)

The safety population included all subjects who had received ≥1 dose of study drug.
*Further investigation revealed that 5 TEAEs believed to be related to rezafungin treatment were associated with the IV saline placebo (for rezafungin) administration.
†Two of the four infusion-related reactions observed in the rezafungin group (including the one drug-related SAE) were determined to have occurred in subjects receiving placebo infusions.
Abbreviations: AEs, adverse events; IV, intravenous; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Figure 1

Figure 1. Incidence of treatment-related adverse events during the first 7 days in the ReSTORE trial (safety population)



The safety population included all subjects who had received ≥1 dose of study drug.

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1. Thompson GR, et al. Rezafungin versus caspofungin for treatment of candidaemia and invasive candidia-sis (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