Poster #P38

Rezafungin Efficacy and Safety in Immunocompromised Patients: Subanalyses of the Phase 3 Trial in the Treatment of Candidemia and Invasive Candidiasis

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INTRODUCTION

- *Candida* infections are very common in immunocompromised patients and are a major cause of morbidity and mortality[1,2]
- Rezafungin is a next-generation echinocandin that is being developed for the treatment of candidemia and invasive candidiasis (IC) and for the prevention of invasive fungal disease caused by *Candida, Aspergillus,* and *Pneumocystis* spp. in patients undergoing bone and marrow transplantation
- The Phase 3 ReSTORE trial (NCT03667690), demonstrated rezafungin once weekly (QWk) to be noninferior to caspofungin once daily (QD) in terms of all-cause mortality and Global Cure in the treatment of patients with candidemia and/or IC[3]
  - Rates of adverse events (AEs) and serious adverse events (SAEs) were similar between study arms
- In this subanalysis of the ReSTORE trial, efficacy and safety outcomes were evaluated in patients who were identified as being immunocompromised

METHODS

- The multicenter, double-blind, double-dummy, randomized ReSTORE trial compared the efficacy and safety of rezafungin vs. caspofungin (with optional oral fluconazole stepdown for caspofungin) in adults (aged ≥18 years) with confirmed candidemia and/or IC (**Table 1**)

Table 1. Treatment Groups for Phase 3 ReSTORE Trial

	Dose Regimen/Schedule
Rezafungin	IV rezafungin 400 mg Week 1 then 200 mg QWk + matching IV caspofungin placebo for a total of 2–4 weeks (for optional step-down, oral fluconazole placebo was given)
Caspofungin	IV caspofungin 70 mg on Day 1, followed by 50 mg QD for ≥14 days but ≤28 days (with optional step-down to oral fluconazole 6 mg/kg + matching placebo for rezafungin after ≥3 days of caspofungin treatment)

IV=intravenous.

- In this subanalysis, efficacy and safety outcomes were compared in:
  - Immunocompromised patients (i.e., those with prior and/or concomitant use of immunosuppressants [e.g., calcineurin inhibitors, corticosteroids] and/or ongoing medical history of neutropenia, bone marrow transplantation, solid organ transplantation, lymphoma, or leukemia at screening)
  - Non-immunocompromised patients (i.e., those with no reported prior or concomitant use of immunosuppressants and no ongoing medical history of neutropenia, bone marrow transplantation, solid organ transplantation, lymphoma, or leukemia at screening)
- Efficacy and safety outcomes are reported for the modified intent-to-treat (mITT) and safety populations, respectively

RESULTS

- Of the 187 patients in the mITT population, 90 were classified as immunocompromised
- In general, efficacy was reduced in immunocompromised vs. non-immunocompromised patients; rates of mycological response at Days 5 and 14 were relatively higher for rezafungin vs. caspofungin in both patient populations (**Table 2**)
- Of the 196 patients in the safety population, 96 were classified as immunocompromised
- Overall, there were no concerning trends in rates of AEs and SAEs between groups; rates of AEs and SAEs were relatively higher in immunocompromised vs. non-immunocompromised patients (**Table 3**)

Table 2. Efficacy Outcomes by Immune Status (mITT Population[a])

	Proportion of Patients, n (%)			
	Immunocompromised		Non-immunocompromised	
Efficacy Outcome	Rezafungin N=45	Caspofungin N=45	Rezafungin N=48	Caspofungin N=49
Day 14 Global Cure	23 (51.1)	25 (55.6)	32 (66.7)	32 (65.3)
Day 5 mycological eradication	29 (64.4)	23 (51.1)	35 (72.9)	35 (71.4)
Day 14 mycological eradication	29 (64.4)	28 (62.2)	34 (70.8)	34 (69.4)

[a]All patients who received any amount of study drug and with documented *Candida* infection.
mITT=modified intent-to-treat

Table 3. Summary of AEs (Safety Population[a])

	Proportion of Patients, n (%)			
	Immunocompromised		Non-immunocompromised	
Adverse Event	Rezafungin N=48	Caspofungin N=48	Rezafungin N=50	Caspofungin N=50
Any TEAE	48 (100)	45 (93.8)	41 (82.0)	38 (76.0)
Any drug-related TEAE	7 (14.6)	4 (8.3)	9 (18.0)	5 (10.0)
Any TEAE leading to study drug discontinuation	6 (12.5)	6 (12.5)	4 (8.0)	4 (8.0)
Any SAE	34 (70.8)	28 (58.3)	21 (42.0)	24 (48.0)

[a]All patients who received any amount of study drug.
SAE=serious adverse event; TEAE=treatment-emergent adverse event.

CONCLUSIONS

- Overall data from the Phase 3 ReSTORE trial demonstrated the efficacy and safety of rezafungin in the treatment of candidemia and IC
- In this exploratory subanalysis from ReSTORE, immunocompromised status was associated with reduced efficacy rates overall, but did not change efficacy rate differences between rezafungin and caspofungin; AE and SAE rates were relatively higher in immunocompromised vs. non-immunocompromised patients
- Data from this subanalysis provide further insights on the efficacy and safety of rezafungin in a high-risk, immunocompromised patient population

REFERENCES

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