P436

Rezafungin Clinical Safety and Efficacy in the Treatment of Candidaemia and/or Invasive Candidiasis: Combined Results from the STRIVE Phase 2 Trial Parts A and B

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INTRODUCTION

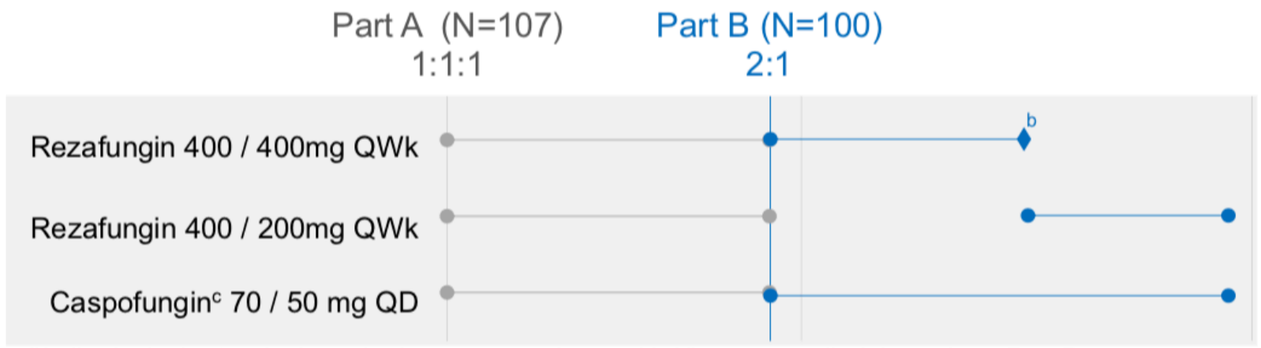
Rezafungin (RZF) is a novel, next-generation echinocandin with distinctive pharmacokinetics/pharmacodynamics, including prolonged half-life and front-loaded plasma exposure, and improved safety and stability over existing systemic antifungals, which allow for once-weekly IV administration and optimized pharmacometrics of efficacy.[1-3]

STRIVE is a global, double-blind, randomized trial (NCT02734862) that evaluated the safety and efficacy of once-weekly RZF in the treatment of candidaemia and/or invasive candidiasis (IC). After successful completion of Part A[4,5], a second randomization (Part B) was conducted. Rezafungin is currently in Phase 3 (Ph3) development.

METHODS

Adults (≥18 y) with systemic signs and mycological confirmation of candidaemia and/or IC were randomized to RZF once-weekly or standard of care (SOC) with caspofungin (CAS) for ≥14 days (≤4 weeks) (**Figure 1**). The study objective was to evaluate the safety and tolerability of RZF and overall success at Day 14 (**Box 1**).

Figure 1. STRIVE Trial of Rezafungin Treatment of Candidaemia and/or Invasive Candidiasis: Part A and Part B Randomization[a] (Intent-to-Treat)



[a]Similar inclusion/exclusion criteria, except patients with IC were enrolled throughout Part B.
[b]In Part B, 400 mg QWk was amended mid-study to 400 mg Wk1/200 mg QWk to align with dosing used in the RZF Ph 3 program.
[c]Caspofungin arm included optional step-down to oral fluconazole.

Box 1. Key Endpoints of the STRIVE Trial

Safety

- Treatment-emergent adverse events (TEAEs), serious AEs (SAEs), and mortality in the Safety Population

Efficacy

- Primary: Overall Response at day 14 in the mITT Population
- Secondary: Principal Investigator (PI)–assessment of clinical response at day 14; all-cause mortality (ACM) at day 30

Overall Response = mycological eradication + resolution of signs of candidaemia and/or IC.
mITT (microbiological intent-to-treat) = all subjects in the Safety Population (those who received any study drug) with a documented *Candida* infection.

RESULTS

Of 207 patients enrolled, 183 patients were included in the mITT population. Treatment groups were well balanced and matched in demographics and baseline characteristics (data not shown), including APACHE II scores (mean±SD: 13.8±7.1, N=207). Patients with IC comprised ~21% of the combined population.

Safety

- No concerning safety trends were observed
- Incidence of ≥1 TEAE was 120/134 (89.6%) among the RZF-treated (pooled) and 55/68 (80.9%) in the SOC group
- Rates of TEAEs leading to study discontinuation were comparable between RZF-treated (pooled) (5.2%) and SOC patients (5.9%)
- SAEs were observed in 47.0% and 42.6% of the RZF-treated and SOC groups, respectively

Efficacy

- RZF 400 mg/200 mg demonstrated greater efficacy than SOC on the primary and key endoints (**Table 1**)
- Across all groups, RZF 400 mg/200 mg had the highest rates of overall success and clinical cure and the lowest rate of 30-day ACM

Table 1. Topline Results from STRIVE – Part A and Part B Combined, mITT Population

Outcome	RZF once weekly 400 mg Wk 1/ 400 mg N=76	RZF once weekly 400 mg Wk 1/ 200 mg N=46	CAS once daily 70 mg D1/50 mg N=61
Overall Success (D14)	46 (60.5)	35 (76.1)	41 (67.2)
PI-assessed Clinical Cure[a] (D14)	53 (69.7)	37 (80.4)	43 (70.5)
All-cause Mortality[b] (D30)	12 (15.8)	2 (4.4)	8 (13.1)

CAS=caspofungin; RZF=rezafungin.
[a]Outcome most closely approximating the primary outcome for the EMA in the Ph3 treatment trial.
[b]The primary endpoint for the US FDA in the Ph3 treatment trial.

CONCLUSIONS

- RZF was safe and efficacious in the Phase 2 STRIVE trial of RZF treatment in patients with candidaemia and/or IC
- No concerning safety trends were observed, and RZF was generally comparable with SOC
- RZF 400 mg/200 mg once weekly, the dosing regimen in the ongoing Ph3 trial (ReSTORE; NCT03667690), demonstrated greater efficacy than SOC and the most favorable efficacy of all treatment arms
- The results from STRIVE Part B, combined with the previous success of Part A, demonstrate the safety and efficacy of RZF and supports its Ph3 development for the treatment of candidaemia and/or IC

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