Rezafungin for the Treatment of Candidemia and/or Invasive Candidiasis: Analysis of the Global, Randomized, Double-Blind, Placebo-Controlled Phase 2 STRIVE Clinical Trial by Geographic Region of Enrollment

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INTRODUCTION

Significant changes in the patient population and disease landscape, and no new antifungal approved in over a decade, have contributed to growing unmet needs in antifungal treatment.

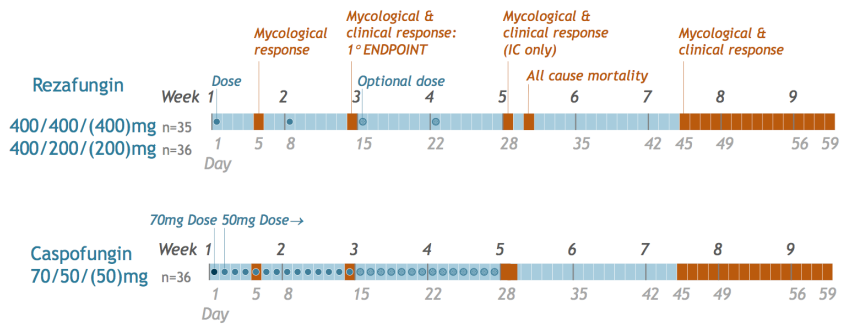
Rezafungin acetate, a novel echinocandin designed to address limitations in the current antifungal armamentarium, has a distinctive PK profile that enables high, front-loaded drug exposure and once-weekly dosing, which correlates with potential benefits to efficacy and safety.[1-3] Rezafungin is being developed for the prevention and treatment of invasive fungal infections. STRIVE (NCT02734862) is a global Phase 2 trial evaluating the safety and efficacy of IV rezafungin in treatment of candidemia and/or invasive candidiasis compared with standard of care (IV caspofungin + optional oral stepdown [fluconazole]).

An analysis by geographic region of the completed Part A of STRIVE was conducted to inform interpretation of results and Phase 3 development.

METHODS

Patients were randomized to 1 of 3 treatment arms according to the study design (Figure 1) as previously described.[4]

Figure 1. STRIVE trial design.



Data were stratified by enrollment region and analyzed for differences in demographics, baseline characteristics, treatment patterns, and outcomes.

RESULTS

Data for 62 patients enrolled in Europe (EU) and 45 patients enrolled in North America (NA) were available for analysis (Table 1).

Table 1. Patient demographics and characteristics at baseline

Parameter		Rezafungin 400/400 mg	Rezafungin 400/200 mg	Caspofungin 70/50 mg	TOTAL
Male, n/N (%)	NA	7/13 (53.8)	11/18 (61.1)	3/14 (21.4)	**21/45 (46.7)**
	EU	14/22 (63.6)	11/18 (61.1)	14/22 (63.6)	**39/62 (62.9)**
Age, y mean ± SD [≥65 y]	NA	46.8 ± 12 y [1 (7.7)]	52.1 ± 14 y [4 (22.2)]	52.4 ± 16 y [5 (35.7)]	**50.7 ± 14 y [10 (22.2)]**
	EU	63.0 ± 15 y [10 (45.5)]	61.9 ±13 y [8 (44.4)]	66.0 ±16 y [14 (63.6)]	**63.7 ±15 y [32 (51.6)]**
Weight, kg mean ± SD	NA	74.6 ± 17.8	85.3 ± 26.5	73.8 ± 13.5	**78.7 ± 21.2**
	EU	72.5 ±15.5	65.8 ± 19.8	75.3 ± 15.9	**71.4 ± 17.2**

Patients in the EU were older than in NA; however, illness severity (APACHE II scores) was similarly distributed between regions. EU patients were predominantly male (62.9%) and white (96.8%). The NA population was balanced between male and female; 26.7% were Black or African-American. In addition to weighing more, NA patients had higher BMI (not shown).

RESULTS (cont'd)

Efficacy (mITT population)

No meaningful trends in efficacy were noted (Table 2); however, subgroup sizes limit interpretation.

Table 2. Rates of overall response by region (mITT).

Overall Response-Success (Day 14)	Rezafungin 400 mg Wk1/ 400 mg QWk	Rezafungin 400 mg Wk 1/ 200 mg QWk	Caspofungin 70 mg/50 mg QD
NA	58.3% (7/12)	64.3% (9/14)	50.0% (5/10)
EU	57.1% (12/21)	76.5% (13/17)	72.2% (13/18)

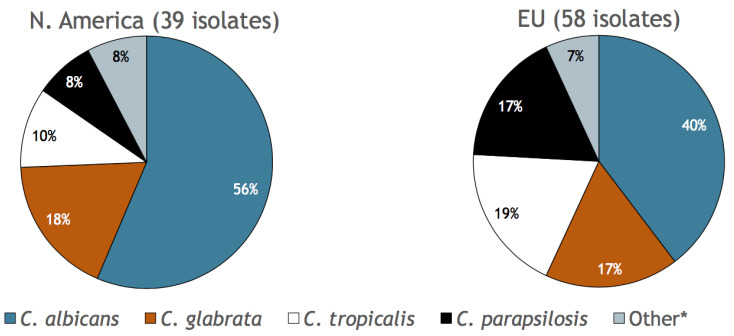
Treatment Patterns (Safety Population)

While most patients overall received 8–14 days of IV treatment; 23% of EU patients received >14 days versus 9% in NA.

Distribution of *Candida* spp. at Enrollment (mITT Population)

Non-*albicans Candida* comprised 60.3% of baseline isolates in the EU with similar proportions of *C. glabrata*, *C. parapsilosis*, and *C. tropicalis*. In NA, *C. albicans* was predominant (56.4%), followed by *C. glabrata* (17.9%) (Figure 1).

Figure 1. *Candida* spp. isolated at Baseline



*In N. America, Other comprised *C. intermedia* (n=1) and *C. dubliniensis* (n=2); in the EU, Other comprised 1 isolate each of *C. dubliniensis, C. guilliermondii, C. krusei, and C. rugosa.*

CONCLUSIONS

- No differentiating trends in illness severity or outcomes by geographic region were seen in STRIVE (Part A)
- In general, EU patients were older and NA patients were heavier
- Non-*albicans Candida* spp. were more prevalent in the EU
- Longer durations of IV treatment were more often administered in the EU
- Subgroups identified by demographics and baseline characteristics may warrant future additional analyses

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ACKNOWLEDGMENTS

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