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Outcomes in Europe from the STRIVE Clinical Trial of Rezafungin Treatment of Candidaemia and/or Invasive Candidiasis

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INTRODUCTION AND PURPOSE

Significant changes in the patient population and disease landscape have exacerbated unmet needs in antifungal treatment. In addition, no new antifungal agents have been approved for treatment of candidemia or invasive candidiasis in over a decade.

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 correlate with potential benefits to efficacy and safety.[1-3] Rezafungin is being developed for prevention and treatment of invasive fungal infections. STRIVE (NCT02734862) is a global, randomized, double-blind, placebo-controlled, 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]).

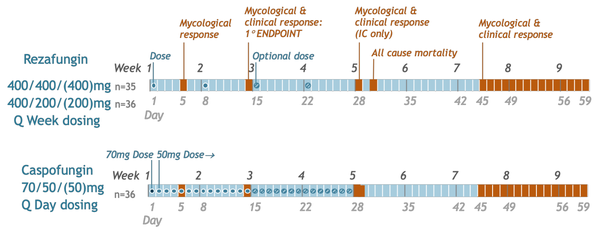
Following completion of the first part of STRIVE ("Part A"), enrollment was continued ("Part B") to achieve the target safety database with Part B completion expected in 2019.

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.



- Intent-to-treat (ITT) population: all randomized subjects
- Safety population: all subjects who received any amount of study drug
- Microbiological ITT (mITT): all subjects in safety population with documented *Candida* infection

METHODS (cont'd)

Data from STRIVE Part A were stratified by enrollment region (Europe [EU] and North America [NA]) and analyzed for differences in demographics, baseline characteristics, treatment patterns, and outcomes.

RESULTS

Patient Population

Results for 62 patients enrolled in EU and 45 patients enrolled in 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 (%)	EU	14/22 (63.6)	11/18 (61.1)	14/22 (63.6)	**39/62 (62.9)**
	NA	7/13 (53.8)	11/18 (61.1)	3/14 (21.4)	**21/45 (46.7)**
Age, y mean ± SD [No. patients ≥65 y (%)]	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)]**
	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)]**
Weight, kg mean ± SD	EU	72.5 ±15.5	65.8 ± 19.8	75.3 ± 15.9	**71.4 ± 17.2**
	NA	74.6 ± 17.8	85.3 ± 26.5	73.8 ± 13.5	**78.7 ± 21.2**
BMI, kg/m^2 mean ± SD (range)	EU	25.3 ± 4.43 (16.4, 32.4)	23.9 ± 7.21 (14.7, 45.3)	27.2 ± 5.43 (17.3, 36.7)	**25.5 ±5.79 (14.7, 45.3)**
	NA	25.1 ± 5.70 (13.9, 35.0)	30.5 ± 10.75 (15.1, 64.4)	26.9 ± 4.67 (20.7, 34.4)	**27.8 ± 8.14 (13.9, 64.4)**
APACHE II score mean	EU	11.81	12.61	14.67	**13.06**
	NA	13.15	15.24	11.67	**13.53**

- Patients in the EU were on average 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%). In contrast, the patient population in NA was balanced between male and female and 26.7% were Black or African-American.
- Patients in NA weighed more and had higher BMI than EU patients.

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 treatment group and region (mITT).

Overall Response at Day 14	n/N (%) Rezafungin 400 mg Wk1/ 400 mg QWk	Rezfungin 400 mg Wk 1/ 200 mg QWk	Caspofungin 70 mg/50 mg QD
EU - Success	12/21 (57.1)	13/17 (76.5)	13/18 (72.2)
Excluding indeterminates*	12/19 (63.2)	13/16 (81.3)	13/18 (72.2)
NA - Success	7/12 (58.3)	9/14 (64.3)	5/10 (50)
Excluding indeterminates*	7/7 (100)	9/12 (75.0)	5/8 (62.5)

*Excludes indeterminates excludes patients for whom outcome could not be assessed due to missing data point(s).

Treatment Patterns (Safety Population)

- While most patients in both regions received 8–14 days of IV treatment, more EU patients received >14 days of IV treatment (**Table 3**).

Table 3. Number of days on IV treatment by region (safety).

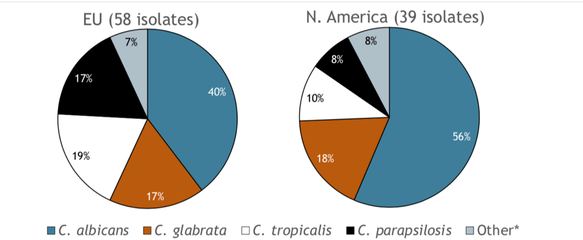
No. of Days on IV Treatment	n/N (%) EU	NA
1-3	5/60 (8.3)	5/44 (11.4)
4-7	3/60 (5.0)	6/44 (13.6)
8-14	38/60 (63.3)	29/44 (65.9)
15-21	12/60 (20.0)	3/44 (6.8)
>21	2/60 (3.3)	1/44 (2.3)

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 2**).

RESULTS (cont'd)

Figure 2. Distribution of *Candida* spp. by region (mITT).



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

CONCLUSIONS

- No differentiating trends in illness severity or outcomes by geographic region were seen in STRIVE (Part A)
- Patients in EU were generally older and weighed less than in NA
- Non-*albicans Candida* spp. were more prevalent in the EU
- Longer durations of IV treatment were observed in the EU
- Subgroups identified by demographics and baseline characteristics may warrant future additional analyses

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ACKNOWLEDGMENTS

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