Rezafungin Clinical Safety and Efficacy in Patients with Candidemia and/or Invasive Candidiasis in the Randomized, Double-blind, Multicenter, Phase 2 STRIVE Trial

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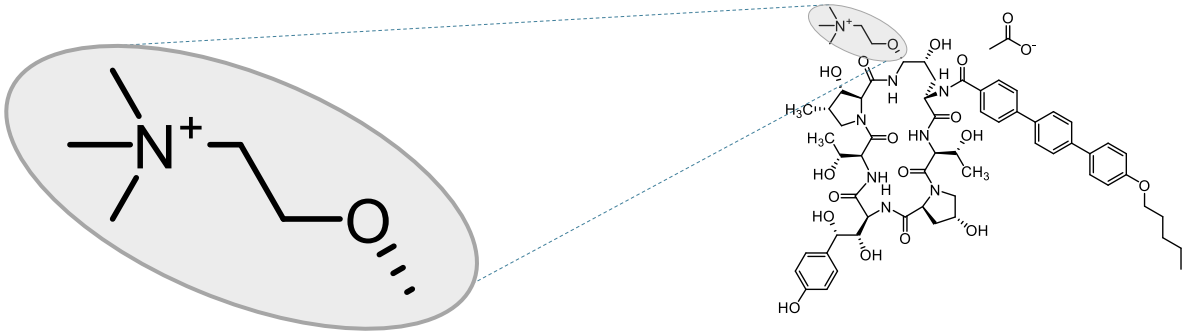
Candidemia and invasive candidiasis

- *Candida* spp. are a leading cause of nosocomial bloodstream infections
- Trends in species distribution
  - *C. albicans* now <50% of isolates in the US
  - Increases in *C. glabrata* (US, Australia, EU, Asia)
  - Increases in *C. parapsilosis* (Latin America, Africa)

Lamoth et al. *J Antimicrob Chemother*. 2018;73 suppl1:i4–i13.

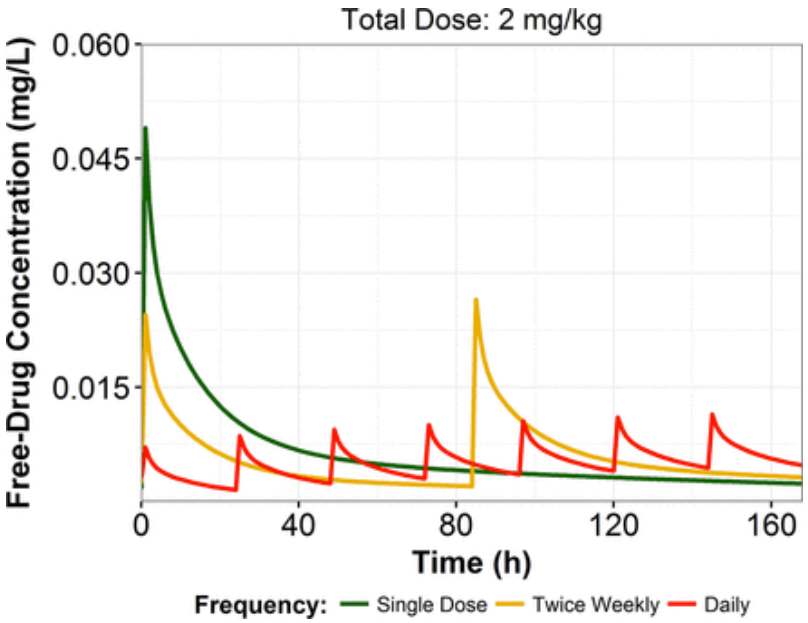
Rezafungin: a novel echinocandin



Structural modification yields improved chemical & biological properties

- Designed for prolonged PK — once weekly dosing in clinical trials
- Designed for high exposures — potential for improved efficacy
- Observed elimination of toxic degradation products — potential for improved safety
- Enables multiple formulations — IV and SC under development

Echinocandin efficacy driven by shape of exposure curve



- Concentration-dependent killing
- Long half-life
- Safety supports front-loaded dosing

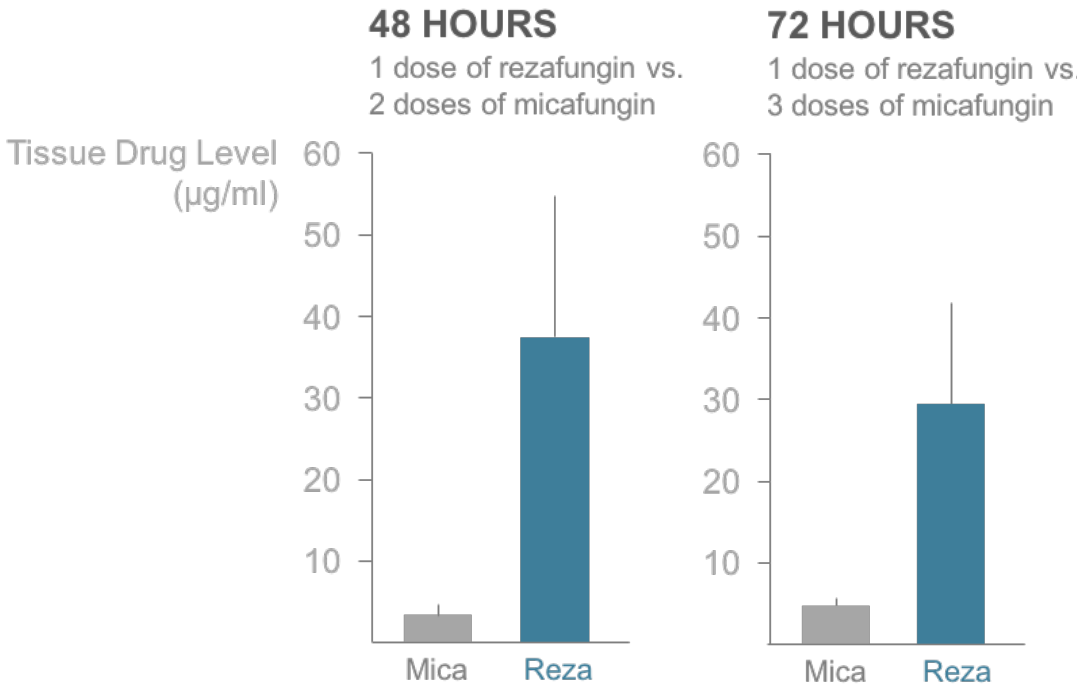
❖ **Once-weekly dosing of rezafungin demonstrated greater fungal killing than divided doses**

❖ **A higher degree of fungal killing achieved with the same amount of weekly exposure**

Lakota et al. *Antimicrob Agents Chemother*. 2017;61:e00758-17.

Rezafungin accumulates at site of infection

Intra-abdominal Invasive Candidiasis Abscess Model



- Exposure at site of infection was 6- to 8-fold higher for rezafungin
- Even multiple doses of micafungin did not reach tissue drug levels achieved with single dose of rezafungin

Zhao et al. *Antimicrob Agents Chemother*. 2017;61:e01009-17.

STRIVE Part A: objectives

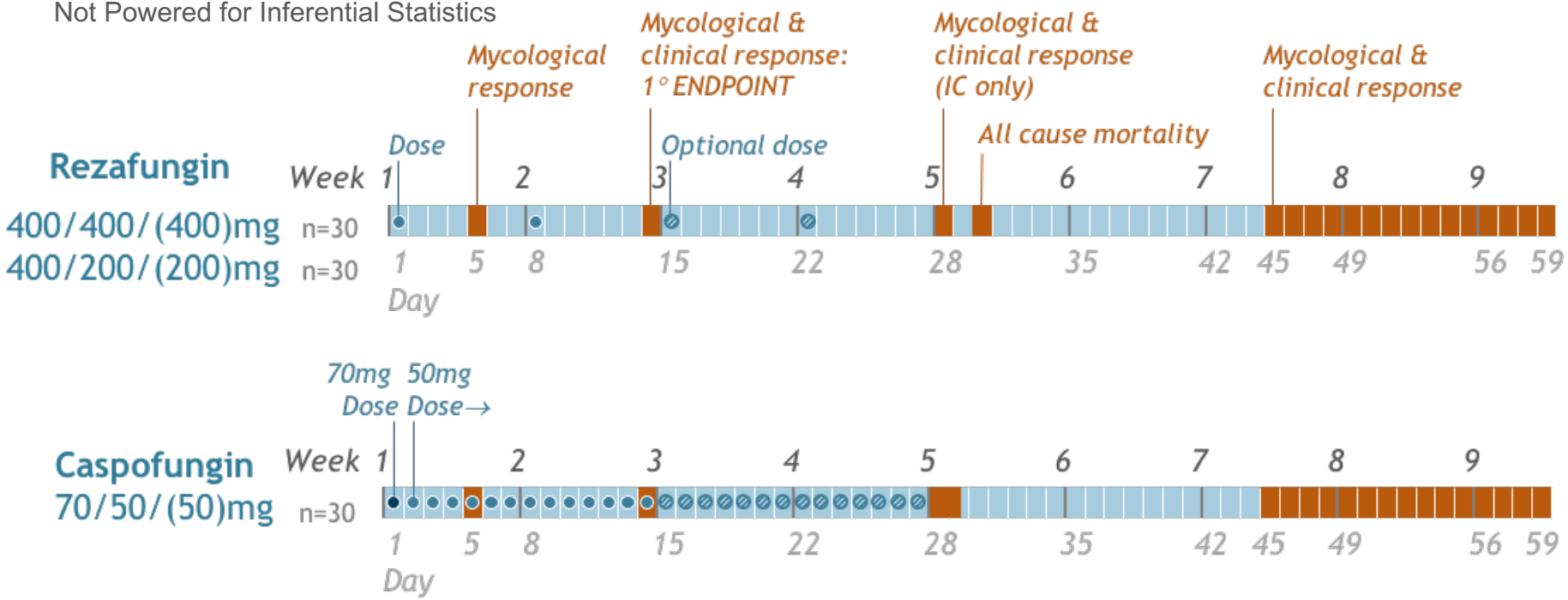
STRIVE is a randomized, double-blind, multicenter, Phase 2 trial of REZAFUNGIN in patients with candidemia and/or invasive candidiasis designed to:

- Establish safety and tolerability in patients
- Establish efficacy (clinical and mycological) across timepoints
- Establish efficacy vs caspofungin
- Establish dosing regimen for Phase 3

Clinicaltrials.gov; NCT02734862

STRIVE Part A: study design

Not Powered for Inferential Statistics



- 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

Subject Demographics and Baseline Characteristics

Parameter		Rezafungin 400 mg/400 mg (QWk) N= 35	Rezafungin 400 mg/200 mg (QWk) N= 36	Caspofungin 70 mg/50 mg (QD) N= 36
		n (%), except where noted		
Age	Mean ± SD [Range]	57 ± 15.9 years [24, 88]	57 ± 14.3 years [26, 84]	61 ± 17.2 years [24, 93]
Diagnosis	Candidemia	32 (91.4)	31 (86.1)	33 (91.7)
	IC	3 (8.6)	5 (13.9)	3 (8.3)
Child-Pugh score[a]	<7	12 (34.3)	10 (27.8)	13 (36.1)
	7-9	15 (42.9)	16 (44.4)	17 (47.2)
	10-15	0	2 (5.6)	1 (2.8)
APACHE II score[a]	0-9	12 (34.3)	9 (25.0)	9 (25.0)
	10-19	16 (45.7)	18 (50.0)	21 (58.3)
	≥20	6 (17.1)	8 (22.2)	3 (8.3)

[a]Numbers of subjects with scores not calculated/missing are not shown.

Overall Response
Day 14- mITT Population

Response	Rezafungin 400 mg/400 mg (QWk) N= 33	Rezafungin 400 mg/200 mg (QWk) N= 31	Caspofungin 70 mg/50 mg (QD) N= 28
	n (%)		
Overall Response- Success	19 (57.6)	22 (71.0)	18 (64.3)
- Failure	7 (21.2)	6 (19.4)	8 (28.6)
- Indeterminate[a]	7 (21.2)	3 (9.7)	2 (7.1)
Excluding Indeterminate Response			
Success	19/26 (73.1)	22/28 (78.6)	18/26 (69.2)
Failure	7/26 (26.9)	6/28 (21.4)	8/26 (30.8)

[a]Indeterminate response indicates inability to assess outcome due to missing data point(s)

Overall Response
Day 5- mITT Population

Response	Rezafungin 400 mg/400 mg (QWk) N=33	Rezafungin 400 mg/200 mg (QWk) N=31	Caspofungin 70 mg/50 mg (QD) N=28
	n (%)		
Overall Response- Success	19 (57.6)	21 (67.7)	15 (53.6)
- Failure	10 (30.3)	8 (25.8)	12 (42.9)
- Indeterminate[a]	4 (12.1)	2 (6.5)	1 (3.6)
Excluding Indeterminate Response			
Success	19/29 (65.5)	21/29 (72.4)	15/27 (55.6)
Failure	10/29 (34.5)	8/29 (27.6)	12/27 (44.4)

[a]Indeterminate response indicates inability to assess outcome due to missing data point(s)

PI Assessment of Clinical Response
Day 14- mITT Population

Response	Rezafungin 400 mg/400 mg (QWk) N= 33	Rezafungin 400 mg/200 mg (QWk) N= 31	Caspofungin 70 mg/50 mg (QD) N= 28
	n (%)		
Clinical Cure[a]	25 (75.8)	24 (77.4)	20 (71.4)
- Failure	7 (21.2)	4 (12.9)	8 (28.6)
- Indeterminate[b]	1 (3.0)	3 (9.7)	0
Excluding Indeterminate Response			
Success	25/32 (78.1)	24/28 (85.7)	20/28 (71.4)
Failure	7/32 (21.9)	4/28 (14.3)	8/28 (28.6)

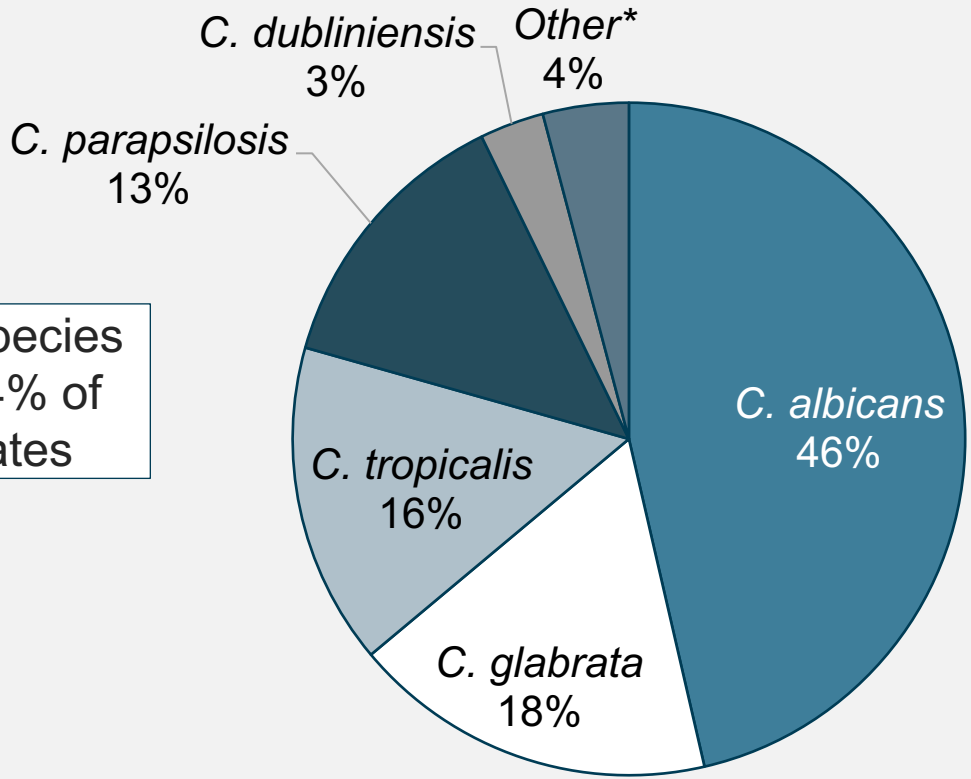
[a]Outcome most closely approximating primary outcome from prior IC/candidemia clinical trials
[b]Indeterminate response indicates inability to assess outcome due to missing data point(s)

Mycological Response
Day 14- mITT Population (Patients with Candidemia Only)

Response	Rezafungin 400 mg/400 mg (QWk) N= 30	Rezafungin 400 mg/200 mg (QWk) N= 26	Caspofungin 70 mg/50 mg (QD) N= 25
	n (%)		
Mycological Success in Candidemia	21 (70.0)	17 (65.4)	18 (72.0)
- Failure	6 (20.0)	6 (23.1)	6 (24.0)
- Indeterminate[a]	3 (10.0)	3 (11.5)	1 (4.0)
Excluding Indeterminate Response			
Success	21/27 (77.8)	17/23 (73.9)	18/24 (75.0)
Failure	6/27 (22.2)	6/23 (26.1)	6/24 (25.0)

[a]Indeterminate response indicates inability to assess outcome due to missing data point(s)

Candida Species at Enrollment
mITT Population

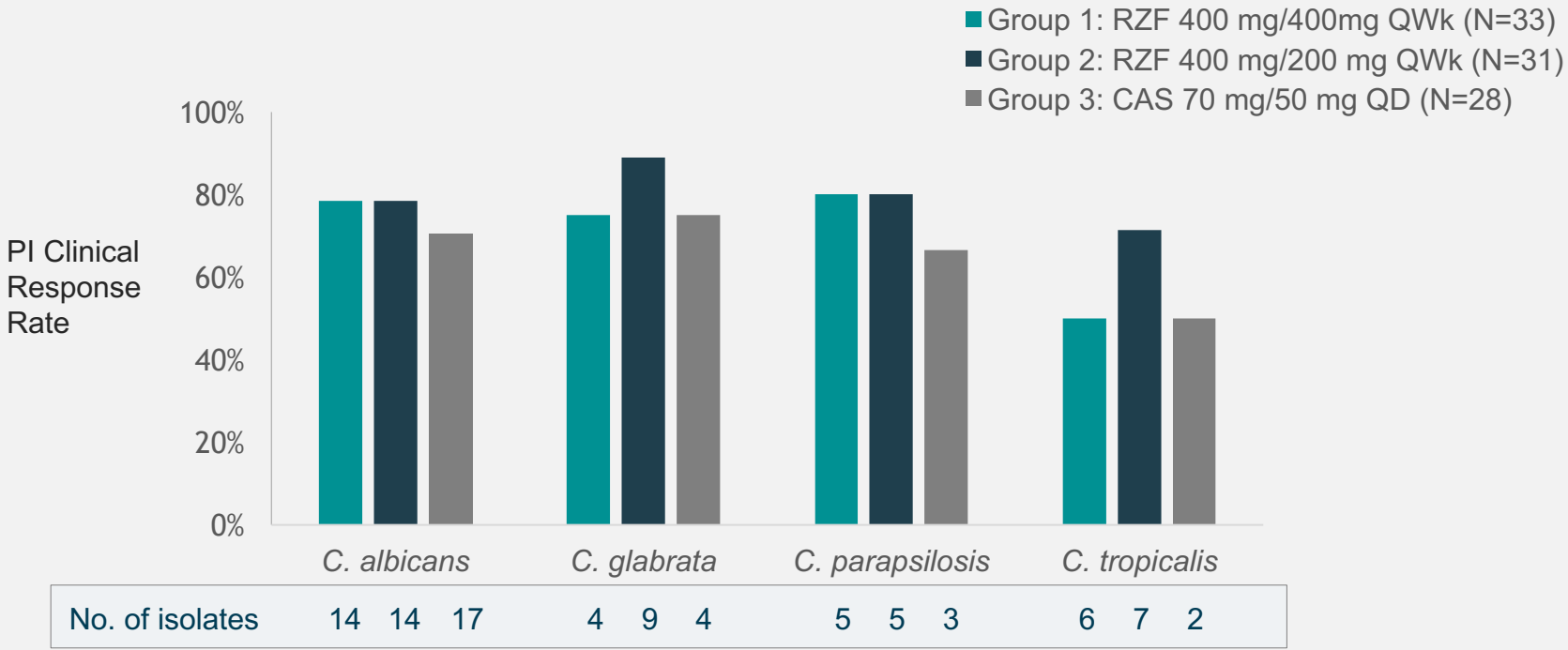


*Other comprised 1 isolate each of *C. guilliermondii*, *C. intermedia*, *C. krusei*, and *C. rugosa*.

Non-*albicans* species comprised ~54% of baseline isolates

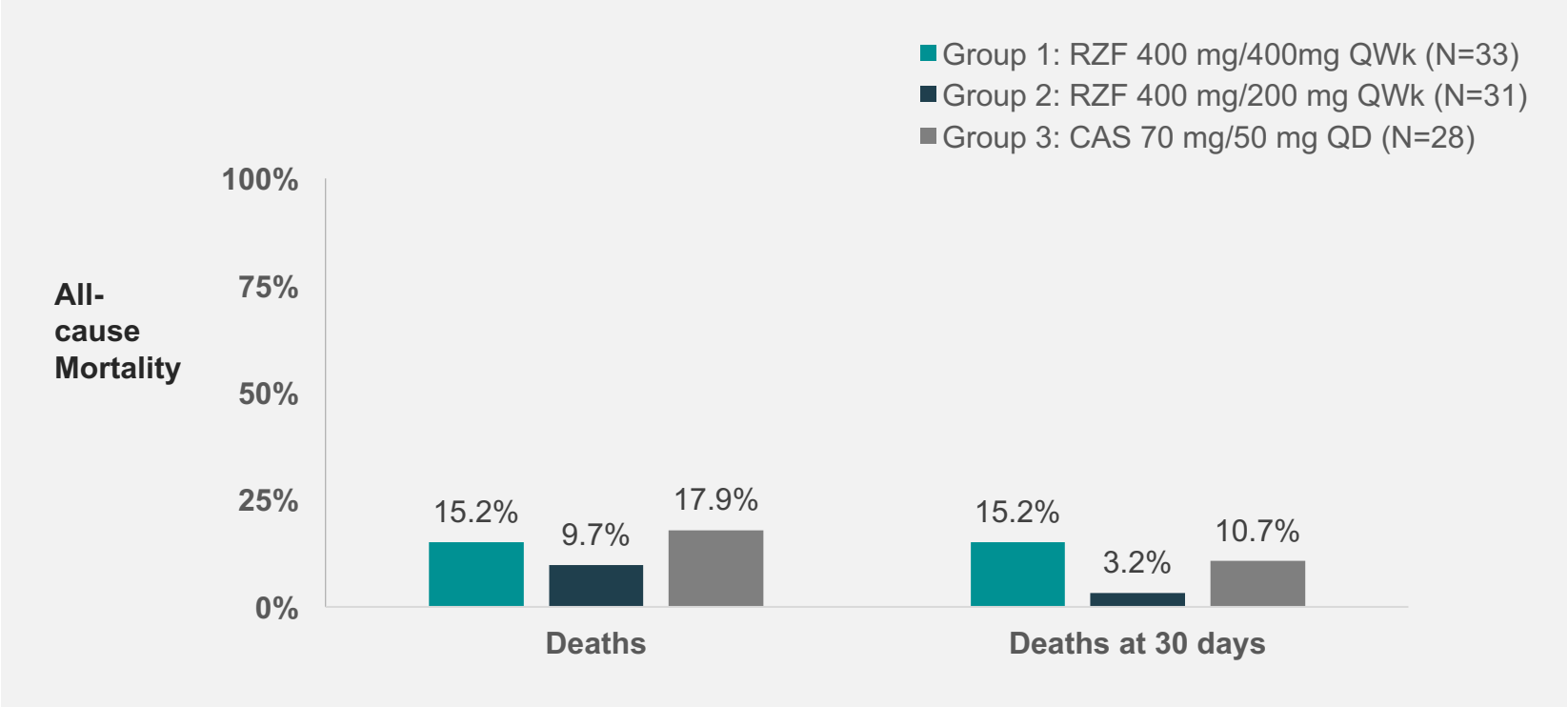
PI Clinical Response by *Candida* Species at Enrollment

Day 14- mITT Population



Not shown: 100% responses against Other isolates in Group 1 (*C. dubliniensis,* n=3; *C. guilliermondii* and *C. rugosa*, n=1 each) and in Group 3 (*C. intermedia* and *C. krusei*, n=1 each)

All-cause Mortality
mITT Population



Adverse Events Summary

Parameter	Rezafungin 400 mg/400 mg (QWk) N= 35	Rezafungin 400 mg/200 mg (QWk) N= 36	Caspofungin 70 mg/50 mg (QD) N= 33
	n (%)		
≥1 TEAE Severe	31 (88.6) 13 (37.1)	34 (94.4) 10 (27.8)	27 (81.8) 13 (39.4)
Study-drug related TEAE	4 (11.4)	6 (16.7)	4 (12.1)
Serious AE Study-drug related SAE	13 (37.1) 0	18 (50.0) 1 (2.8)	13 (39.4) 1 (3.0)

Most Frequent (≥10%) Adverse Events
Safety Population

Preferred Term	Rezafungin 400 mg/400 mg (QWk) N= 35	Rezafungin 400 mg/200 mg (QWk) N= 36	Combined Rezafungin Groups N=71	Caspofungin 70 mg/50 mg (QD) N= 33
	n (%)			
Hypokalemia	5 (14.3)	7 (19.4)	**12 (16.9)**	**3 (9.1)**
Diarrhea	3 (8.6)	7 (19.4)	**10 (14.1)**	**8 (24.2)**
Nausea	2 (5.7)	6 (16.7)	**8 (11.3)**	**3 (9.1)**
Anemia	4 (11.4)	4 (11.1)	**8 (11.3)**	**1 (3.0)**
Edema/swelling peripheral	5 (14.3)	2 (5.6)	**7 (9.9)**	**2 (6.1)**
Vomiting	2 (5.7)	4 (11.1)	**6 (8.5)**	**5 (15.2)**

Conclusions

- STRIVE Part A met its objectives of establishing
  - Clinical safety and tolerability
  - Efficacy (clinical and mycological) across timepoints and versus caspofungin
  - Dosing regimen for Phase 3 (400 mg/200 mg)
- These findings support and inform the continued development of rezafungin in treatment and prevention of invasive fungal infections.