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ISHAM INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

CIDARA THERAPEUTICS

Rezafungin: a Novel, Once-weekly Echinocandin in Phase 3 Development for Treatment and Prevention of Invasive Fungal Disease

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Chief Medical Officer

Cidara Therapeutics, Inc.

Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requirements differ internationally

Presenter Disclosures

- Employee and shareholder of Cidara Therapeutics, Inc.

What's Changed for Systemic Fungal Infections in the Past 20 Years?

2001 → Today

Clinical Landscape[1-3]

Evolving epidemiology

- Rising predominance of non-*albicans Candida*
- Increasing MICs
- Resistance - *FKS* mutations, pan-azole resistance
- New threat: *Candida auris*

Complexity of Care

- Older patient population
- Improved outcomes and survival
- Longer periods of neutropenia
- Drug—drug interactions (CYP family)
- Therapeutic drug monitoring needs
- Evidence of inadequate drug exposure in the critically ill, special populations

→ Increased risk of IFI

↔ Tidal wave of novel chemotherapeutics (midostaurin, vincristine, venetoclax, nilotinib, ibrutinib, and more…)

1. Bassetti et al. *J Antimicrob Chemother.* 2018;73:i14-i25. **2.** Stemler et al. *Ann Hematol*. 2020;99:1429-1440. **3.** Pea and Lewis. *J Antimicrob Chemother.* 2018;73:i33-i43.

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Antifungal drug approvals[4]

Voriconazole, Posaconazole, Caspofungin, Micafungin, Anidulafungin, Isavuconazole

1. Bassetti et al. *J Antimicrob Chemother.* 2018;73:i14-i25. **2.** Stemler et al. *Ann Hematol.* 2020;99:1429-1440. **3.** Pea and Lewis. *J Antimicrob Chemother.* 2018;73:i33-i43. **4.** US Food and Drug Administration. Available at https://www.fda.gov/drugs/development-approval-process-drugs/drug-approvals-and-databases. Accessed June 24, 2021.

Rezafungin: A Novel Long-Acting Echinocandin With Distinctive Properties in Phase 3

Structural modification increases stability and yields unique chemical & biological properties

Properties	Evidence
Long-acting PK	Once-weekly dosing as in ongoing Phase 3 clinical trials*
Front-loaded plasma drug exposure	Efficacy: Shorter time to negative blood culture in Phase 2
Broad spectrum activity	*In vivo* efficacy vs. *Candida*, *Aspergillus*, and *Pneumocystis* spp.
Observed absence of toxic degradation products	Safety: lack of hepatotoxicity
No DDIs and favorable hepatic and renal safety	Compatibility with other medications

* ReSTORE: 1st line treatment of candidemia and/or invasive candidiasis
ReSPECT: 1st line prophylaxis for *Candida*, *Aspergillus,* and *Pneumocystis* spp., in allogeneic blood and marrow transplant patients

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Rezafungin Targets the Fungal Cell Wall

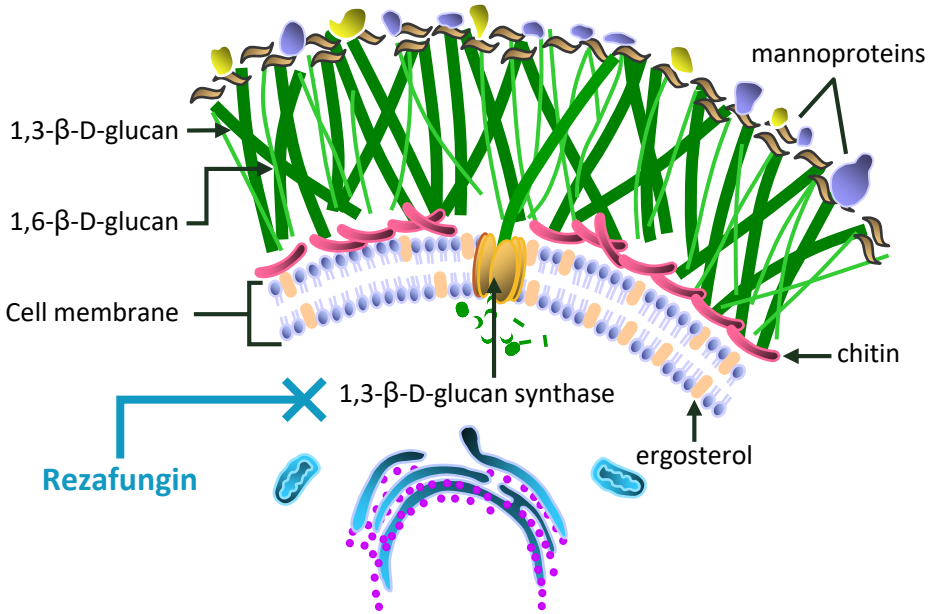

Image adapted from Diamond RD, ed. Atlas of Infectious Diseases: Fungal Infections. Copyright 2000 Springer Science+Business Media New York.

Rezafungin inhibits production of 1,3-β-D-glucan[2]

Increased permeability of the cell wall causes osmotic imbalance[2]

Fungal cell lysis occurs[2]

- **Fungicidal against *Candida* spp.**
- **Fungistatic against *Aspergillus* spp.[2]**
- **Active against *Pneumocystis* spp.[3,4]**

1. Diamond RD, ed. *Atlas of Infectious Diseases: Fungal Infections*. 1st ed. Current Medicine Group; 2000. **2.** Patil, et al. *J Pharm Pharmacol*. 2017 Dec;69(12):1635-1660.
3. Cushion, et al. ASH 2019; Orlando, Florida. **4.** Sandison, et al. ICHS 2021.

Rezafungin: Potent, Broad-Spectrum Activity Against Candida Species

In Vitro Activity Comparable With Current Echinocandins

	MIC_{90} (µg/mL)[1-3*]									
	C. albicans (n=835)[2†]	*C. glabrata* (n=374)[2†]	*C. tropicalis* (n=196)[2†]	*C. krusei* (n=77)[2†]	*C. parapsilosis* (n=329)[2†]	*C. kefyr* (n=52)[3‡]	*C. lusitaniae* (n=46)[3‡]	*C. guilliermondii* (n=27)[3‡]	*C. dubliniensis* (n=22)[3‡]	*C. auris* (n=19)[3‡]
Rezafungin	**0.06**	**0.12**	**0.06**	**0.06**	**2**	**0.12**	**0.25**	**1**	**0.06**	**0.25**
Anidulafungin	0.03	0.12	0.06	0.12	2	0.06	0.06	2	0.03	0.25
Caspofungin	0.03	0.06	0.06	0.25	0.5	0.5	1	1	0.25	1
Micafungin	0.03	0.03	0.06	0.12	1	0.12	0.25	2	0.03	0.5

*CLSI broth microdilution methodology was employed for MIC determination (M27-A3).1-3
†Clinical isolates collected internationally in the JMI Laboratories SENTRY Antimicrobial Surveillance Program (2016-2018).2
‡Clinical isolates collected in Hungary (2005-2018), except for C. auris obtained from the National Mycology Reference Laboratory (Bristol, UK), tested as part of a retrospective study.3
CLSI, Clinical and Laboratory Standards Institute; MIC, minimal inhibitory concentration.
1. Berkow, et al. Diagn Microbiol Infect Dis. 2018;90:196-197. 2. Pfaller, et al. Antimicrob Agents Chemother. 2020;pii: AAC.00099-20. 3. Toth, et al. J Antimicrob Chemother. 2019;74:3505-3510.

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Rezafungin: Potent Activity Against *Aspergillus* Species

In Vitro Activity Includes Azole-Resistant Strains and Cryptic Species

	MEC_{90}/MIC_{90} (µg/mL)*	
	A. fumigatus (n=183)[1†]	*A. flavus* (n=45)[1†]
Rezafungin	**0.03**	**0.015**
Anidulafungin	0.03	0.015
Caspofungin	0.03	0.03
Micafungin	0.015	0.03

	MEC_{90}/MIC_{90} (µg/mL)*		
	Azole-resistant *A. fumigatus* (n=31)[2‡]	*A. lentulus* (n=11)[2‡]	*A. calidoustus* (n=11)[2‡]
Rezafungin	**0.12**	**≤0.015**	**0.06**
Posaconazole	4	0.5	4
Voriconazole	>16	8	4
Micafungin	0.06	≤0.015	0.03

*CLSI broth microdilution methodology was employed for MEC and MIC determination (M38-A2).[2]

†Clinical isolates collected internationally in the JMI Laboratories SENTRY Antimicrobial Surveillance Program (2016-2018).[1]

‡Clinical isolates collected in the US and resistance genotypes confirmed by DNA sequence analysis (CYP51A only, n=13; TR_{34}/L98H, n=2; TR_{46}/Y121F/T289A, n=2; resistant/no CYP51A mutation, n=6; resistant/CYP51A status unknown, n=8).[3]

CLSI, Clinical and Laboratory Standards Institute; CYP, cytochrome P450; MEC, minimal effective concentration; MIC, minimal inhibitory concentration.

1. Pfaller, et al. *Antimicrob Agents Chemother*. 2020;pii: AAC.00099-20. **2.** Wiederhold, et al. *J Antimicrob Chemother*. 2018b;73:3063-3067.

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Rezafungin: *In Vivo* Efficacy

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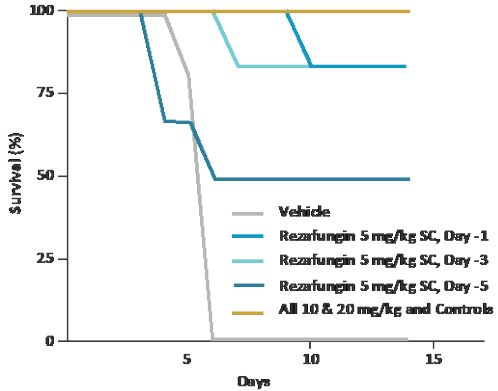
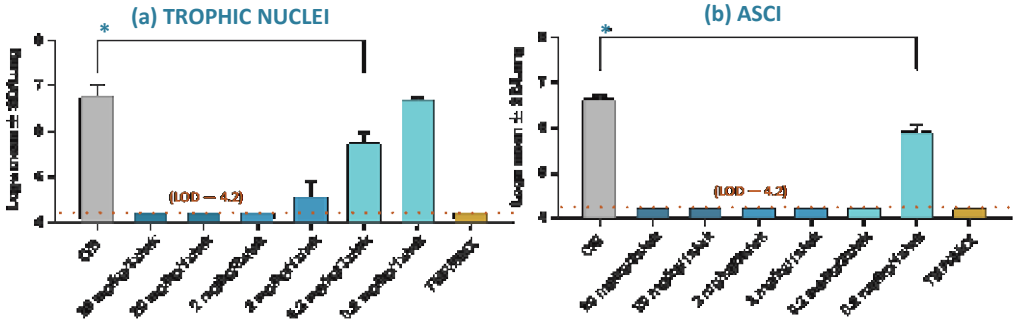
Efficacy of Rezafungin in Prophylactic Mouse Models of Invasive Candidiasis, Aspergillosis, and *Pneumocystis* Pneumonia

Lynn Miesel,[a] Melanie T. Cushion,[b,c] Alan Ashbaugh,[b,c] Santiago R. Lopez,[d] Voon Ong[e]

Survival – *A. fumigatus* (ATCC 13073) 1.85x10^4 on Day 0



Kidney Tissue Fungal Burden – *Pneumocystis murina* 2x10^6 on Day 0



- 100% prophylaxis efficacy against *A. fumigatus* at human equivalent doses (10 and 20 mg/kg)[1]
- Prophylaxis efficacy against *Pneumocystis* comparable to TMP-SMX (standard of care) at human equivalent doses

*p<0.05 vs. control.
C/S, control steroid; CPM, cyclophosphamide; LOD, limit of detection; TMP/SMX, trimethoprim-sulfamethoxazole.

1. Miesel, et al. *Antimicrob Agents Chemother*. 2021;65:e01992-20.

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Rezafungin: PK/PD

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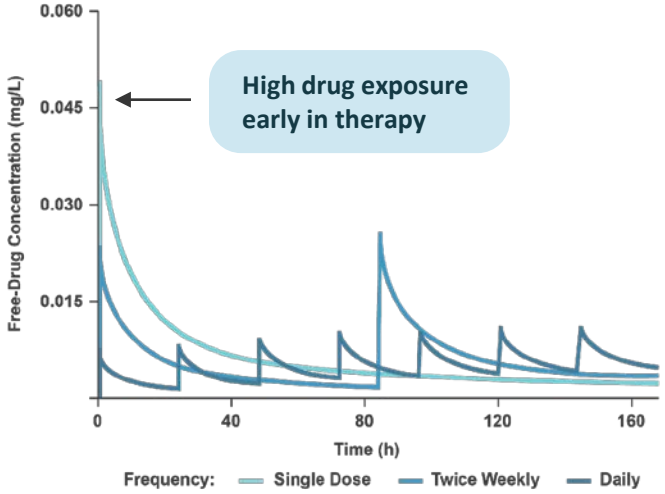
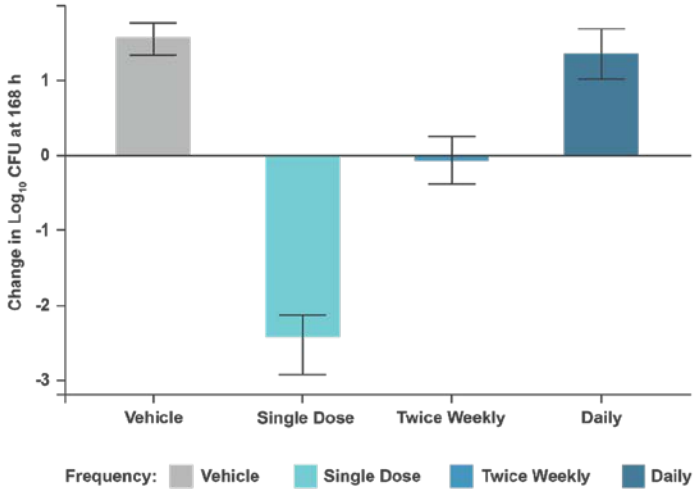
Rezafungin High Exposure for Sustained Fungicidal Activity

Exposure Shape Matters for Antifungal Efficacy

High drug exposure following once-weekly dosing resulted in greater fungal killing than divided doses



Simulated dose fractionation of rezafungin in healthy mice, total dose 2 mg/kg

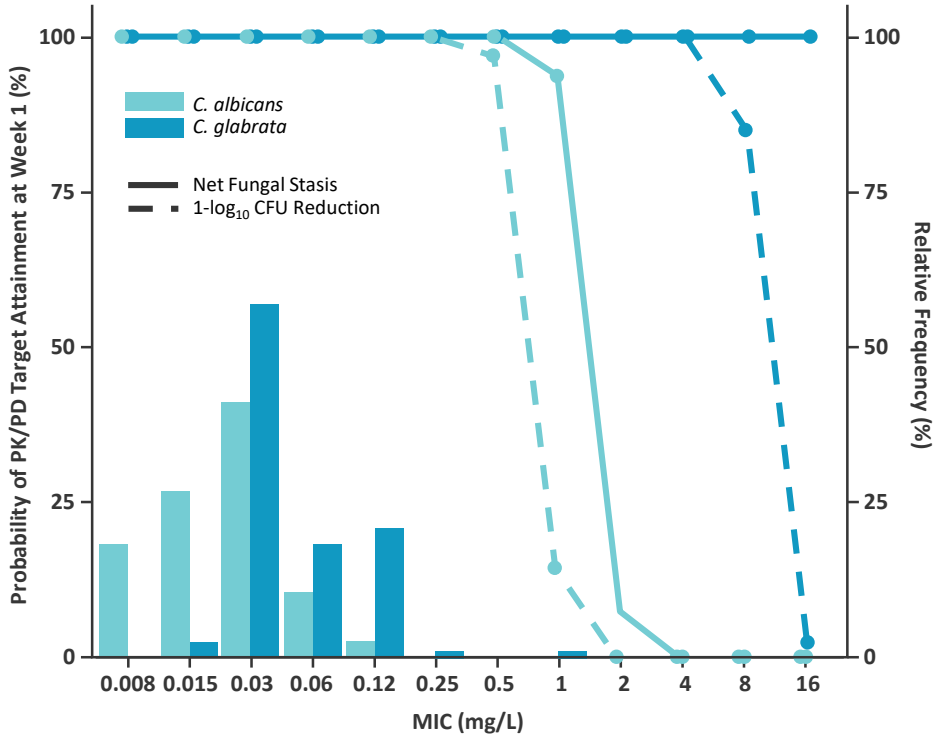


Fungal burden in neutropenic mice following *Candida albicans* infection and 2 mg/kg rezafungin

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

Rezafungin PK/PD Target Attainment by MIC Associated With Net Fungal Stasis and CFU Reductions From Baseline

Percent Probability Against Worldwide *C. albicans* and *C. glabrata* MIC Distributions



Study Design

- Population PK model, non-clinical PK/PD targets, and *in vitro* surveillance data used to simulate probabilities of target attainment
- Simulated administration of rezafungin 400 mg
- Highest rezafungin MIC values in *fks* mutants observed were 0.25 mg/L for *C. albicans* and 2 mg/L for *C. glabrata*

Rezafungin 400 mg simulated to achieve high percent probabilities of PK/PD target attainment, providing efficacy for majority of patients

Single dose of rezafungin 400 mg simulated to reduce fungal burden, even in some *fks* mutant *Candida* isolates

CFU, colony-forming units; MIC, minimal inhibitory concentration; PD, pharmacodynamic; PK, pharmacokinetic.

1. Bader, et al. Antimicrob Agents Chemother. 2018;62:e02614-17.

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Rezafungin Demonstrates High Probability of PK/PD Target Attainment

Percent Probability Against *Candida albicans* and *C. glabrata* 1 Week After Dose Based on Non-Clinical PK/PD Targets

MIC (µg/mL)	*C. albicans*[1,2]			
	Micafungin	Anidulafungin	Caspofungin	Rezafungin
0.008	99.4	100[a,b]	100	100
0.015	71.2	99.1	100	100
0.03	10.1	52.7	100	100
0.06	0.1	0.90	97.9	100
0.12	0	0	76.7	100
0.25	0	0	35.7	100
0.5	0	0	12.1	100
1	0	0	4.4	76.5
2	0	0	1.35	1.00
4	0	0	0.25	0
8	0	0	0.05	0

MIC (µg/mL)	*C. glabrata*[1,2]			
	Micafungin	Anidulafungin	Caspofungin	Rezafungin
0.008	100	100	100	100
0.015	100	100	100	100
0.03	97.5	99.2	100	100
0.06	49.9	54.3	100	100
0.12	3.40	0.95	100	100
0.25	0	0	100	100
0.5	0	0	97.0	100
1	0	0	73.2	100
2	0	0	33.9	100
4	0	0	11.3	100
8	0	0	4.35	100

Shading reflects relative probability of PK/PD target attainment 1 week after dose (stasis).

Rezafungin high probability of PK/PD target attainment against *C. albicans* and *C. glabrata* in Monte Carlo simulations

MIC, minimal inhibitory concentration; PD, pharmacodynamic; PK, pharmacokinetic.
1. Bader, et al. IDWeek 2017; poster 833. **2.** Bader, et al. *Antimicrob Agents Chemother*. 62:e02614-17.

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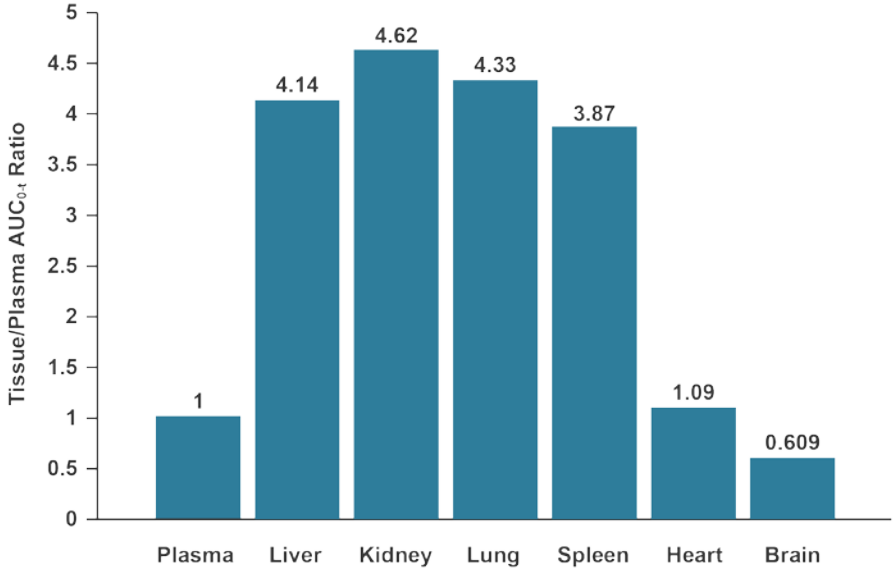
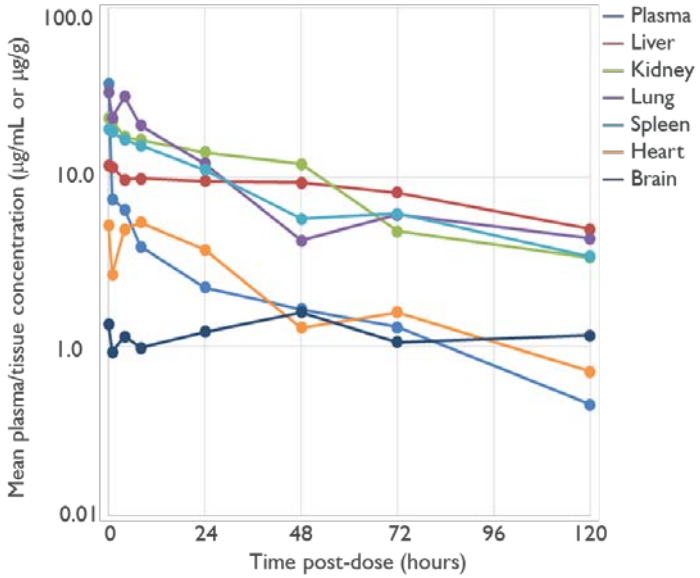
Rezafungin Sustained Tissue Distribution *In Vivo*

Rat PK Models

Uniform tissue distribution across liver, kidney, lungs, and spleen[1]



Similar half-life/elimination in organs[2]



AUC, area under the curve.

1. Ong, et al. *Antimicrob Agents Chemother*. 2017;61:e01626-16. **2.** Ong, et al. *Biol Blood Marrow Transplant*. 2018;24:S291–S459.

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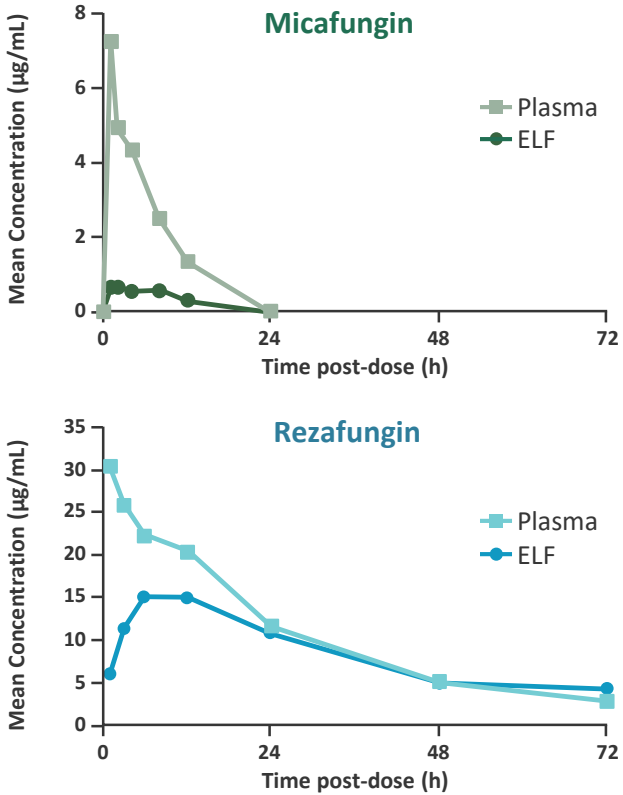
Rezafungin Distribution to Key Sites in Infection

Drug Concentrations in Plasma and ELF[1]



Study Design

- Study drugs administered IP as a single dose in CD-1 mice
  - Micafungin 5 mg/kg (≈ human dose of 100 mg)
  - Rezafungin 20 mg/kg (≈ human dose of 400 mg)
- Comparable levels in humans expected after 1 week due to rezafungin plasma half-life (133 h in human, 21 h in mouse)

Micafungin distribution into mouse ELF is similar to that observed in humans, suggesting that this model may be predictive of distribution in humans

Rezafungin concentrations >20-fold higher than MEC_{90} (0.015 µg/mL) against *Aspergillus fumigatus* and *A. flavus* in plasma (3 µg/mL) and ELF (4 µg/mL) after 3 days

High levels and long duration in ELF reinforce potential for rezafungin efficacy with once-weekly dosing

ELF, epithelial lining fluid; MEC, minimal effective concentration.

1. Ong, et al. HTIDE, 2018; poster.

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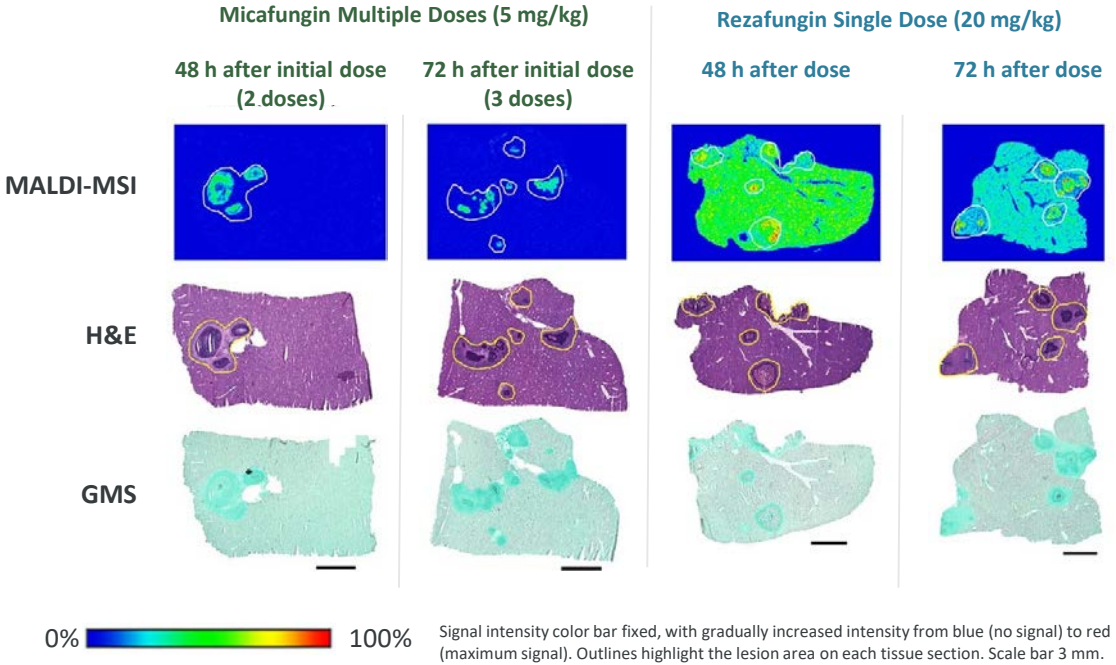
Rezafungin Tissue Penetration With a Single Dose (Zhao et al, 2017)

In vivo Comparison of Drug Penetration in the Liver



Signal intensity color bar fixed, with gradually increased intensity from blue (no signal) to red (maximum signal). Outlines highlight the lesion area on each tissue section. Scale bar 3 mm.

Study Design

- CD-1 mice, no immunosuppression
- *C. albicans* (SC5314), $1x10^7$ on Day 0
- Study drugs administered on Day 3 post-infection
  - Micafungin 5 mg/kg 2-3 daily doses (5 mg/kg ≈ human dose of 100 mg)
  - Rezafungin 20 mg/kg single dose (20 mg/kg ≈ human dose of 400 mg)
- MALDI-MSI to assess drug penetration at infection site

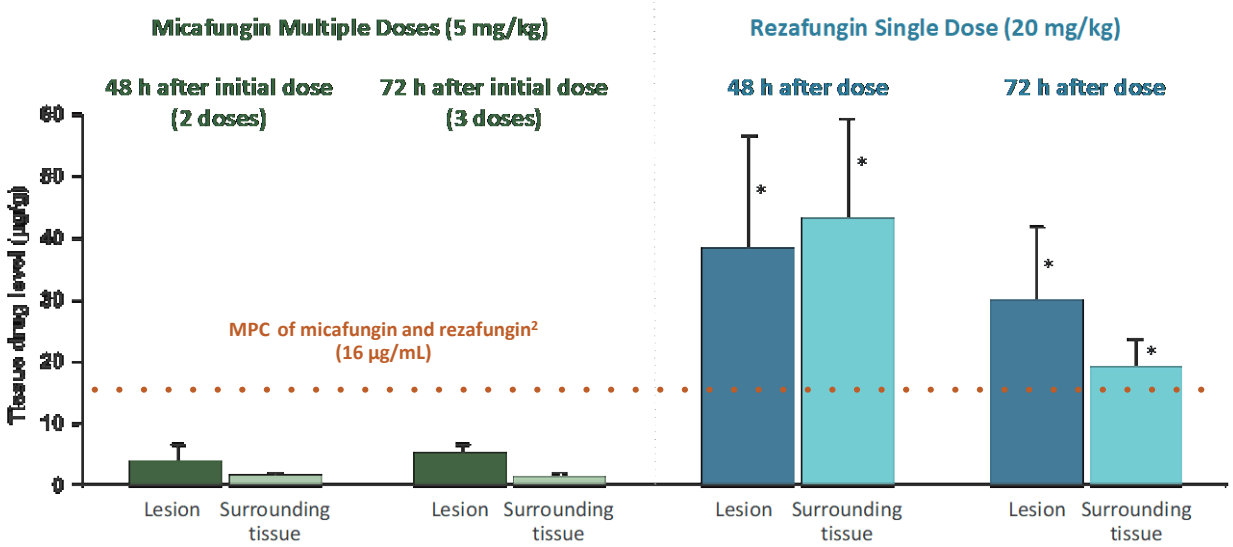
- **Multiple doses of micafungin did not reach tissue drug levels achieved with single dose of rezafungin**
- **Rezafungin accumulated in necrotic areas of each lesion at 48 and 72 hours**

GMS, Gomori methenamine silver; H&E, hematoxylin and eosin; MALDI-MSI, matrix-assisted laser desorption ionization mass spectrometry imaging.

1. Zhao, et al. *Antimicrob Agents Chemother*. 2017;61(10).

Rezafungin Tissue Penetration With a Single Dose (Zhao et al, 2017)

Drug Levels of Rezafungin and Micafungin vs Mutant Prevention Concentration[1]



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  - Rezafungin 20 mg/kg single dose (20 mg/kg ≈ human dose of 400 mg)
- Tissue drug levels measured at infection site, in lesions and in uninvolved/surrounding tissues

Rezafungin drug levels above the MPC for *C. albicans* and *C. glabrata*

*p<0.001.
MALDI-MSI, matrix-assisted laser desorption ionization mass spectrometry imaging.
1. Zhao, et al. *Antimicrob Agents Chemother*. 2017;61(10). **2.** Zhao, et al. *Cell MIcrobio*. 2016;18(9).

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Rezafungin: Phase 1 Data

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Rezafungin Phase 1 Development

Evidence of Rezafungin Safety and Consistent Drug Exposures Across Populations

Pharmacokinetics	Consistent rezafungin exposures observed, including in a wide range of renal function
Hepatic Impairment	No clinically relevant differences in mean exposure observed between moderate or severe hepatic impairment and healthy controls
Drug-Drug Interaction Studies	No notable drug interactions No dose adjustments with rezafungin coadministration
QT Interval Study	Lack of effect on QT interval in healthy adults

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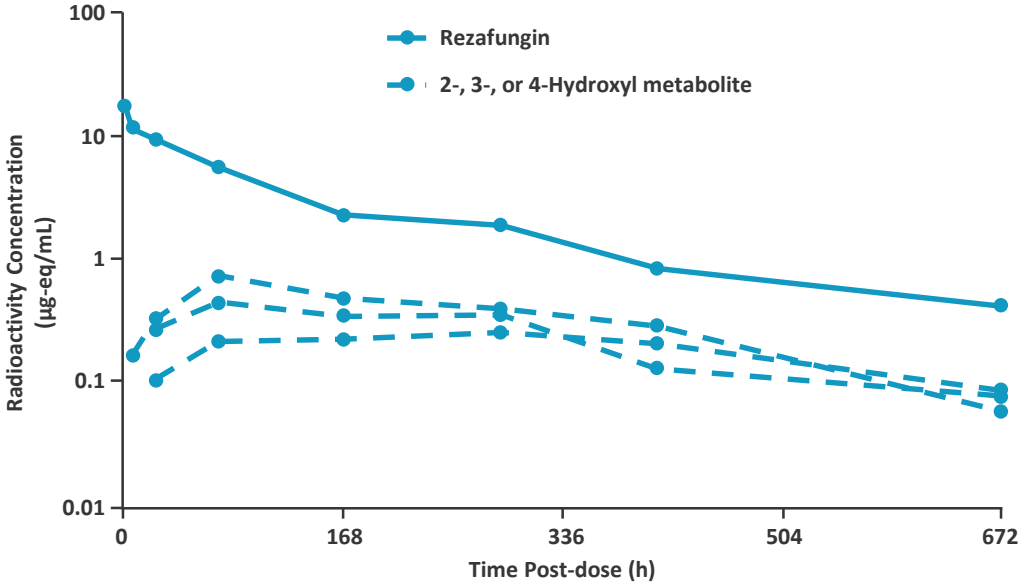
Rezafungin PK Profile in Healthy Adults

Long Plasma Half-Life and Minimal Metabolism Following IV Administration



Study Design[1]

- Healthy human subjects, N=9
- Single 400 mg dose of radiolabeled rezafungin administered IV
- Collected blood, urine, and fecal samples over 60 days

Rezafungin accounted for ~77% total radiocarbon AUC[1]

Metabolites accounted for <10% total plasma radioactivity AUC exposure[1]

Consistent rezafungin exposures observed over a wide range of renal function[2]

Rezafungin minimally metabolized and mainly excreted unchanged in feces

No dose adjustment expected for renal impairment

AUC, area under the curve.

1. Ong, et al. IDWeek 2020; Poster 1286. **2.** Flanagan, et al. ICHS 2021; Poster.

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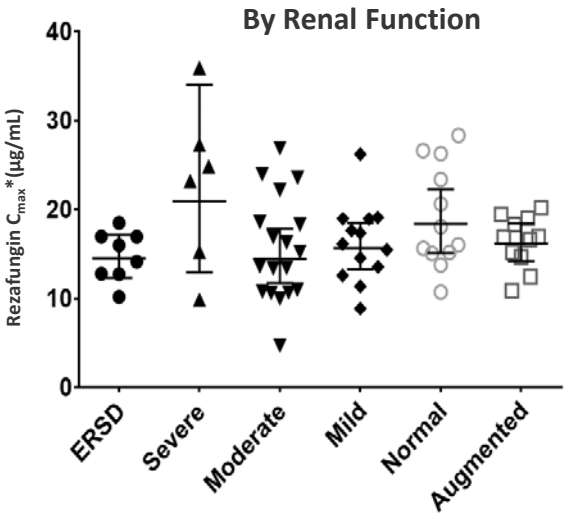
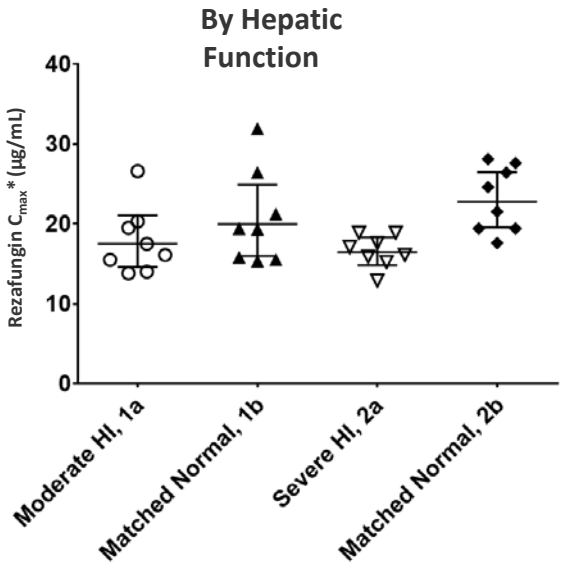
Rezafungin in Renal and Hepatic Impairment





Details of Analyses

- Exposure (C_{max}) following rezafungin 400 mg
  - By Renal Function: from subjects in STRIVE, estimated using a population PK model and Bayesian estimation
  - By Hepatic Function: from subjects with moderate or severe hepatic impairment (HI; Child-Pugh class B or C) and healthy matched controls in an open-label study

Consistent RZF exposures over a wide range of renal function were observed in STRIVE data

Mean RZF exposure in moderate or severe HI was modestly reduced (up to ~30% lower) vs matched healthy subjects

Of 9 AEs in 7 subjects, 1 was considered related to rezafungin (mild headache in subject with moderate HI)

Renal impairment did not appear to affect rezafungin safety or efficacy in STRIVE

Differences in mean exposure in moderate or severe HI and healthy controls were not clinically relevant

*Geometric Means with 95% confidence intervals.

Flanagan et al, SCCM 2020; Flanagan et a ICHS 2021; Cidara Therapeutics, Data on file (submitted, TIMM 2021)

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Rezafungin Demonstrated No Notable Drug-Drug Interactions

Drug Interaction Study In Healthy Adults

DRUG	POSSIBLE MECHANISM(S)	OBSERVATIONS	SUGGESTED ACTION
Tacrolimus	CYP3A4, P-gp	↔ C_{max} ↓ AUC ~15%	No change in dose
Repaglinide	CYP2C8, OATP	↔ C_{max} ↑ AUC ~15%	No change in dose
Metformin	OCT, MATEs	↔ C_{max} ↔ AUC	No change in dose
Rosuvastatin	BCRP, OATP	↑ C_{max} ~12% ↑ AUC ~15%	No change in dose
Pitavastatin	OATP	↔ C_{max} ↔ AUC	No change in dose
Caffeine	CYP1A2	↔ C_{max} ↔ AUC	No change in dose
Efavirenz	CYP2B6	↔ C_{max} ↔ AUC	No change in dose
Midazolam	CYP3A	↔ C_{max} ↔ AUC	No change in dose
Digoxin	CYP2B6	↔ C_{max} ↔ AUC	No change in dose

Single-center, open-label trial (N=26). Substrate drugs dosed alone for 3 weeks, then with rezafungin for 3 weeks.[1]

No dose adjustments required for these commonly used drugs when rezafungin is co-administered

AUC, area under the curve; BCRP, breast cancer resistance protein; C_{max}, maximum plasma concentration; CYP, cytochrome P450; MATEs, multidrug and toxin extrusion protein; OATP, organic anion transporting polypeptides; OCT, organic cation transporter; P-gp, P-glycoprotein.

1. Ong, et al. EBMT19 2019; poster B196.

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Rezafungin Phase 2 Treatment Trial

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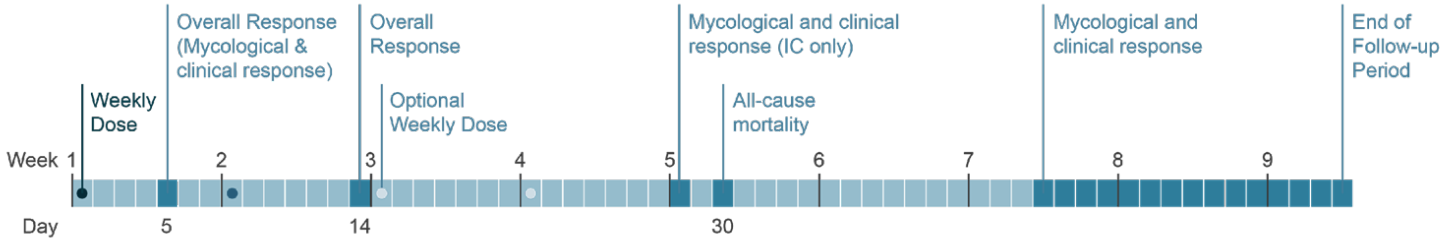
Trial Not Powered for Inferential Statistical Analysis

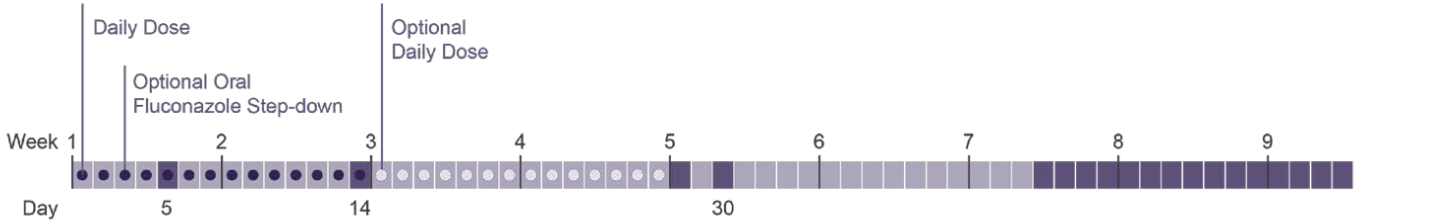
mITT N=183[1]

REZAFUNGIN
(N=122)*
400/400 mg N=76
400/200 mg N=46



CASPOFUNGIN
(N=61)*
70/50 mg

Optional Oral
Fluconazole Step-down
800/400 mg



Analysis Population	Definition	N
• Intent-to-treat (ITT)	All Randomized	207
• Safety	and received ≥1 dose of study drug	202 (97.6%)
• Microbiological Intent-to-treat (mITT)	and had documented *Candida* infection	183 (88.4%)

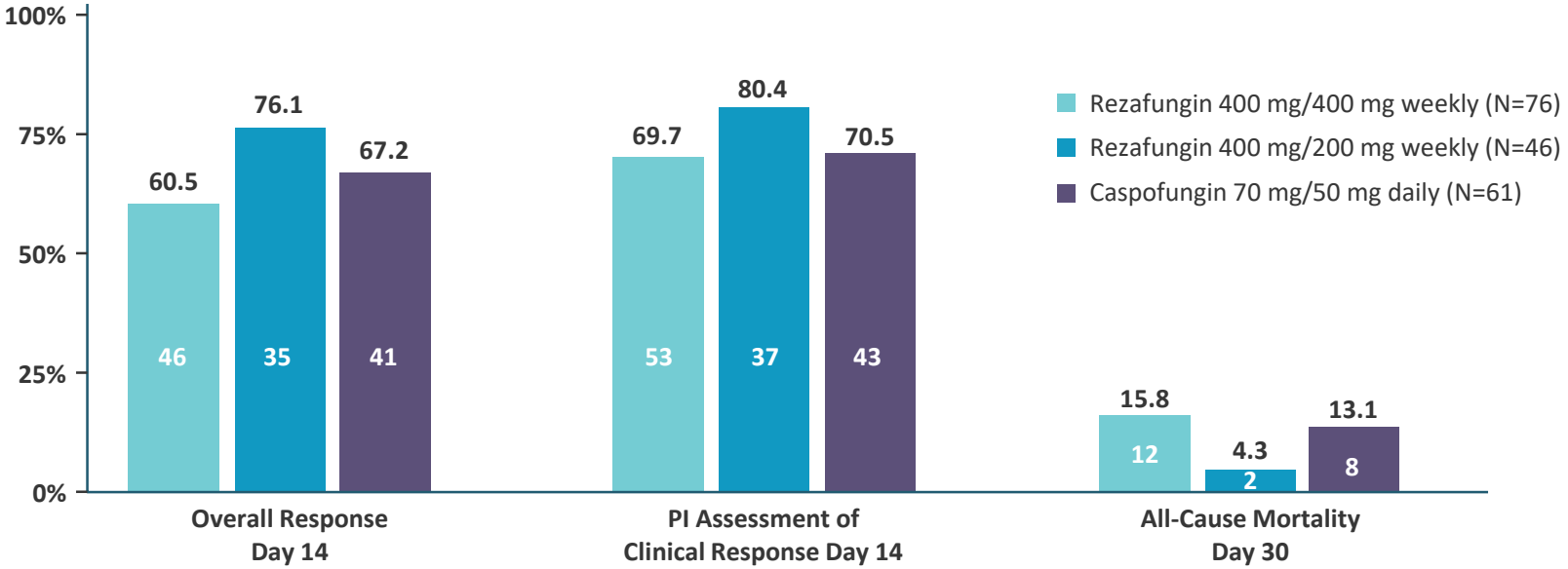
***~21% invasive candidiasis (ITT)**

*N values of the mITT population.
IC, invasive candidiasis; ITT, intent-to-treat; mITT, microbiological intent-to-treat

1. Thompson, et al. *Clin Infect Dis*. 2020, ciaa1380, https://doi.org/10.1093/cid/ciaa1380.

Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requiremer
differ internationally

Summary of Rezafungin Efficacy (mITT Population)[1]



Rezafungin demonstrated similar efficacy vs. caspofungin

EMA, European Medicines Agency; FDA, Food and Drug Administration; mITT, microbiological intent-to-treat; PI, principal investigator.

1. Thompson et al. *Clin Infect Dis*. 2020, ciaa1380, https://doi.org/10.1093/cid/ciaa1380.

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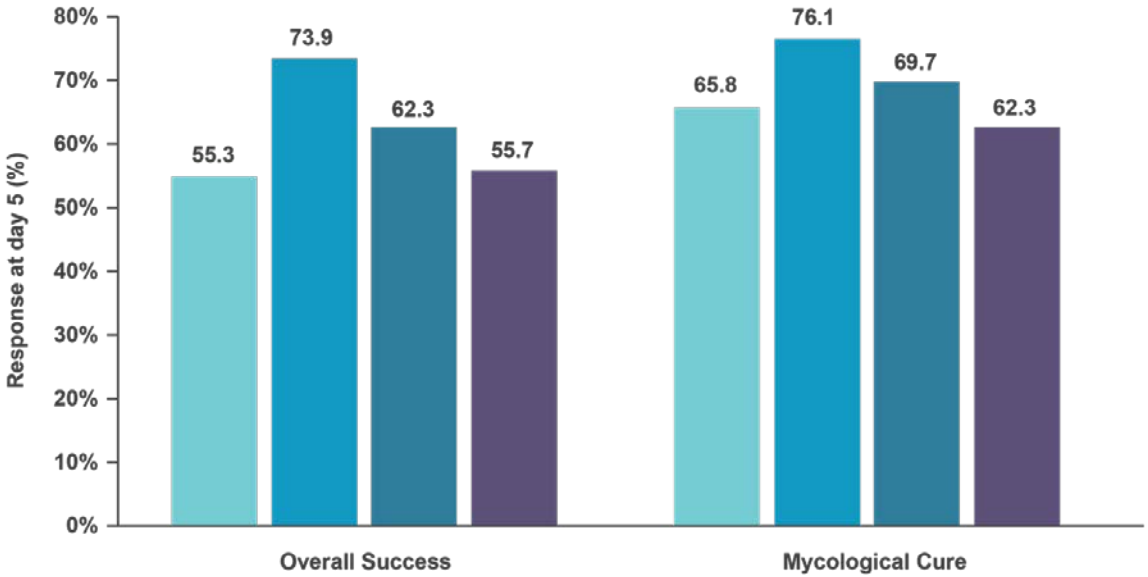
differ internationally

Efficacy Outcomes at Day 5 (mITT Population)[1]



Note initial dose of 400 mg in both rezafungin-treated arms.

Rezafungin efficacy compared with caspofungin evident by day 5

mITT, microbiological intention-to-treat.

1. Thompson, et al. *Clin Infect Dis*. 2020, ciaa1380, https://doi.org/10.1093/cid/ciaa1380.

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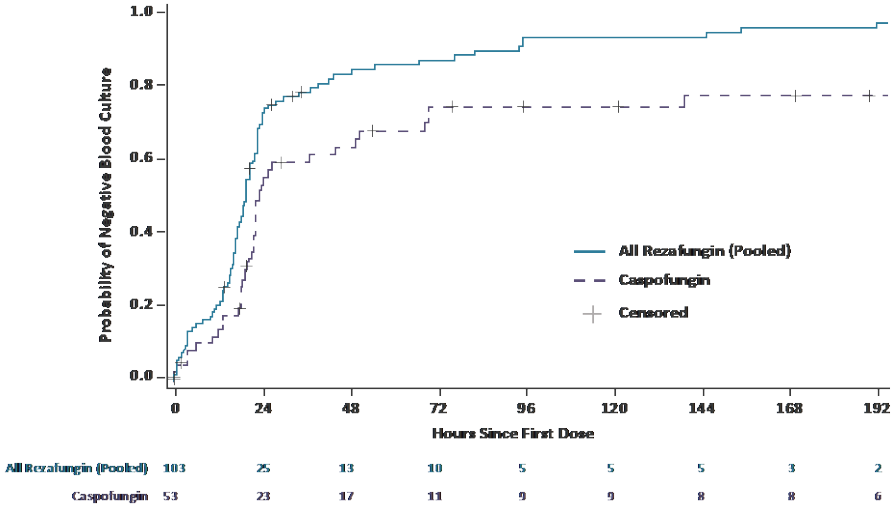
Time to Negative Blood Culture[1]

mITT: All randomized patients who received study drug and had documented C*andida* infection



Pooled rezafungin vs **Caspofungin** (*p*=0.0016 posthoc log-rank test)

- **Rezafungin efficacy early in treatment course suggests clinical effect of high, front-loaded plasma drug exposure**

mITT, microbiological intention-to-treat.

1. Thompson, et al. *Clin Infect Dis.* 2020, ciaa1380, https://doi.org/10.1093/cid/ciaa1380.

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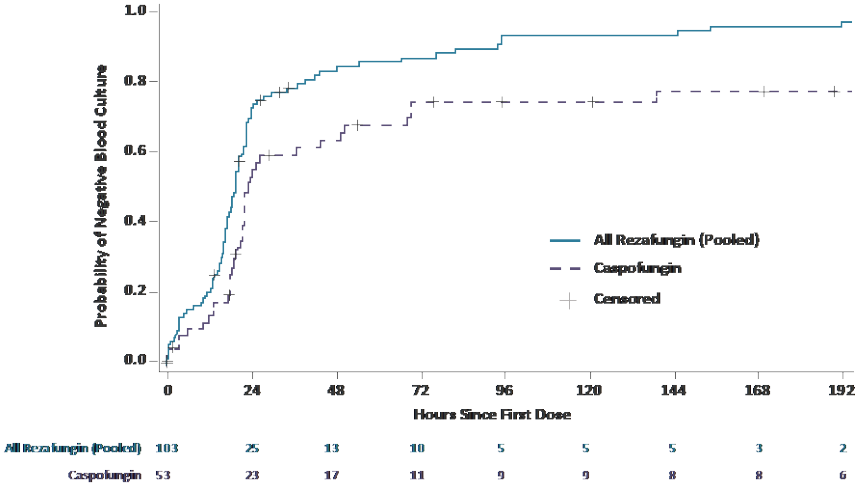
Time to Negative Blood Culture[1]

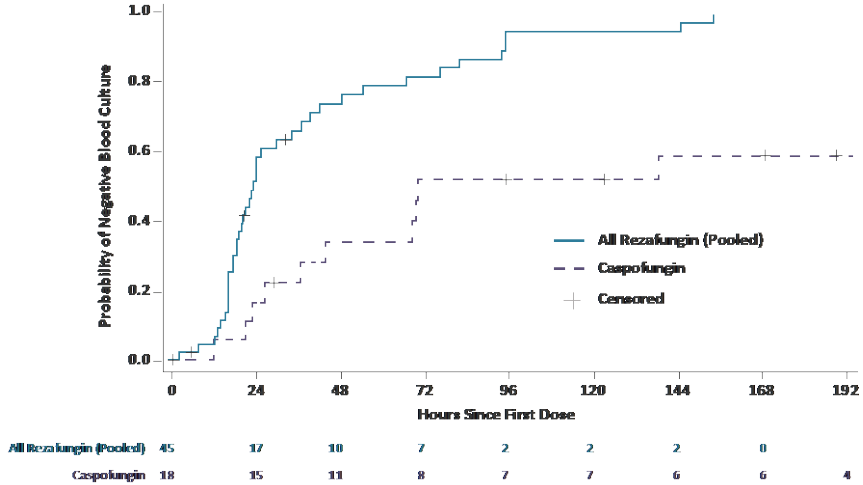
mITT: All randomized patients who received study drug and had documented *Candida* infection



Pooled rezafungin vs **Caspofungin** (*p*=0.0016 posthoc log-rank test)

- Rezafungin efficacy early in treatment course suggests clinical effect of high, front-loaded plasma drug exposure

mITT2: Patients in mITT with positive blood culture within 12h before and 72h after enrollment



Pooled rezafungin vs **Caspofungin** (*p*<0.0001 posthoc log-rank test)

- **More pronounced effect in mITT2 suggests patients with active infection may be more likely to benefit from potential clinical effect of front-loaded exposure**

mITT, microbiological intention-to-treat.

1. Thompson, et al. *Clin Infect Dis*. 2020, ciaa1380, https://doi.org/10.1093/cid/ciaa1380.

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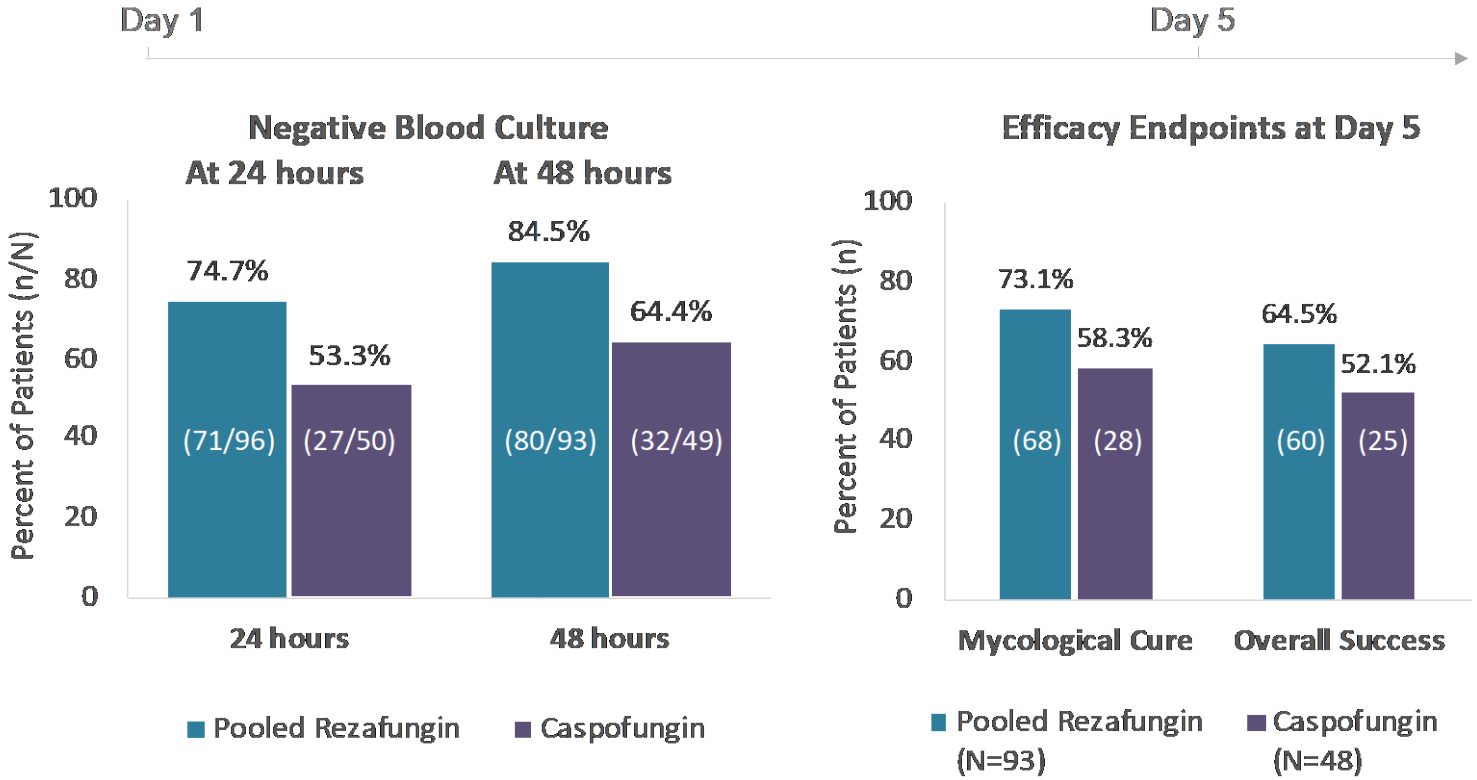
differ internationally

Efficacy Endpoints During Initial Days of Treatment (mITT Population – Patients with Candidemia Only)

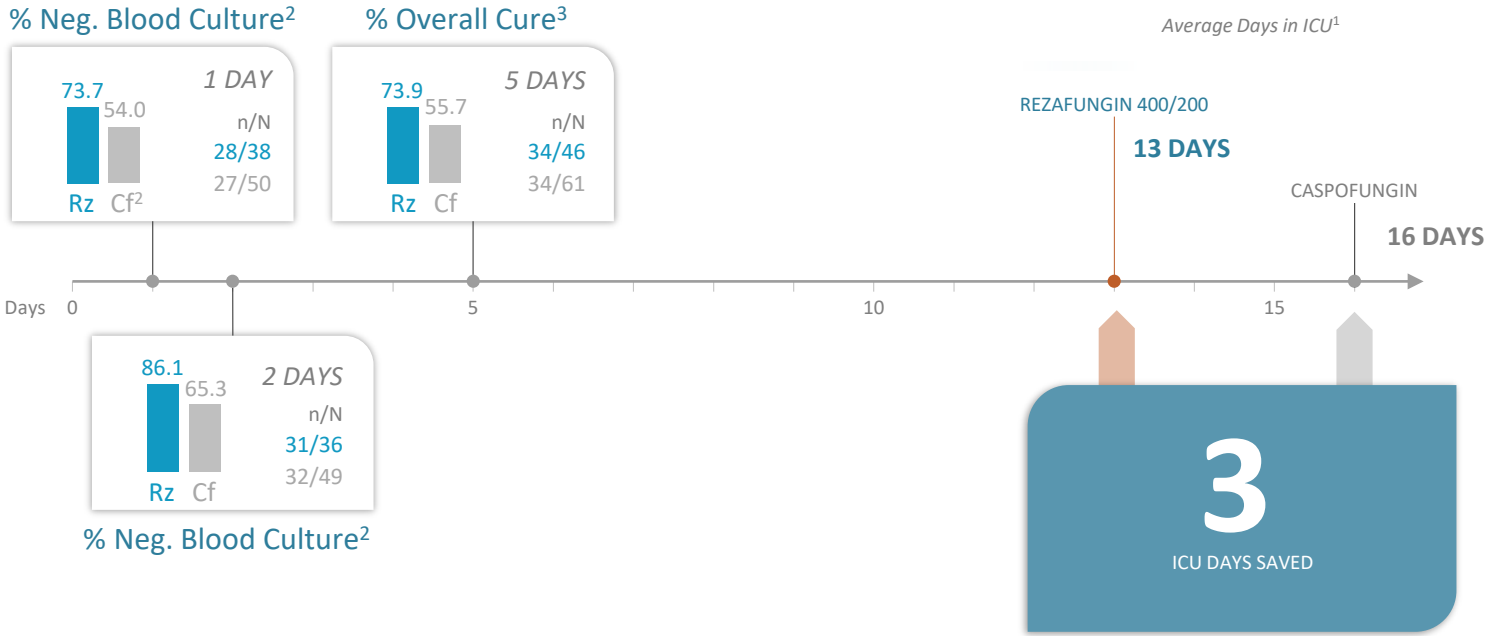


mITT, microbiological intention-to-treat.

1. Soriano, et al. Presented at ECCMID 2021.

Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requiren
differ internationally

Time to Negative Blood Culture (mITT Population)[1]



1. Data on file from STRIVE Phase 2 clinical trial.
2. Data on file. Of patients with confirmed *Candida* infection (positive blood culture), mITT population (%; n/N).
3. STRIVE Phase 2: CID September, 2020.

Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requirem
differ internationally

Summary of Adverse Events (Safety Population)[1]

Adverse Event	Rezafungin 400 mg/400 mg Weekly N=81	Rezafungin 400 mg/200 mg Weekly N=53	All Rezafungin (Pooled) N=134	Caspofungin 70 mg/50 mg Daily N=68
	n (%)			
≥1 TEAE	71 (87.7)	49 (92.5)	120 (89.6)	55 (80.9)
Severe	29 (35.8)	17 (32.1)	46 (34.3)	26 (38.2)
Study drug-related	7 (8.6)	6 (11.3)	13 (9.7)	9 (13.2)
Serious AE	35 (43.2)	28 (52.8)	63 (47.0)	29 (42.6)
Study drug-related	1 (1.2)	1 (1.9)	2 (1.5)	2 (2.9)

No concerning trends with rezafungin safety

TEAE, treatment-emergent adverse event.

1. Thompson, et al. *Clin Infect Dis*. 2020, ciaa1380, https://doi.org/10.1093/cid/ciaa1380.

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differ internationally

Treatment-Emergent Adverse Events (≥10%, Safety Population)[1]

Treatment-emergent Adverse Event	Rezafungin 400 mg/400 mg Weekly N=81	Rezafungin 400 mg/200 mg Weekly N=53	All Rezafungin (Pooled) N=134	Caspofungin 70 mg/50 mg Daily N=68
	n (%)			
Hypokalemia	13 (16.0)	9 (17.0)	22 (16.4)	9 (13.2)
Diarrhea	7 (8.6)	11 (20.8)	18 (13.4)	10 (14.7)
Vomiting	6 (7.4)	8 (15.1)	14 (10.4)	5 (7.4)
Pyrexia	9 (11.1)	4 (7.5)	13 (9.7)	6 (8.8)
Anemia	6 (7.4)	7 (13.2)	13 (9.7)	4 (5.9)
Nausea	4 (4.9)	8 (15.1)	12 (9.0)	6 (8.8)
Abdominal Pain	5 (6.2)	6 (11.3)	11 (8.2)	5 (7.4)
Septic Shock	9 (11.1)	1 (1.9)	10 (7.5)	3 (4.4)

No concerning trends with rezafungin safety

1. Thompson, et al. *Clin Infect Dis*. 2020, ciaa1380, https://doi.org/10.1093/cid/ciaa1380.

Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requireme
differ internationally

Conclusions[1]

Rezafungin 400 mg/200 mg dose demonstrated highest overall response, lowest all-cause mortality, and more rapid clearance of candidemia in STRIVE trial

Rezafungin 400 mg/200 mg dose now in Phase 3 trials

Adverse event data demonstrate the safety of rezafungin and its once-weekly dosing regimen

1. Thompson, et al. *Clin Infect Dis*. 2020, ciaa1380, https://doi.org/10.1093/cid/ciaa1380.

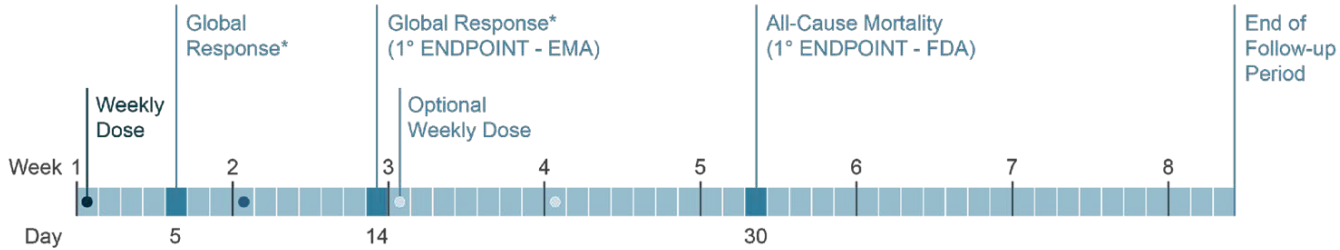
Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requirements differ internationally

Rezafungin Phase 3 Treatment Trial

Rezafungin is in Phase 3 clinical development. Not registered in any country Registration requirements differ internationally

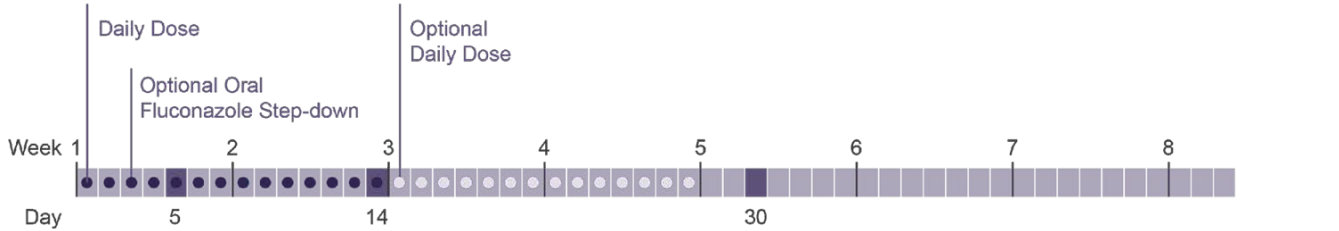
Phase 3 Trial Design Mirrors STRIVE Phase 2 Trial
Prospective, randomized, double-blind, international, >100 centers

REZAFUNGIN
N=92 in mITT population
400/200 mg



CASPOFUNGIN
N=92 in mITT population
70/50 mg

Optional Oral
Fluconazole Step-down
6 mg/kg to nearest 200 mg



*Global Response is defined as Clinical Response (as assessed by the Primary Investigator), Mycological Response and Radiological Response (for qualifying invasive candidiasis patients only).
EMA, European Medicines Agency; FDA, Food and Drug Administration.

1. Clinicaltrials.gov NCT 03667690 accessed 5 Feb 2021.

Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requirement internationally

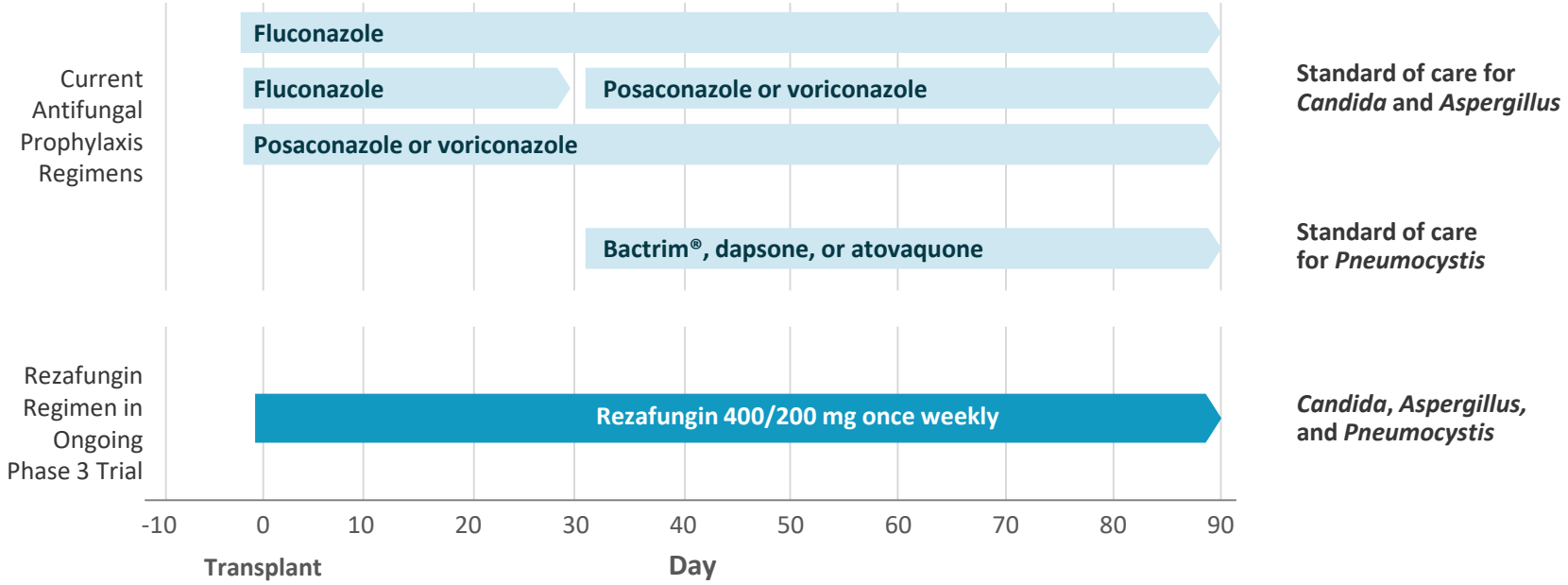
Rezafungin Phase 3 Prophylaxis Trial in Allogeneic BMT

ReSPECT

Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requirements differ internationally

Rezafungin: The Potential For a Simplified Single Drug Paradigm

Antifungal Prophylaxis in Allogeneic Blood and Marrow Transplant Setting[1,2]



1. Sandison. RICAI 2019 presentation. **2.** Tomblyn, et al. *Biol Blood Marrow Transplant*. 2009;15:1143-238.

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differ internationally

Trial Design

Ongoing Phase 3 Trial
IFD Prophylaxis in allogeneic BMT

Phase 3, Prospective, Randomized, Double-Blind, International, Multicenter Trial[1]

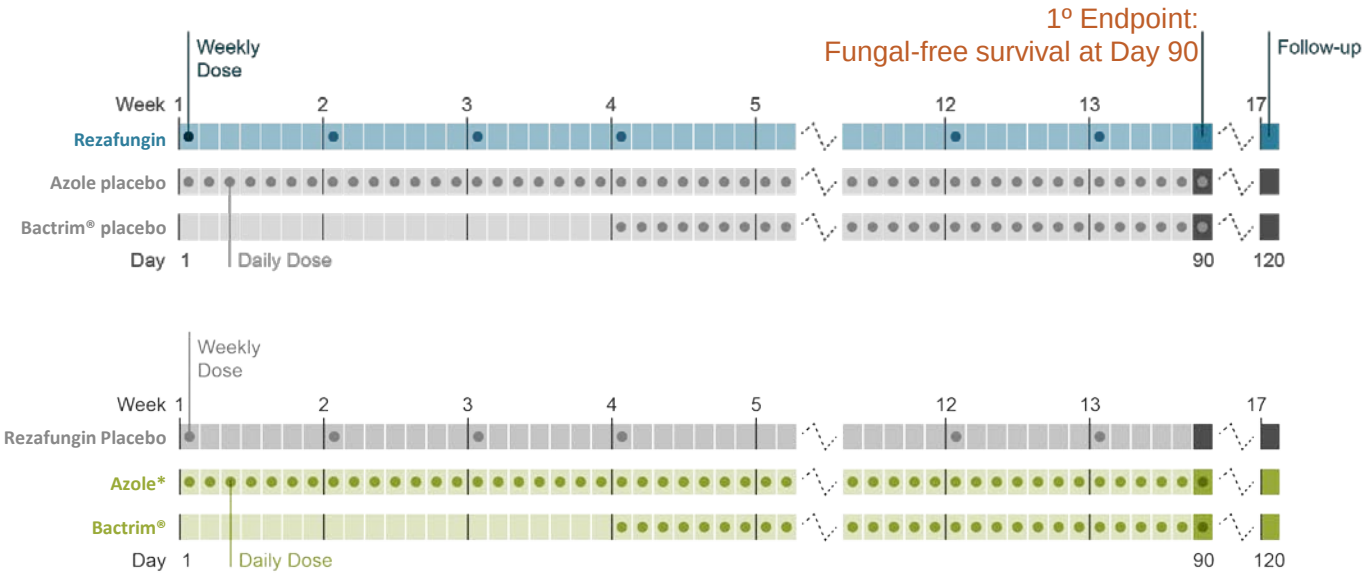
462 patients enrolled

To evaluate efficacy and safety of rezafungin vs standard of care (azole plus TMP/SMX) against IFD caused by *Aspergillus*, *Candida*, and *Pneumocystis* in allogeneic BMT patients

REZAFUNGIN
(N=308)
400/200 mg once weekly

COMPARATOR
(N=154)
400 mg fluconazole QD*
80 mg TMP/400 mg SMX QD

*Patients with acute GVHD can be switched to posaconazole



GVHD, graft-versus-host disease; IFD, invasive fungal disease; SMX, sulfamethoxazole; TMP, trimethoprim.

1. Clinicaltrials.gov NCT04368559 accessed 4 Feb 2021.

Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requireme differ internationally

Rezafungin for Treatment and Prophylaxis

Unique Properties of a Next-Generation Echinocandin

- **Potent and broad-spectrum activity against *Candida*, *Aspergillus*, and *Pneumocystis***
  includes *C. auris,* subset of azole- and echinocandin-resistant isolates, *Aspergillus* activity includes azole-resistant species
- **Enhanced PK**
  extended half-life (~130 hours), once-weekly front-loaded dosing, and greater tissue penetration compared with micafungin
  - Front-loaded dosing may improve early outcomes, time to negative blood culture, and day 5 outcomes compared with caspofungin
- **Safety and DDI profile of the echinocandin class**
  may spare myelosuppression, TDM, hepatic and renal toxicity, non-compliance, and complications of managing/avoiding DDIs
- **Dosing and administration**
  once-weekly use inpatient and outpatient may support earlier hospital discharge
- **Phase 2 STRIVE trial**
  demonstrated rezafungin safety and efficacy for 1st line treatment of documented candidemia and/or invasive candidiasis
- **Phase 3 ongoing**
  - ReSTORE: 1st line treatment of candidemia and/or invasive candidiasis v caspofungin, 2-4 weeks
  - ReSPECT: 1st line prophylaxis of *Candida*, *Aspergillus*, and *Pneumocystis* in alloBMT ± GVHD, vs fluconazole/posaconazole/Bactrim®, 90 days

Rezafungin is in Phase 3 clinical development. Not registered in any country. Registration requirements differ internationally