ReSTORE: Efficacy and Safety Results of the Phase 3, Noninferiority Trial of Rezafungin in the Treatment of Candidemia and/or Invasive Candidiasis (IC)

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Acknowledgments and Disclosures

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Disclosures

- Presenter (G.R. Thompson, III): Research grants (Astellas, Cidara, Mayne, Merck, Scynexis, F2G); Advisory (Astellas, Cidara, Mayne, F2G, Pfizer)

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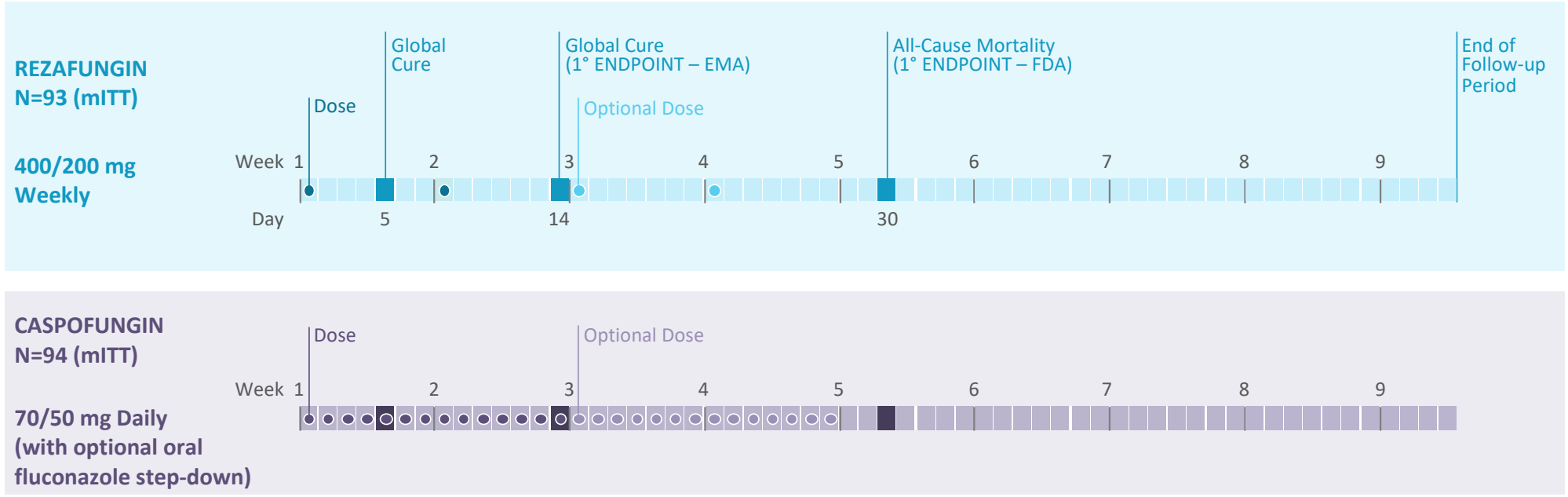
ReSTORE: a Phase 3 Global Trial of Rezafungin in the Treatment of Candidemia and/or IC

- Rezafungin is a next-generation echinocandin in development for treatment of candidemia and IC and for prevention of invasive fungal disease caused by *Candida*, *Aspergillus*, and *Pneumocystis* spp. in blood and marrow transplantation
- Study Objective: To evaluate the efficacy and safety of rezafungin once weekly vs caspofungin once daily, with optional oral step-down to fluconazole in the caspofungin arm[a], in the treatment of documented candidemia and/or IC

Study Design of ReSTORE (NCT03667690)

- Prospective, multicenter, double-blind, double-dummy, 1:1 randomized, controlled, non-inferiority trial



- Study arms were well matched at baseline (as shown in Table 1 of the Poster Abstract)

[a]To maintain blinding, the rezafungin arm included oral placebo administered once daily.

Documented candidemia and/or IC based on systemic signs and mycological confirmation.

N values are presented for the mITT population, comprising all subjects in safety population who had documented *Candida* infection.

Global Cure defined as Clinical Cure (as assessed by the Primary Investigator), Mycological Eradication and Radiological Cure (for qualifying invasive candidiasis patients only).

Primary Endpoints: Global Cure at Day 14 and All-Cause Mortality at Day 30

Modified Intent-To-Treat (mITT) Population

Global response at Day 14 (±1 day)

Endpoint	Proportion of Patients, % (n)	
	Rezafungin 400/200 mg weekly N=93	Caspofungin 70/50 mg daily N=94
Global Cure[a] at Day 14	59.1 (55)	60.6 (57)
Difference (95% CI)[b]	–1.1 (–14.9 to 12.7)	
Failure	30.1 (28)	30.9 (29)
Indeterminate	10.8 (10)	8.5 (8)

Non-inferiority (NI) achieved; lower bound of 95% CI was within 20% NI margin

All-cause mortality at Day 30 (–2 days)

Endpoint	Proportion of Patients, % (n)	
	Rezafungin 400/200 mg weekly N=93	Caspofungin 70/50 mg daily N=94
ACM at Day 30	23.7 (22)	21.3 (20)
Difference (95% CI)	2.4 (–9.7, 14.4)	
Known deceased	20.4 (19)	18.1 (17)
Unknown survival	3.2 (3)	3.2 (3)
Alive	76.3 (71)	78.7 (74)

Non-inferiority (NI) achieved; upper bound of 95% CI was within the 20% NI margin

[a]Defined as 1) clinical cure as assessed by the investigator; 2) radiological cure for those patients with IC documented by radiologic/imaging evidence at baseline; and 3) mycological eradication, as confirmed by an independent DRC.

[b]Adjusted for the two randomization strata and APACHE II score/ANC at screening.

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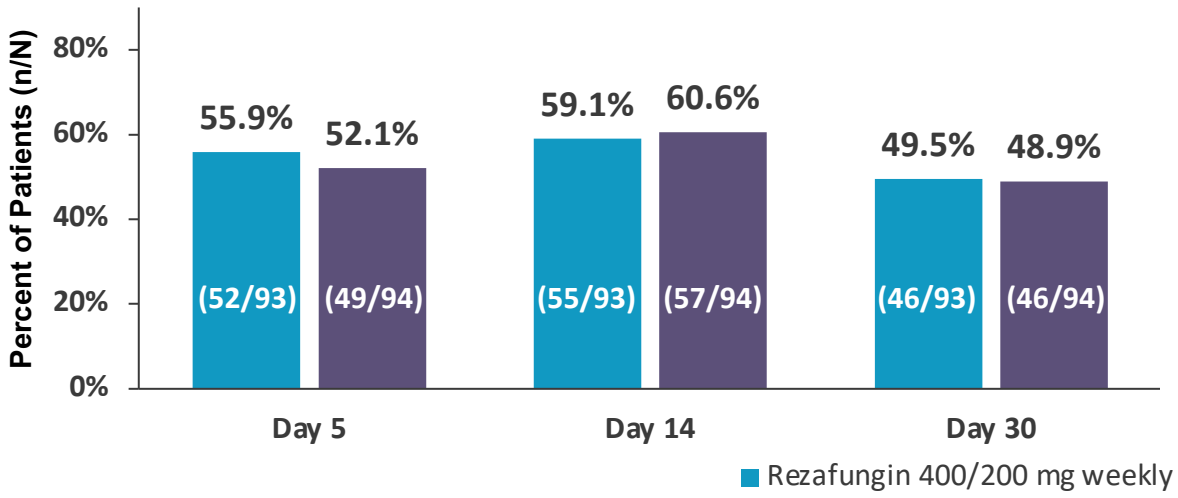
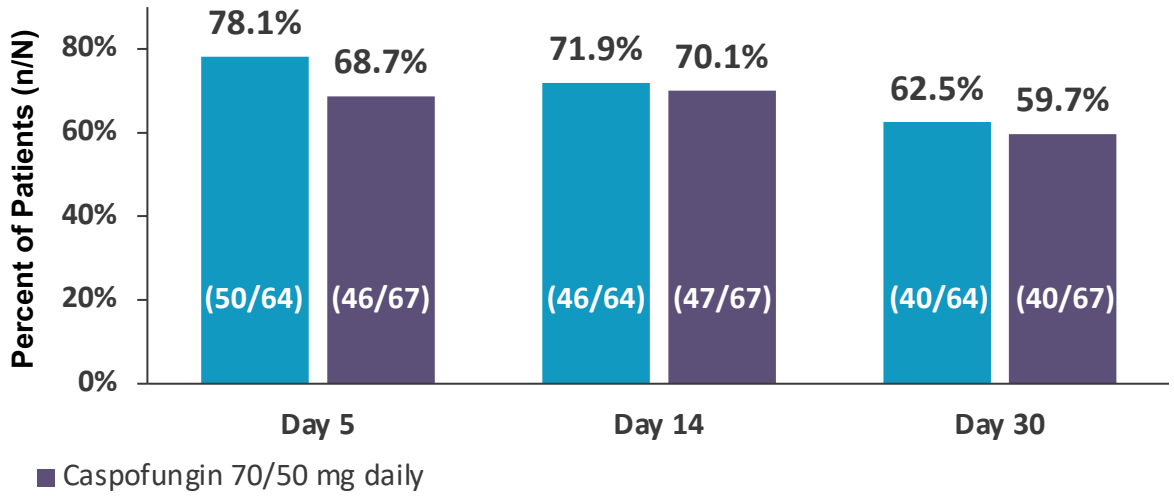
Global Cure and Mycological Eradication at Days 5, 14, and 30

mITT Population – Secondary and Exploratory Endpoints

Global cure[a]



Mycological Eradication[b]



[a]Defined as 1) clinical cure as assessed by the investigator; 2) radiological cure for those patients with IC documented by radiologic/imaging evidence at baseline; and 3) mycological eradication, as confirmed by an independent DRC.

[b]Subjects with candidemia only.

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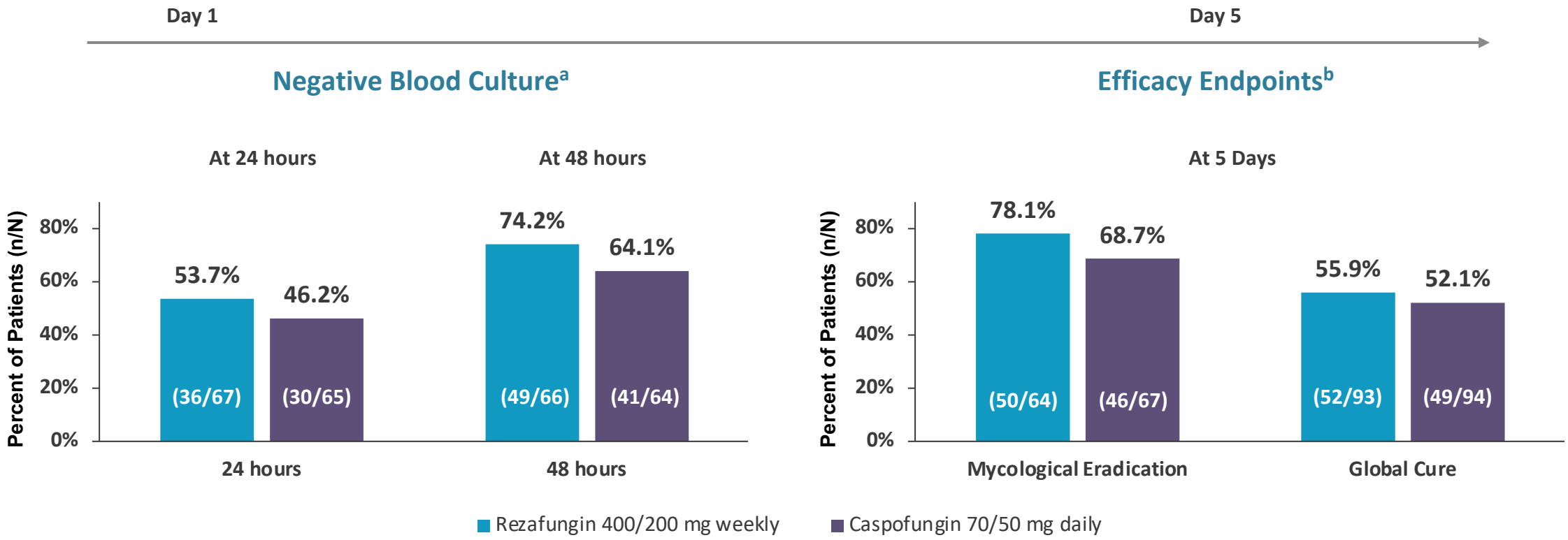
Outcomes in the Initial Days of Treatment

mITT Population – Secondary and Exploratory Endpoints



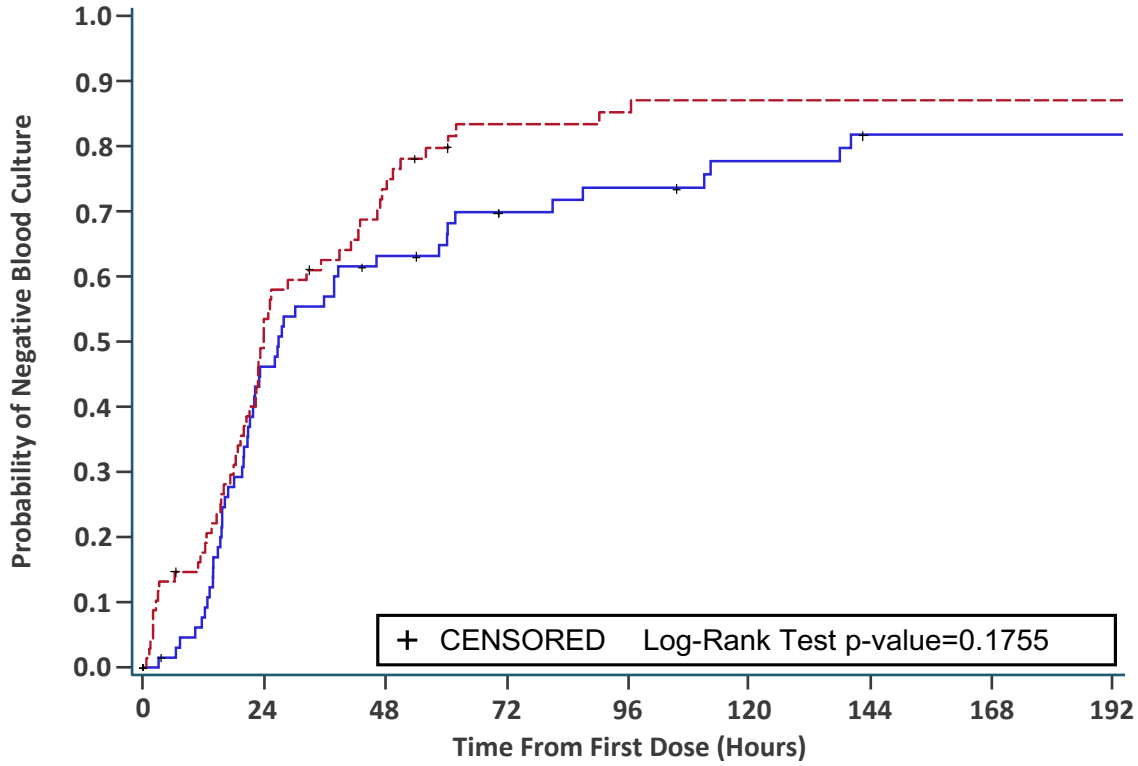
[a]Subjects with positive blood culture before randomization.

[b]Mycological eradication rates for subjects with candidemia only.

Time to Negative Blood Culture

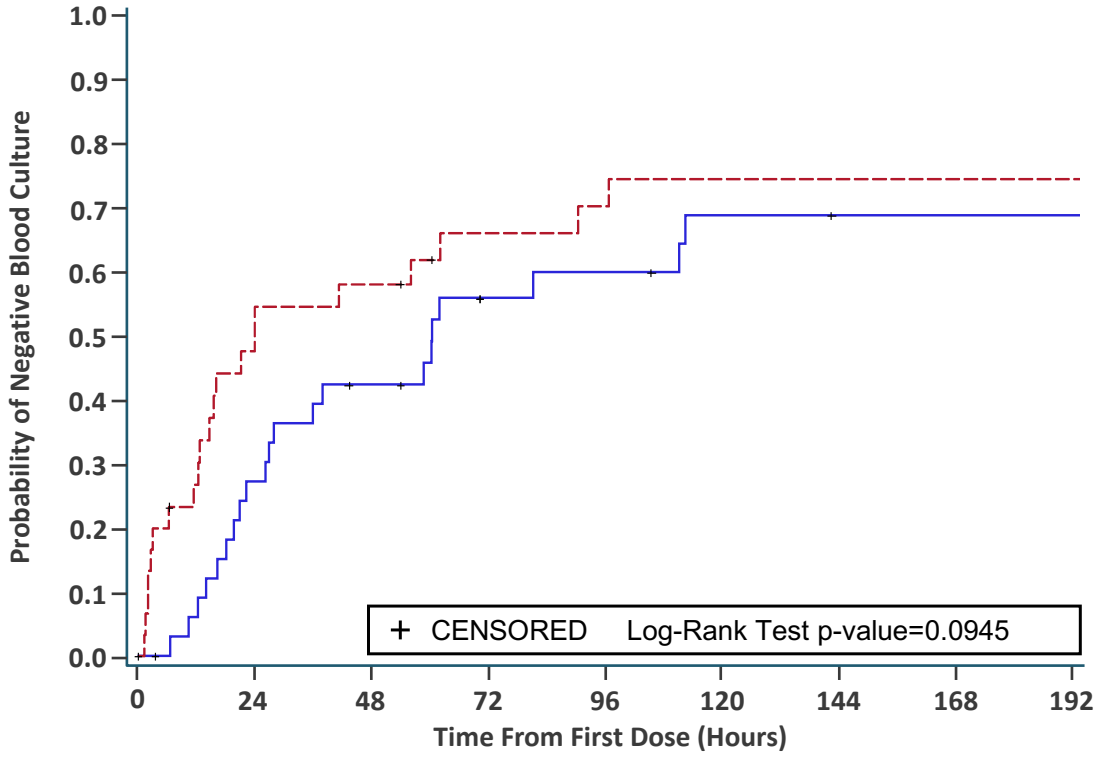
mITT and mITT2 – Exploratory Endpoint – Subjects with Positive Blood Culture Before Randomization (Candidemia-only)

mITT



Rezafungin	69	31	17	9	8	7	7	7	7
Caspofungin	69	35	23	16	14	11	8	8	8

mITT2



Rezafungin	30	13	12	8	7	6	6	6	6
Caspofungin	35	24	18	11	10	7	6	6	6

Treatment ---- REZAFUNGIN —— CASPOFUNGIN

- mITT: Subjects who received at least one dose of study drug and had a positive culture from blood or other normally sterile site up to 96 hours before randomization.
- mITT2: Subjects in mITT who had a positive blood culture within 12h prior to or within 72h after randomization.

Safety Overview: Summary of AEs

Adverse Event (AE)	Proportion of Patients Who Experienced an AE, n (%)	
	Rezafungin 400/200 mg weekly N=98	Caspofungin 70/50 mg daily N=98
≥1 TEAE	89 (90.8)	83 (84.7)
Study drug-related[a]	16 (16.3)	9 (9.2)
Serious AE	55 (56.1)	52 (53.1)
Study drug-related[a]	2 (2.0)	3 (3.1)
AE leading to study drug discontinuation	13 (13.3)	11 (11.2)

[a]Study drug-related AEs may be considered related to study drug or placebo due to investigator blinding.
5 AEs in the rezafungin arm were considered related to placebo administration.
0 AEs in the caspofungin arm were considered related to placebo administration.

AE: adverse event; TEAE: treatment-emergent AE.

Summary

- Rezafungin is a next-generation once-weekly echinocandin in development for treatment of candidemia and IC and for prevention of invasive fungal disease caused by *Candida*, *Aspergillus*, and *Pneumocystis* spp. in blood and marrow transplantation
- The ReSTORE trial evaluated the efficacy and safety of rezafungin QWk vs caspofungin QD in the treatment of documented candidemia and/or IC
- Rezafungin was found to be non-inferior to caspofungin for both of its primary endpoints (all-cause mortality at Day 30, US FDA; global cure at Day 14, EMA)
- Exploratory endpoints of early efficacy (mycological eradication and global cure at Day 5, time to negative blood culture) support the conclusion that rezafungin is efficacious for the treatment of candidemia and IC
- Rates of AEs and SAEs were similar between study arms

25 April 2022, 8:30 – Session "*Emerging Clinical Data and Interventional Studies*"

Results from Integrated Analysis of Rezafungin Ph2/Ph3 Trials