Exebacase (Lysin CF-301) Improved Clinical Responder Rates In Methicillin Resistant *Staphylococcus Aureus* (MRSA) Bacteremia Including Endocarditis Compared To Standard Of Care Antibiotics (SOC) Alone In A First-in-Patient Phase 2 study

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for the Exebacase Phase 2 Study Group

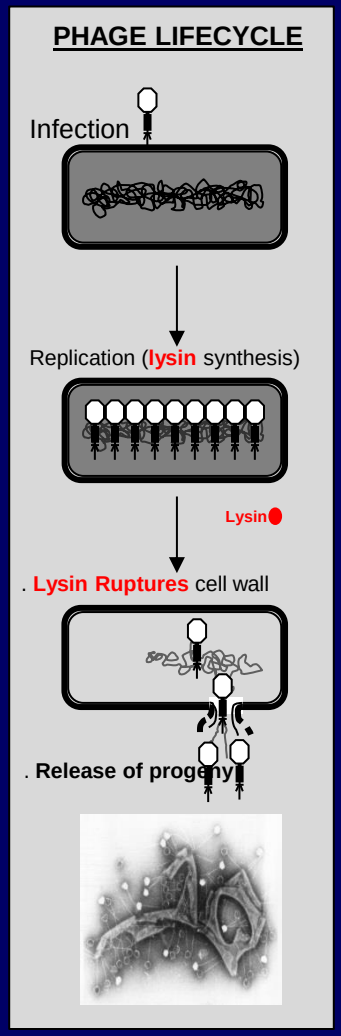
Disclosures

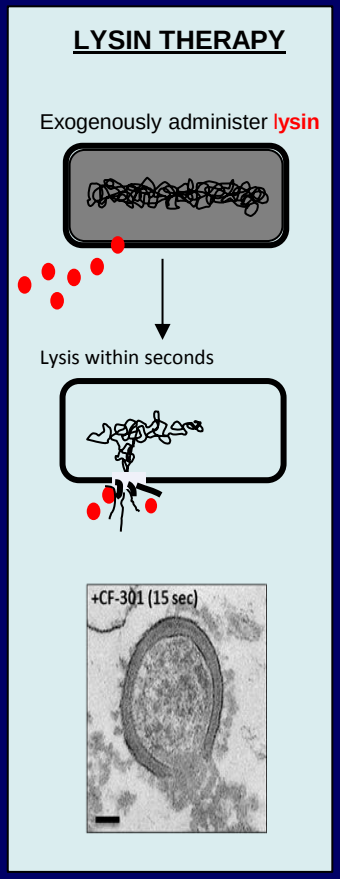
Nature of Relevant Financial Relationship	Commercial Interest
Grant or research support	ContraFect; Cerexa/Actavis, Cubist/Merck; Genentech; Karius; MedImmune, NIH
Paid consultant	Achaogen, Astellas, Arsanis; Affinergy; Basilea; Bayer; Cerexa, ContraFect; Cubist; Debiopharm, Durata, Grifols; Genentech; MedImmune, Merck, Medicines Co; Pfizer, Novartis, Novadigm, Theravance; xBiotech,
Speaker's Bureau	None
Employment	Duke University
Honoraria	Theravance; Green Cross
Membership on advisory committees or review panels, board membership,	Chair- Merck V710 Advisory Board Committee
Ownership Interest (e.g., stocks, stock options or other interests	NONE
Other relevant financial interests	Patent pending in sepsis diagnostic

BACKGROUND
S. aureus Bacteremia (SAB) & Endocarditis

- Common & potentially lethal
- Standard of Care (SOC) therapy suboptimal
- MRSA particularly problematic
- New treatments are required

Lysins – A New Class of Antibacterials





Potent cell wall hydrolase enzymes derived from bacteriophage

- *In nature – highly potent bacterial killer in bacteriophage armamentarium*
- *New technology – recombinantly produced and purified biologic therapy*

Novel MOA – peptidoglycan hydrolysis leading to osmotic lysis

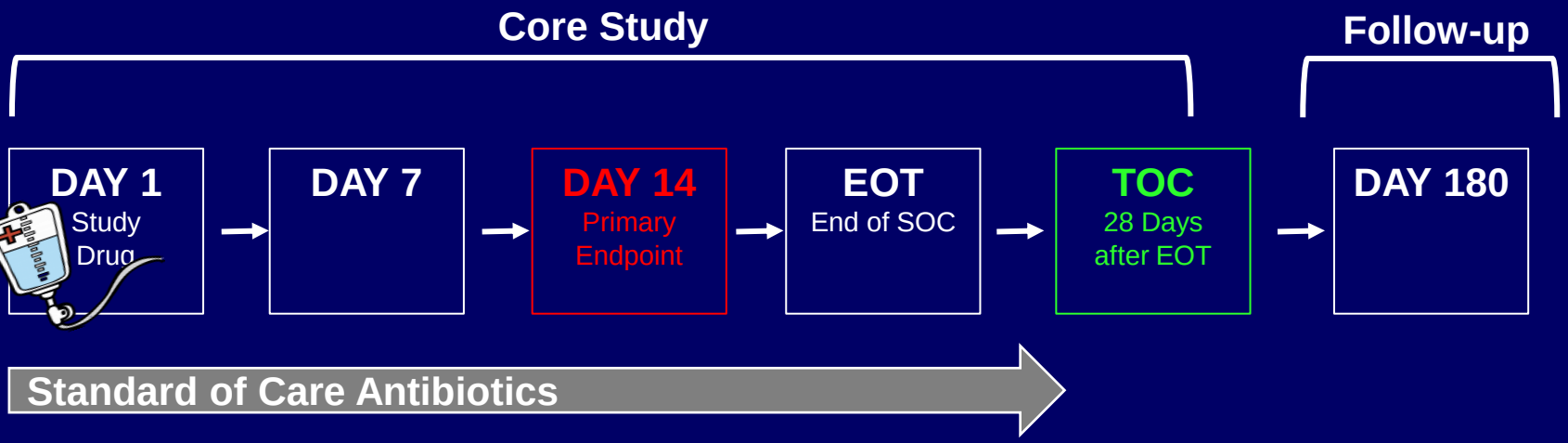
Hallmark Features

- *Rapid, targeted, species-specific killing*
- *Potent eradication of biofilms*
- *Synergy with conventional antibiotics*
- *Low propensity for resistance*

Study Design

- Phase II Randomized, double-blind, placebo-controlled, superiority design Proof of Concept study
  - *Compares exebacase (EXE) + standard of care antibiotics (SOC) vs SOC*
- Study population
  - *Adults with documented S. aureus bacteremia including endocarditis*
- Study objectives
  - *Describe safety/tolerability*
  - *Estimate clinical outcome at Day 14 after study drug administration*
  - *Describe the pharmacokinetic parameters of EXE*
- Primary endpoint – Clinical Responder Rate at Day 14
  - *"Improvement/resolution of signs/symptoms, no new metastatic foci or complications, and no changes in antibiotic treatment or further medical intervention due to lack of response in patients alive at time of evaluation"*
  - Determined by independent, blinded Adjudication Committee

Study Schema



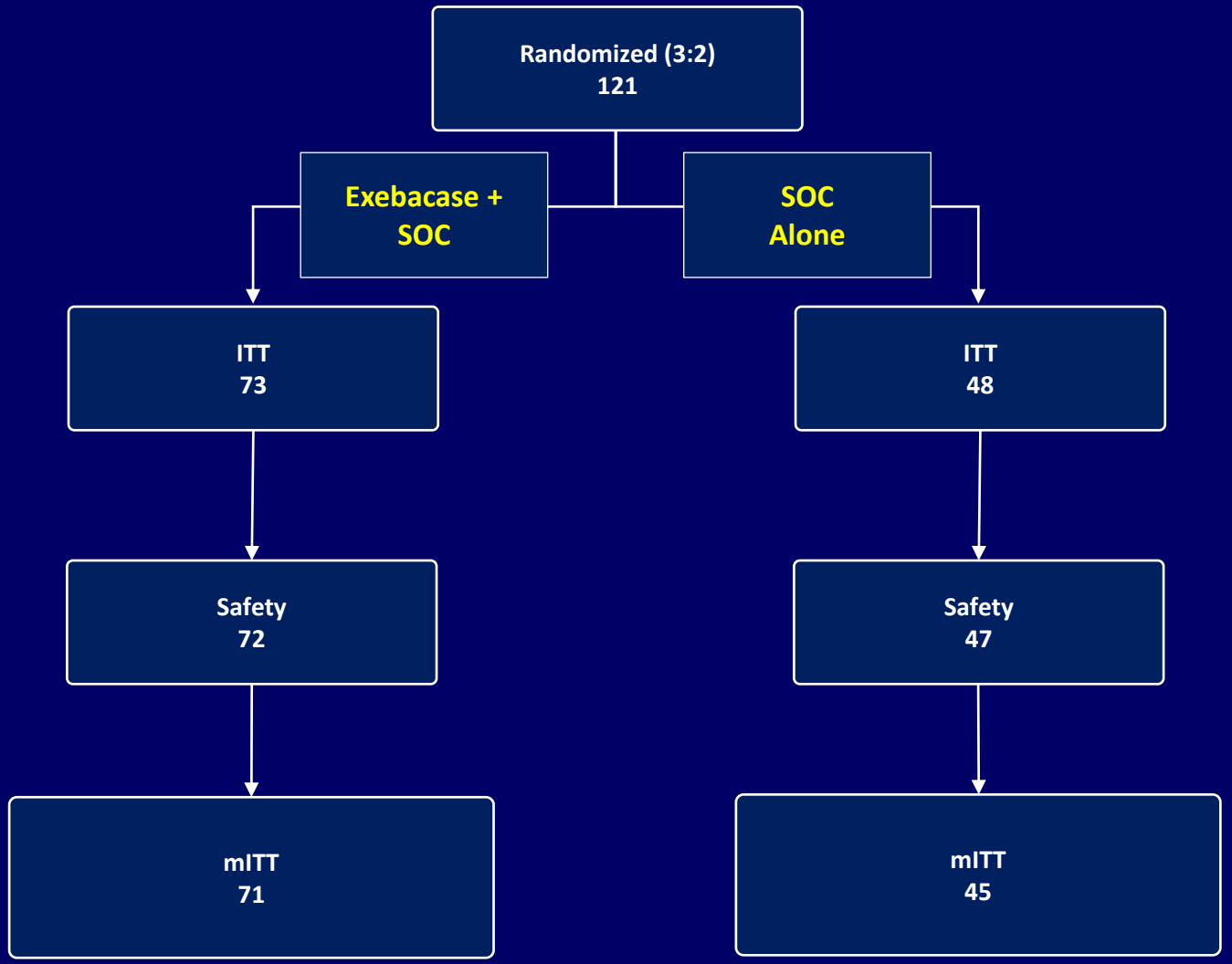
Number of days of SOC antibiotic treatment varied widely: mean days, (range)

EXE + SOC : 33.3 days, (2 - 181)

SOC Alone: 30.5 days, (3 - 91)

Results

Patient Disposition



Demographics were Similar in Both Groups

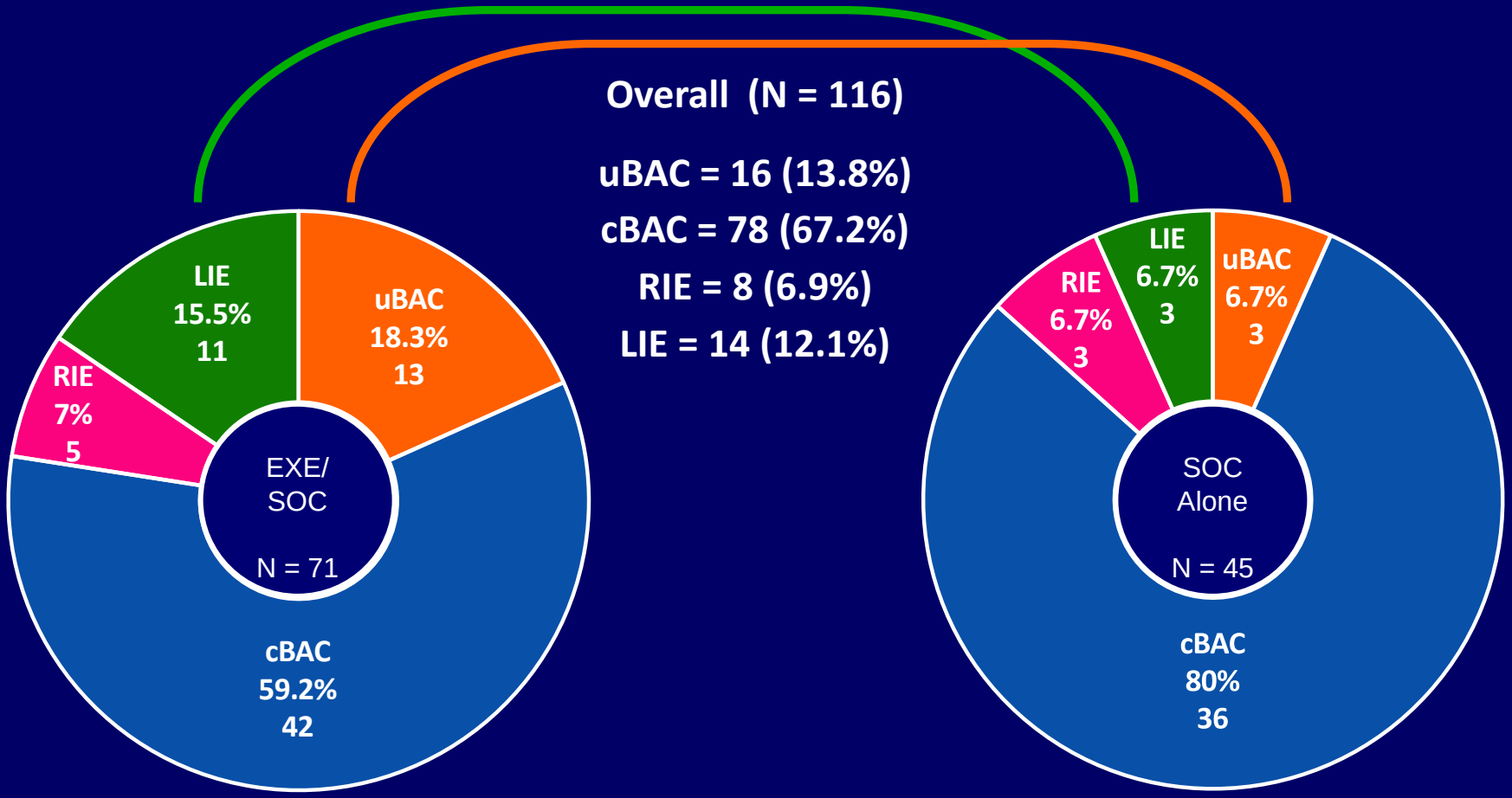
	Exebacase + SOC N = 73	SOC Alone N = 48
Age (years, mean)	56.6	55.0
Age > 50 (n, %)	47 (64.4)	34 (70.8)
Gender (n, %)		
Female	23 (31.5)	16 (33.3)
Male	50 (68.5)	32 (66.7)
Race (n, %)		
Black	14 (19.2)	8 (16.7)
White	51 (69.9)	30 (62.5)
Other	8 (11.0)	10 (20.8)
CrCl (ml/min, n, %)		
<30	28 (38.4)	12 (25.0)
30 to <60	13 (17.8)	7 (14.6)
60 to <90	5 (6.9)	4 (8.3)
≥90	24 (32.9)	23 (47.9)
Missing	3 (4.1)	2 (4.2)

Risk Factors and Infecting Pathogen (mITT)

	Exebacase + SOC N = 71	SOC Alone N = 45
	n (%)	n (%)
Risk Factor		
Poorly controlled diabetes mellitus[1]	20 (32.3)	8 (20.5)
Injection drug use[1]	6 (9.7)	5 (12.8)
Pre-existing valvular heart disease	1 (1.4)	3 (6.7)
Surgery within prior 30 days	11 (15.5)	5 (11.1)
Extravascular foreign material	9 (12.7)	9 (20.0)
Diagnosis of AIDS[1]	2 (3.2)	1 (2.6)
Hemodialysis	21 (29.6)	8 (17.8)
SIRS[1]	45 (72.6)	27 (69.2)
Infecting Pathogen[2]		
MRSA	27 (38.0)	16 (35.6)
MSSA	44 (62.0)	30 (66.7)

[1] Risk factor not included in Protocol Amendment 4; denominator is 62 for exebacase and 39 for antibiotics alone.
[2] One patient in the placebo group had both MRSA and MSSA.

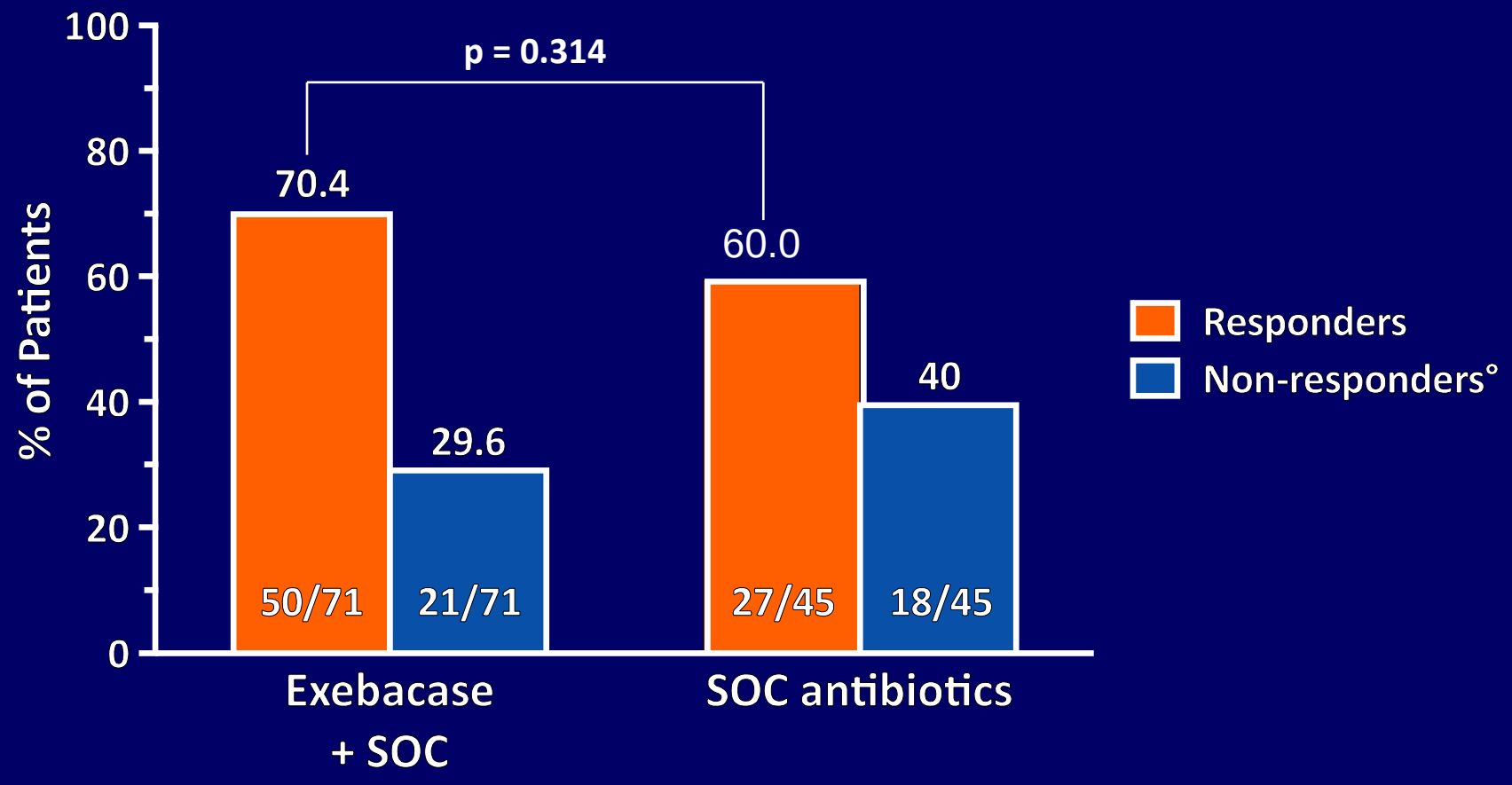
Distribution of Final Diagnoses* Differed Between Groups



* As assessed by blinded Adjudication Committee

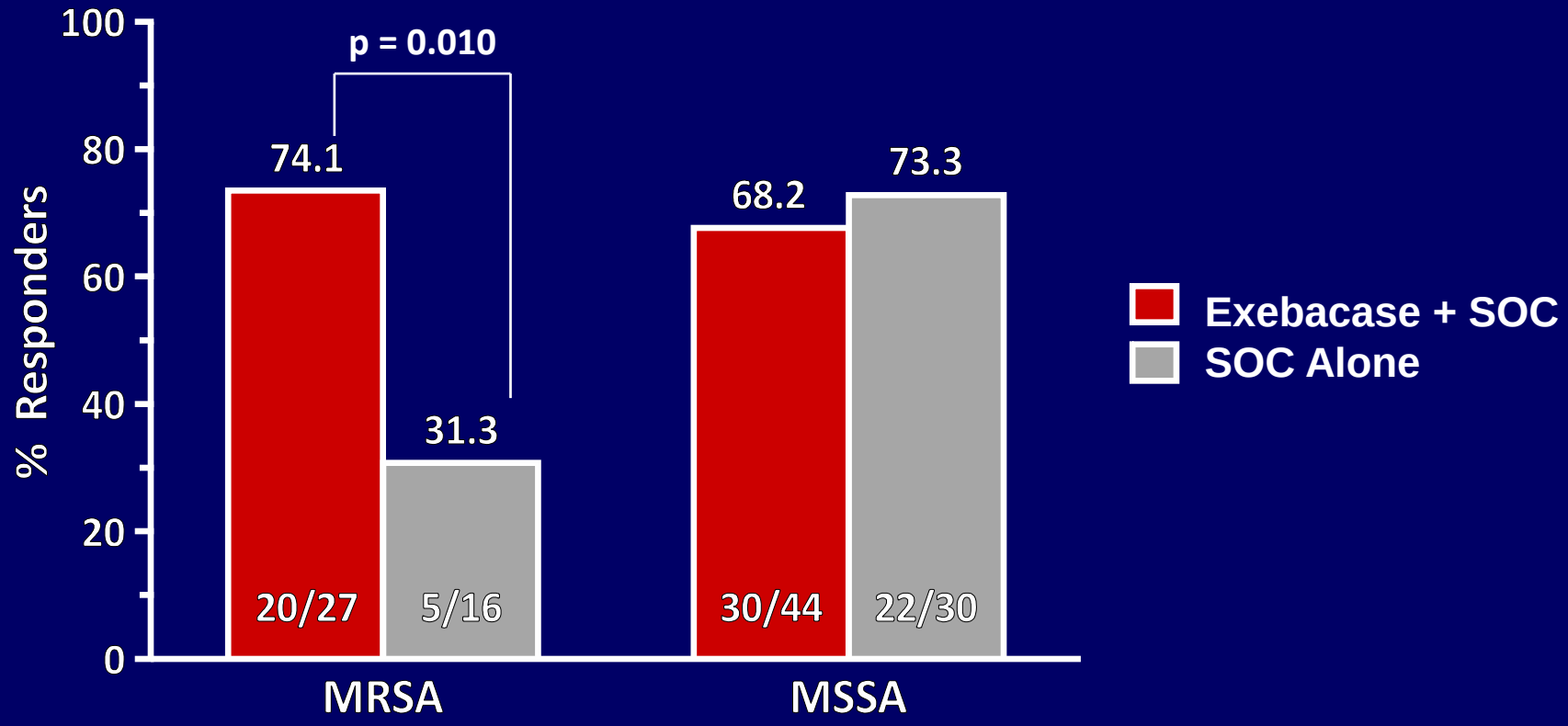
uBAC = uncomplicated bacteremia
cBAC = complicated bacteremia
RIE = right-sided endocarditis
LIE = left-sided endocarditis

Primary Efficacy Endpoint: Clinical Responder Rates at Day 14 (mITT)

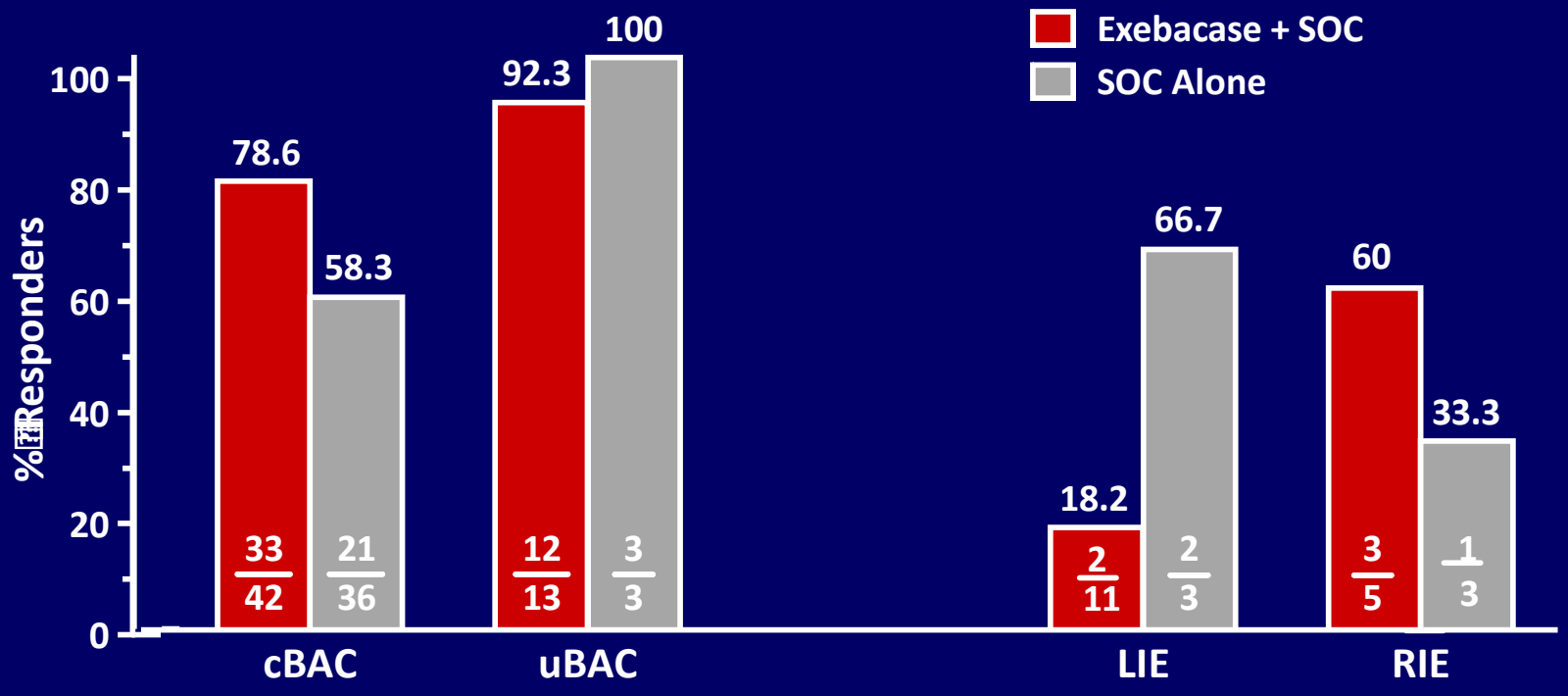


° indeterminates included with non-responders
(3 in Exebacase group, 5 in antibiotics alone group)

Clinical Responder Rates at Day 14
Prespecified MRSA Subgroup Analysis

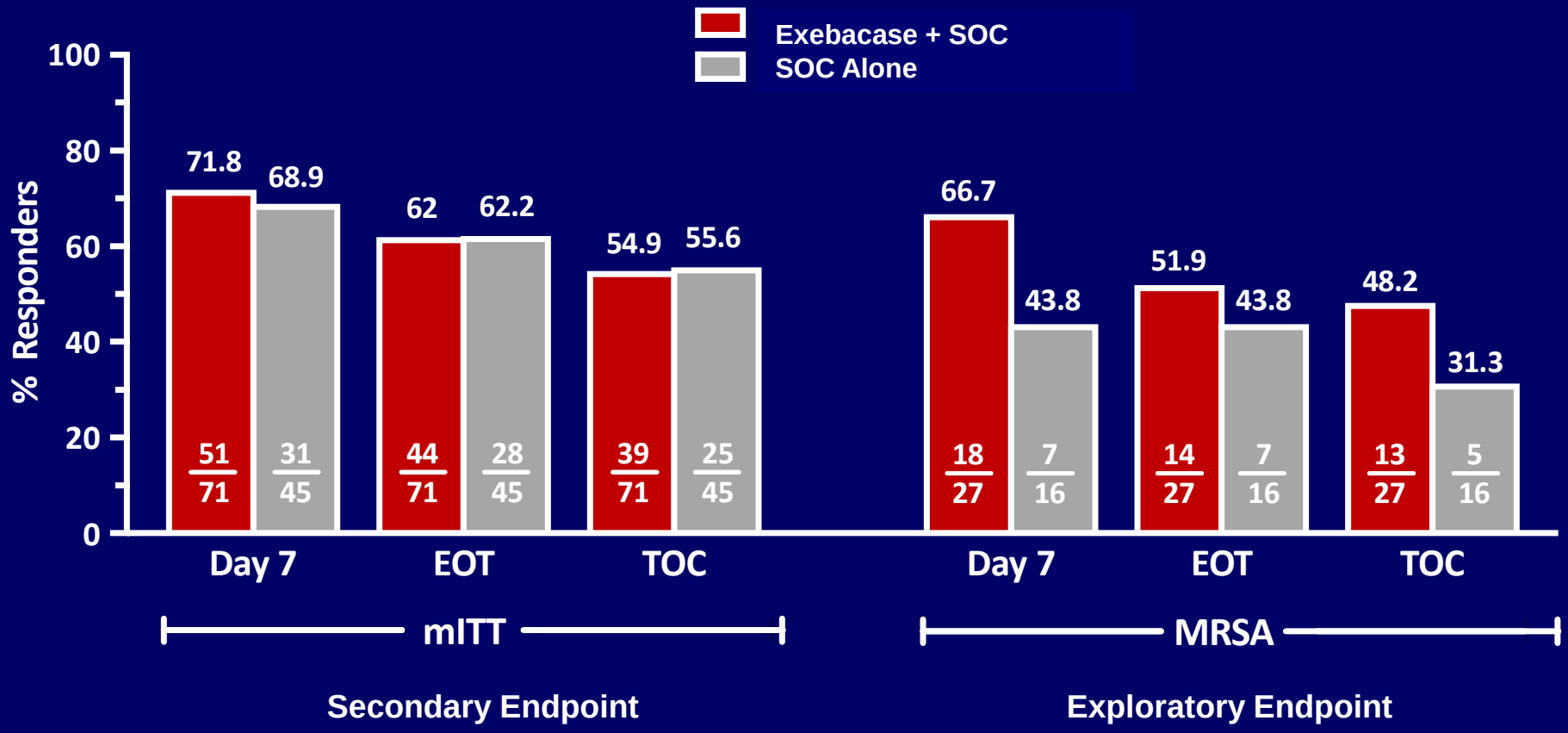


Clinical Responder Rates at Day 14
Prespecified Final Diagnosis* Subgroups



* As assessed by blinded Adjudication Committee

Clinical Responder Rates at Day 7, EOT and TOC



Safety Summary

	Exebacase + SOC N = 72 n (%)	SOC Alone N = 47 n (%)
TEAE through TOC	64 (88.9)	40 (85.1)
TEAE through Day 7	48 (66.7)	31 (66.0)
Serious TEAE through TOC	33 (45.8)	21 (44.7)
AE leading to discontinuation of study drug	0	0
Total Deaths through TOC	14 (19.4)	7 (14.9)

TEAE = treatment emergent adverse event

Summary and Conclusions: Exebacase

- **A first in class direct lytic agent**

- **In this Phase 2 trial, a single IV dose of exebacase + SOC to treat *S. aureus* SAB/IE:**

  - was well tolerated

  - resulted in 42.8% higher clinical responder rate in prespecified MRSA subgroup vs SOC alone

- **Results support further evaluation of exebacase in a definitive Phase 3 study**