

**Exebacase Reduced Length of Stay and 30-Day Readmission Rates for US Patients with MRSA Bacteremia Including Endocarditis Compared to Standard of Care Antibiotics Alone in a Phase 2 Study**

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## BACKGROUND - *S. aureus* Bacteremia (SAB) & Endocarditis

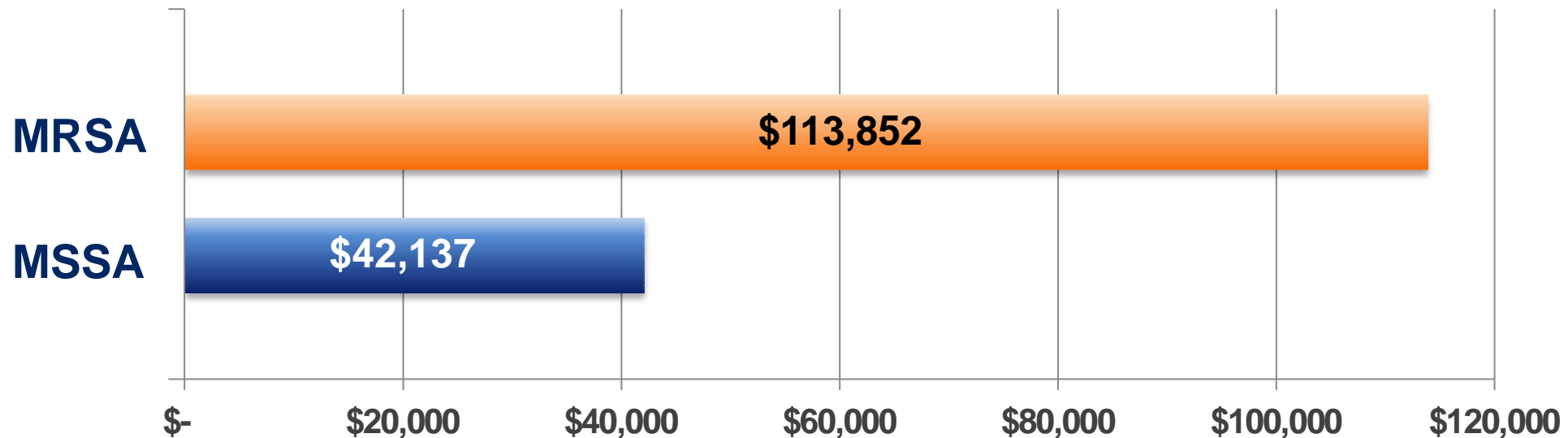
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- Common & potentially lethal
- Standard of Care (SOC) therapy suboptimal
- MRSA particularly problematic
- No new treatments in over a decade

# MRSA Bacteremia: High Societal and Economic Costs

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## Hospital Cost for ICU Patients with a Nosocomial *Staphylococcus aureus* Bloodstream Infection (BSI)<sup>(1)</sup>

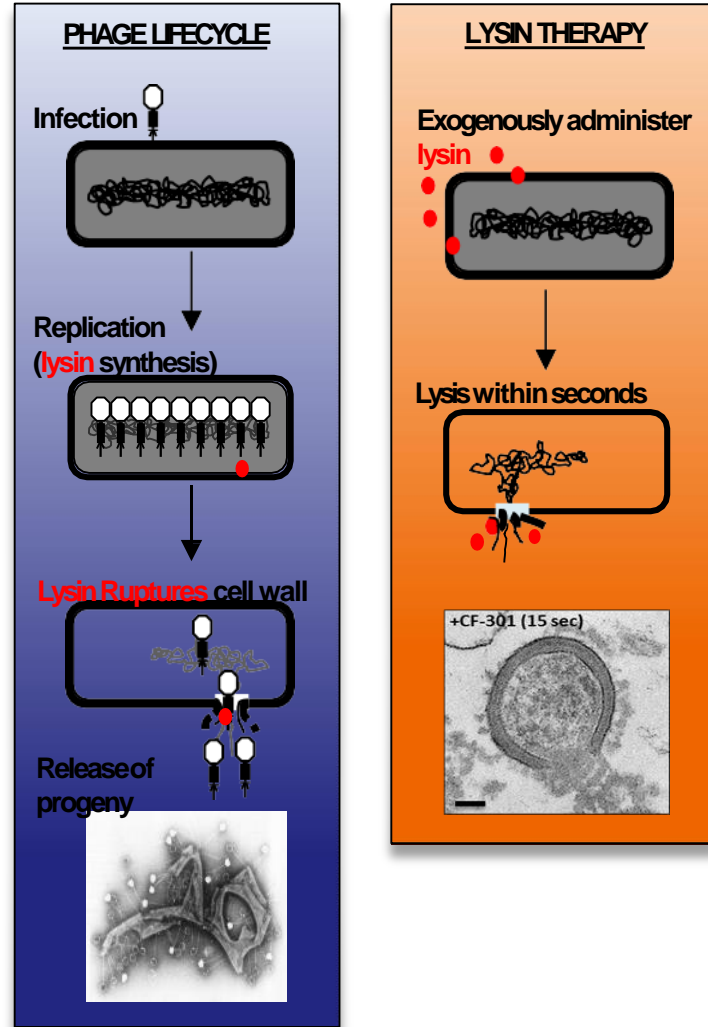


**MRSA surgical site and central line-associated bloodstream infections were found to increase length of stay the most (up to 23 days) and be the highest cost (up to \$175,000)<sup>(2)</sup>**

Sources: (1) Ben-David, Infection Control and Hospital Epidemiology, May 2009, Vol. 30, No. 5, pp. 453-460

(2) Zimlichman, JAMA Internal Medicine, September 2, 2013

# Lysins – A New Class of Highly Differentiated Antibacterials



## Lysins are Direct Lytic Agents

- *Potent cell wall hydrolase enzymes*

## New modality with novel MOA

- *Peptidoglycan hydrolysis leading to osmotic lysis*
- *New Technology – Recombinantly produced and purified protein therapeutic*

## Hallmark features

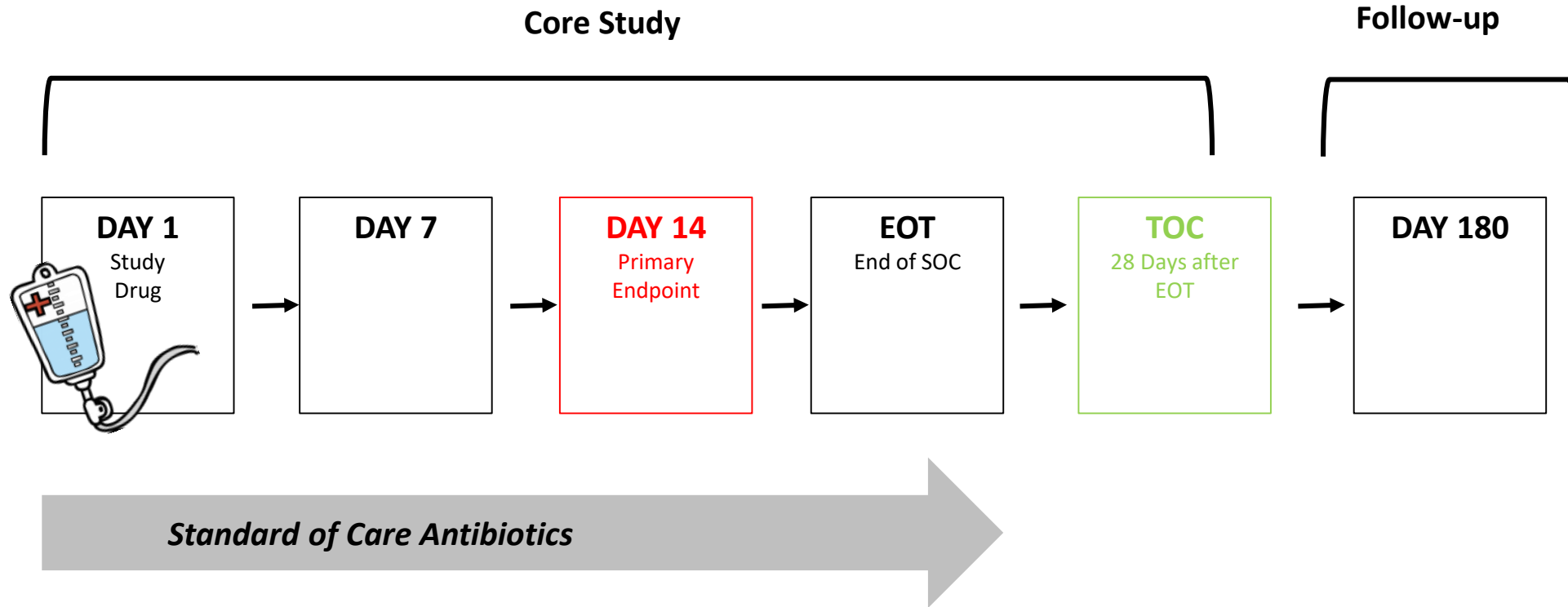
- *Rapid, targeted, species-specific killing*
- *Potent eradication of biofilms*
- *Synergy with conventional antibiotics*
- *Low propensity for resistance*

# A Superiority Design Study

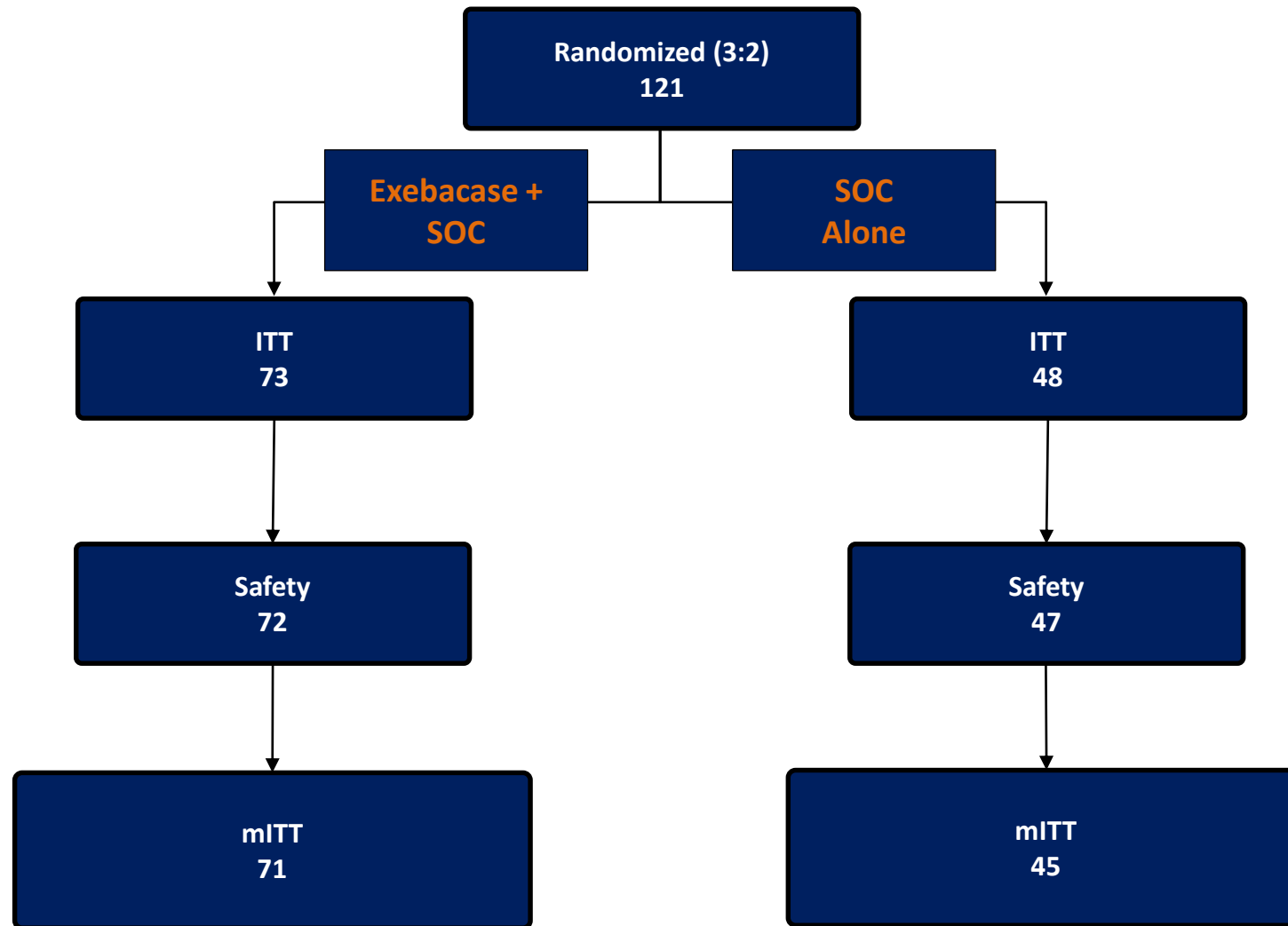
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- **Randomized, double-blind, placebo-controlled, superiority-design Phase 2 study**
  - *Compared exebacase (EXE) + standard of care antibiotics (SOC) vs SOC antibiotics alone*
- **Study population**
  - *Adults with documented Staph aureus bacteremia including endocarditis*
- **Study objectives**
  - *Describe safety and tolerability*
  - *Estimate clinical outcome rates after study drug administration*
  - *Describe the pharmacokinetic parameters*
- **Primary endpoint – Clinical Responder Rate at Day 14**
  - *Determined by independent, blinded Adjudication Committee*
  - *Defined as “Improvement/resolution of signs/symptoms, no new metastatic foci of infection or complications, and no changes in antibiotic treatment or further medical intervention due to lack of response in patients alive at time of evaluation”*

# Study Schema



# Patient Disposition



# Demographics were Similar in Both Groups (ITT)

	Exebacase +Antibiotics N = 73	Antibiotics Alone N = 48
<b>Region (n,%)</b>		
<b>United States (US)</b>	<b>58 (79.5%)</b>	<b>38 (79.2%)</b>
<b>Age (years, mean)</b>	<b>56.6</b>	<b>55.0</b>
<b>Gender (n, %)</b>		
<b>Male</b>	<b>50 (68.5)</b>	<b>32 (66.7)</b>
<b>Race (n, %)</b>		
<b>Black</b>	<b>14 (19.2)</b>	<b>8 (16.7)</b>
<b>White</b>	<b>51 (69.9)</b>	<b>30 (62.5)</b>
<b>Other</b>	<b>8 (11.0)</b>	<b>10 (20.8)</b>
<b>CrCl (ml/min, n, %)</b>		
<b>&lt;30</b>	<b>28 (38.4)</b>	<b>12 (25.0)</b>
<b>30 to &lt;60</b>	<b>13 (17.8)</b>	<b>7 (14.6)</b>
<b>60 to &lt;90</b>	<b>5 (6.9)</b>	<b>4 (8.3)</b>
<b>≥90</b>	<b>24 (32.9)</b>	<b>23 (47.9)</b>



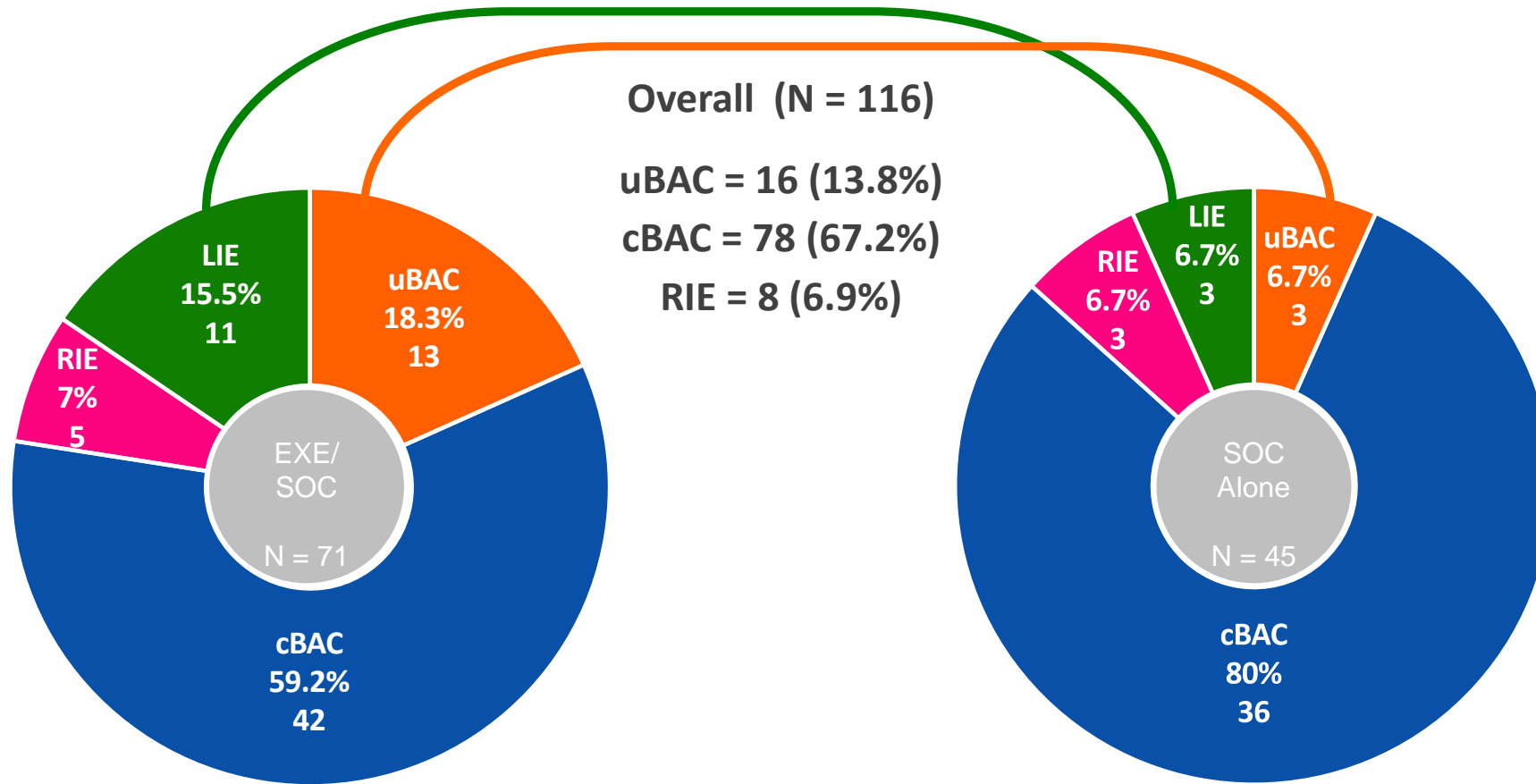


# Risk Factors by Infecting Pathogen (mITT)

	Exebacase +Antibiotics N = 71	Antibiotics Alone N = 45
	n (%)	n (%)
<b>Risk Factor</b>		
Poorly controlled diabetes mellitus <sup>1</sup>	20 (32.3)	8 (20.5)
Injection drug use <sup>1</sup>	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 <sup>1</sup>	2 (3.2)	1 (2.6)
Hemodialysis	21 (29.6)	8 (17.8)
SIRS <sup>1</sup>	45 (72.6)	27 (69.2)
<b>Infecting Pathogen<sup>2</sup></b>		
MRSA	27 (38.0)	16 (35.6)
MSSA	44 (62.0)	30 (66.7)



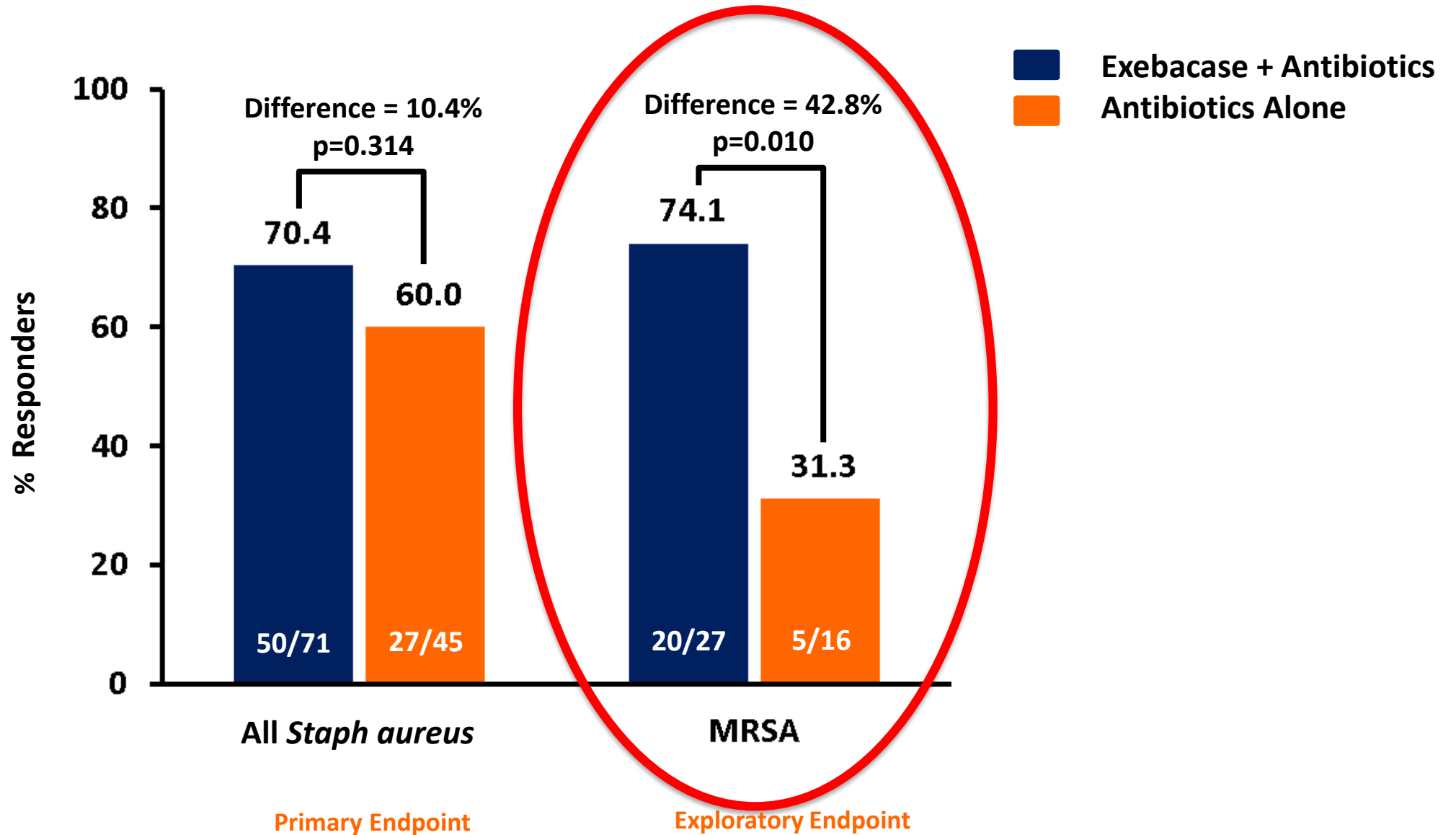
# Distribution of Final Diagnoses\* Differed Between Groups



\* As assessed by blinded Adjudication Committee

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

# 42.8% Higher Clinical Responder Rate at Day 14 with Exebacase in Prespecified MRSA Subgroup

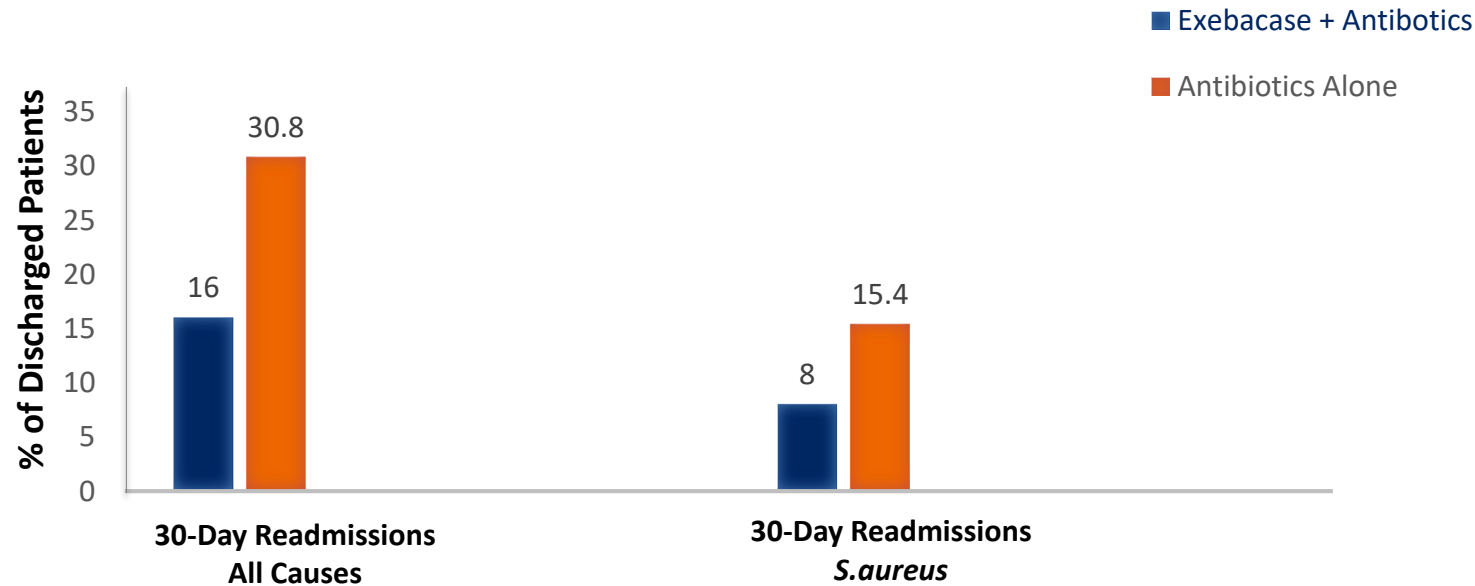


# Exebacase Was Safe and Well Tolerated in MRSA Patients

	<b>Exebacase + Antibiotics N = 27 % (n)</b>	<b>Antibiotics Alone N = 16 % (n)</b>
Treatment Emergent Adverse Events (TEAEs)	88.9 (24)	98.3 (15)
AEs leading to study drug discontinuation	0	0
Hypersensitivity AEs related to EXE	0	N/A
Serious Adverse Events (SAEs) through Day 180	63.0 (17)	75.0 (12)
SAEs determined to be related to EXE	0	N/A
Total deaths through TOC	18.5 (5)	31.3 (16)

# Exebacase Reduced Length of Stay and 30 Day Readmissions for US MRSA Patients Discharged Alive from the Hospital

- In-hospital mortality for US MRSA patients was 3.8% (1/26) and 13.3% (2/15), in the EXE-treated and Antibiotics alone groups, respectively
- Median length of stay was reduced by 4 days with exebacase
  - Median number of hospital days from Day 1 through discharge was 6.0 vs 10 days in the EXE-treated vs Antibiotics alone groups
- 30-day hospital readmission rates were lower among EXE-treated patients



# Outpatient Health Resource Utilization by US MRSA Patients

	Exebacase + Antibiotics N = 25 % (n)	Antibiotics Alone* N = 13 % (n)
<b>Discharge location</b>		
Home	56.0 (14)	46.1 (6)
Skilled Nursing Facility or Rehabilitation	36.0 (9)	38.5 (5)
Other	8.0. (2)	6.7 (1)

88.0% (22/25) of EXE-treated patients and 76.9% (10/13) patients treated with antibiotics alone were discharged prior to completion of SOC antibiotics.

- Outpatient parenteral antibiotic therapy (OPAT) was provided to all except 1 patient in the EXE group, who received oral antibiotics only after discharge.
- Median duration of OPAT therapy was 24 days in EXE-treated group and 27.5 days among patients who received antibiotics alone

\*Data not available for 1 patient in Antibiotic Alone Group



# Exebacase – A Potential New Treatment Paradigm for Serious, Antibiotic-Resistant Bacterial Infections

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- **A first in class direct lytic agent**
- **In Phase 2, exebacase used in addition to SOC antibiotics:**
  - was safe and well tolerated
  - resulted in a 42.8% higher responder rate vs antibiotics alone at Day 14 in the prespecified MRSA subgroup
  - reduced length of stay and 30-day hospital readmission rates in MRSA patients
- **Results support a definitive Phase 3 study focused on MRSA**
- **Establishes Proof of Concept for direct lytic agents as potential therapeutics**

