

*Comparison of Glycopeptide or Lipopeptide versus
Beta-Lactam for the Treatment of Enterococcus Faecalis
Bacteremia: A National Retrospective Cohort Study of
Veterans Affairs*

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Disclosure

- The speaker has no actual or potential conflicts of interest in relation to this presentation

Project Background

- High incidence of 30-day all-cause mortality in enterococcal bacteremia (7-40%)
- Optimal therapy for *Enterococcus faecalis* (EF) has not been well studied
- Recent studies report mixed results comparing mortality risk of glycopeptide vs. beta-lactam therapy for enterococcal bacteremia
- No studies to date have compared outcomes for lipopeptides vs. beta-lactam or glycopeptide therapies for enterococcal bacteremia

Previous Studies

Study	N	Enterococcus Infection	Outcome
Foo et al. 2014 <i>Two-centers,</i> <i>Australia</i>	172	100% <i>E. faecalis</i> (33% polymicrobial)	30-day all-cause mortality: 15% <ul style="list-style-type: none"> Glycopeptide 26.1% vs. β-lactam 11.1% (p=0.015)
Fletcher et al. 2018 <i>Single-center,</i> <i>US</i>	186	95% <i>E. faecalis</i> (% polymicrobial not defined)	30-day all-cause mortality: 7% <ul style="list-style-type: none"> Glycopeptide 6.7% vs. β-lactam 7.1% (p=0.922)
Petersiel et al. 2019 <i>Single-center,</i> <i>Israel</i>	516	77% <i>E. faecalis</i> (38% polymicrobial)	30-day all-cause mortality: 40% <ul style="list-style-type: none"> Glycopeptide 40.8% vs. β-lactam 39% (p=0.692)

Purpose

Study Objective

- To compare outcomes in patients with ampicillin-susceptible, vancomycin-susceptible *Enterococcus faecalis* bacteremia treated with intravenous glycopeptide, lipopeptide, or beta-lactam therapy

Inclusion and Exclusion Criteria

Inclusion Criteria



- Patients age ≥ 18 years admitted to VAMC
- Clinically significant EF bacteremia
- EF susceptible to ampicillin (or penicillin) and vancomycin (daptomycin, if reported)
- Appropriate therapy with glycopeptide, lipopeptide, or beta-lactam antibiotic

Exclusion Criteria



- Subsequent episodes of EF bacteremia within the study period
- Treatment with combination of beta-lactam plus glycopeptide or lipopeptide
- Antibiotic therapy < 5 days
- Polymicrobial bacteremia

Methods

- Retrospective review of national database of patients admitted to Veterans Affairs Medical Centers
 - **January 1, 2012 to December 31, 2017**
- Treatment Groups

Beta-lactam Therapy

- Ampicillin
- Ampicillin/sulbactam

Glycopeptide Therapy

- Vancomycin

Lipopeptide Therapy

- Daptomycin

End Points

- Primary
 - 30-day all-cause mortality
- Secondary
 - Recurrent *Enterococcus faecalis* bacteremia
 - Hospital mortality
 - One-year all-cause mortality
 - Incidence of *C. difficile* infection
 - Hospital and ICU length of stay
 - Duration of bacteremia

Statistics

- Power calculation
 - 208 patients needed for 80% power to detect a 15% difference in 30-day all-cause mortality

Primary Outcome	Type of Data	Statistical Test
30-day all-cause mortality	Non-continuous	Fisher's exact or Chi-squared Kaplan-Meier with log-rank test
Secondary Outcomes	Type of Data	Statistical Test
Incidence of recurrent bacteremia	Non-continuous	Fischer's exact or Chi-squared
Incidence of C. difficile infection		
Hospital mortality		Kaplan-Meier with log-rank test
One-year all-cause mortality		
Hospital and ICU length of stay	Continuous	T-test or Mann-Whitney U test
Duration of bacteremia		

Results

1,038 unique patients
hospitalized with *E.*
faecalis bacteremia
meeting study criteria

Ampicillin

n = 112

Vancomycin

n = 908

Daptomycin

n = 18

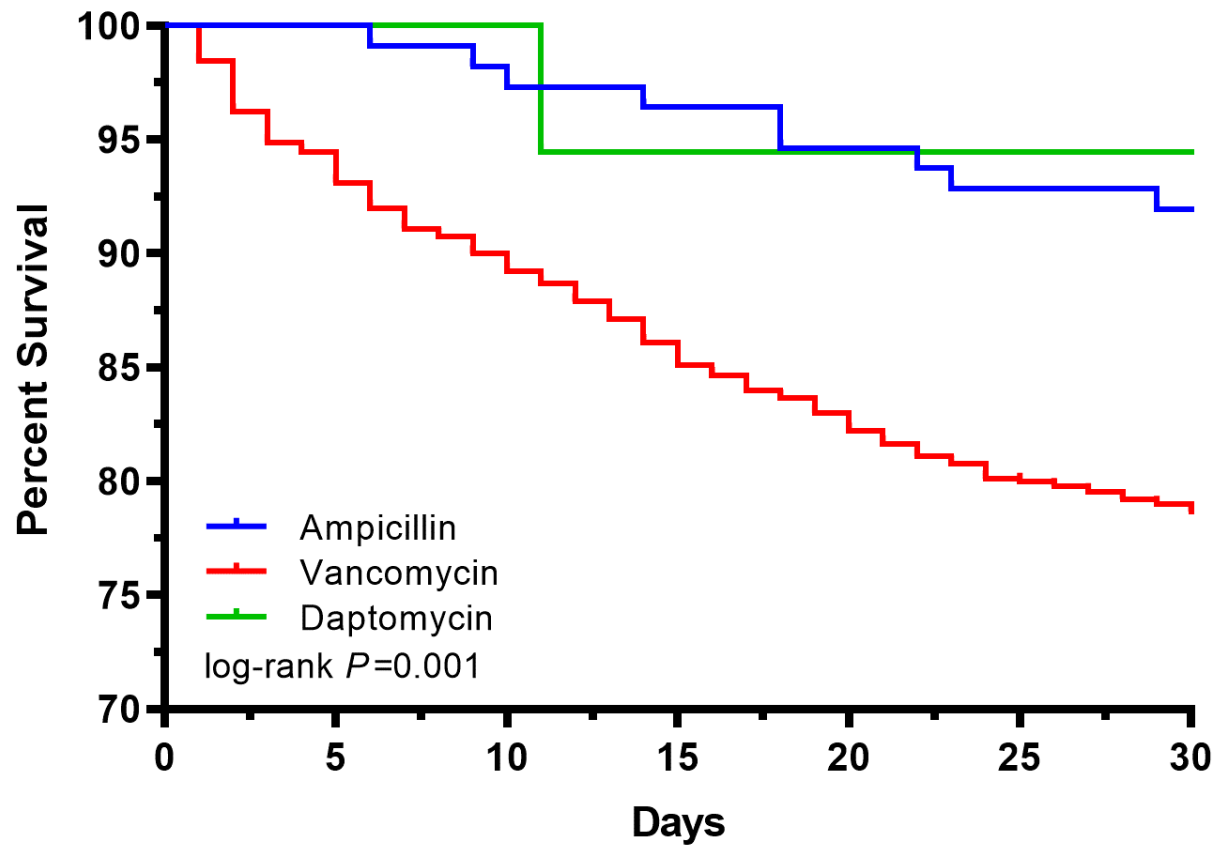
Patient Demographics

Characteristics	Ampicillin (n=112)	Vancomycin (n=908)	Daptomycin (n=18)
Age, mean years \pm SD	72.7 \pm 11.1	73.2 \pm 11.5	72.4 \pm 11.1
Male, n (%)	111 (99.1)	891 (98.1)	17 (94.4)
ICU admission location, n (%)	15 (13.4)	229 (25.2)	3 (16.7)

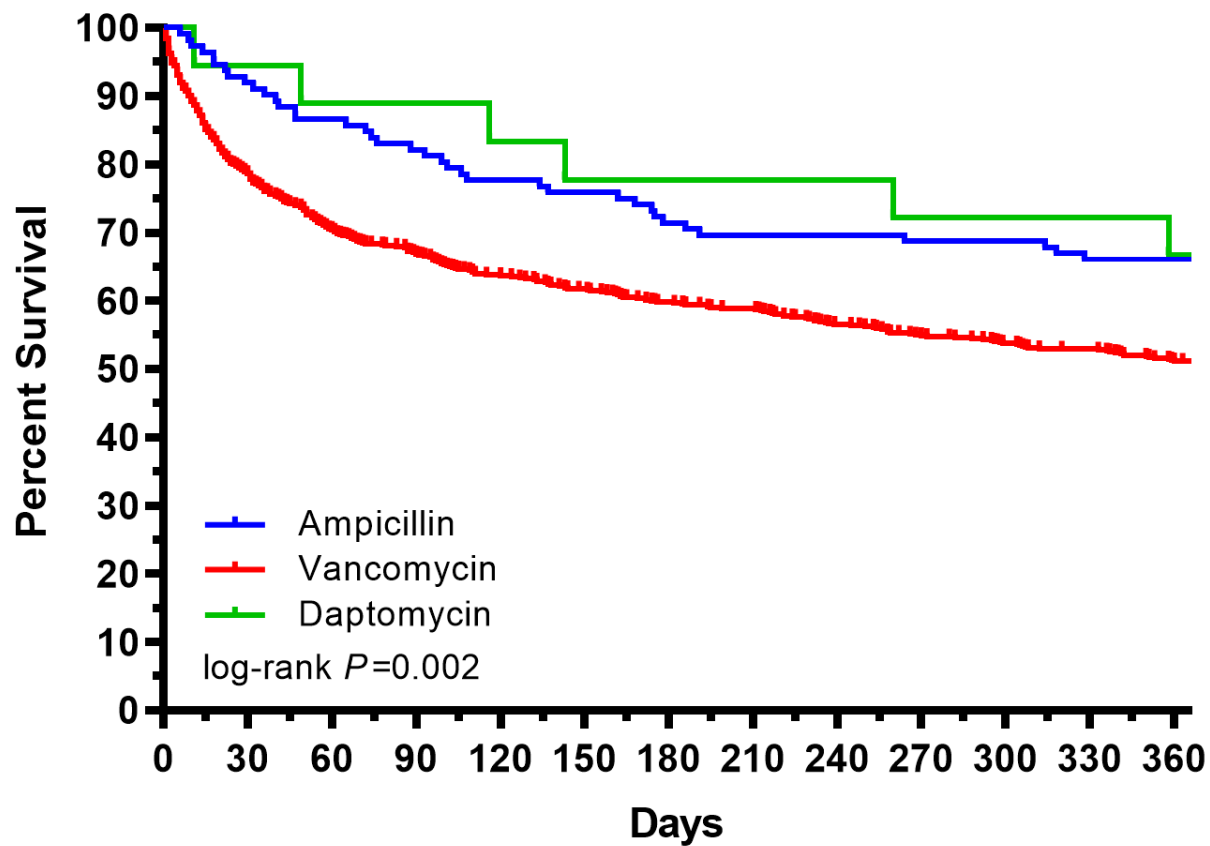
Results

Outcome	Ampicillin (n=112)	Vancomycin (n=908)	Daptomycin (n=18)	P-value
30-day all-cause mortality, n (%)	9 (8.0)	200 (22.0)	1 (5.6)	0.001
1-year all-cause mortality, n (%)	38 (33.9)	448 (49.3)	6 (33.3)	0.004
Hospital mortality, n (%)	5 (4.5)	138 (15.2)	1 (5.6)	0.005

Results



Results



Results

- Comparison of 30-day all-cause mortality between ampicillin and vancomycin treatment groups by multivariable logistic regression

Variable	Adjusted Odds Ratio (95% confidence interval)	P-value
Vancomycin treatment	2.80 (1.37-5.71)	0.005
ICU admission	3.68 (2.64-5.14)	<0.001
Age	1.03 (1.01-1.05)	<0.001
Male gender	1.36 (0.41-4.49)	0.617

Conclusion

- Vancomycin is associated with increased mortality compared to ampicillin for the treatment of clinically significant ampicillin-susceptible, vancomycin-susceptible *Enterococcus faecalis* bloodstream infection
- Lowest mortality numerically observed in daptomycin group, but limited by power

Future Directions

- Further collection and adjustment for confounding factors between groups
- Expansion of cohort years included to increase daptomycin sample
- Evaluation of effect of vancomycin dosing on outcomes

Limitations

- Retrospective study
- Limited data available at this time
- VA patient population

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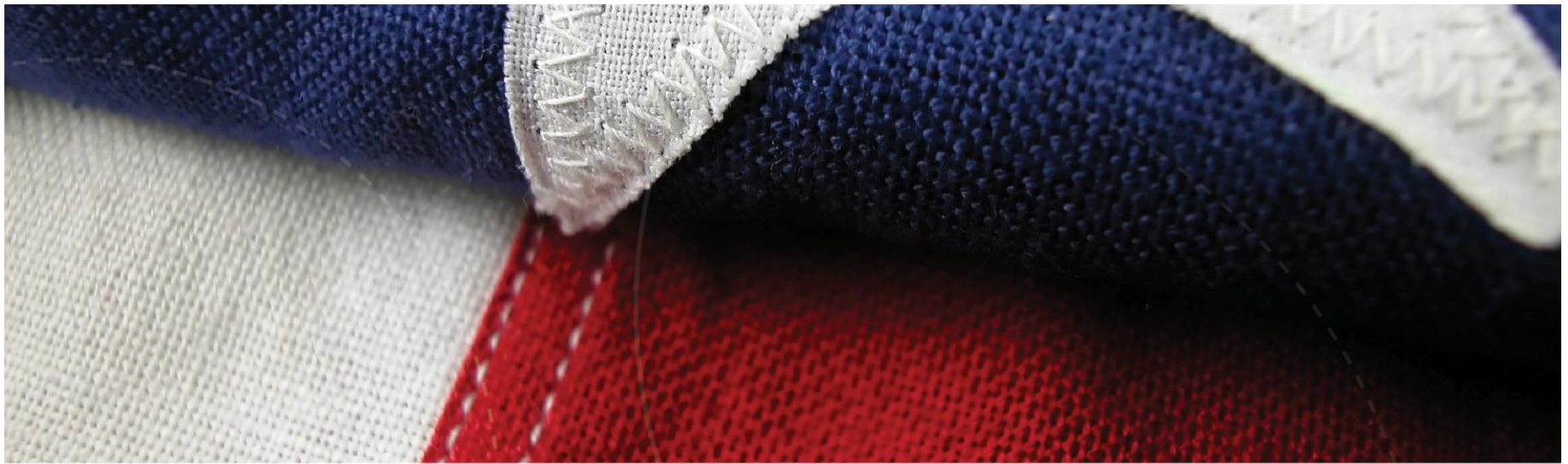
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Questions?

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