Abstract #295

Clinical outcomes of bloodstream infections (BSI) due to Vancomycin-resistant *Enterococcus faecium* (VRE)

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LIFE CHANGING MEDICINE

INTRODUCTION

- Vancomycin-resistant Enterococci (VRE) are common causes of hospital-acquired infections
- The front-line agents to treat VRE infections include daptomycin and linezolid; however, the preferred agent for bacteremia is unclear
- Completed studies have provided conflicting evidence to support the use of one agent over the other
  - Existing literature is limited by small, retrospective studies

OBJECTIVE

Our objective was to compare the clinical outcomes and survival of patients with VRE bloodstream infections, particularly those treated with daptomycin and linezolid

METHODS

Design: Retrospective cohort study

Setting: University of Pittsburgh Medical Center (UPMC)- Presbyterian campus

Study Period: 2012 – 2015

Inclusion Criteria:
- Adult patients with any positive blood culture for vancomycin-resistant *Enterococcus faecium* with signs and symptoms of infection

Exclusion Criteria:
- Positive blood cultures deemed to be a result of contaminated catheters

Primary Outcome:
- 30-day survival

Secondary Outcomes:
- Clinical success was defined as 30-day survival AND improvement in signs and symptoms of infection, microbiologic clearance of blood cultures within 7 days, and the absence of recurrent VRE infections within 30-days
- Recurrent bloodstream infections within 90 days of index VRE bloodstream infection
- Rates of early treatment discontinuation

Statistical Analysis:
- Univariate analysis: Mann Whitney U, Chi square, and Fisher's exact tests; significant two-tailed *p*-value: <0.05
- Multivariate logistic regression with backward selection procedures were performed with variables demonstrating *p*-values <0.30 in univariate analysis

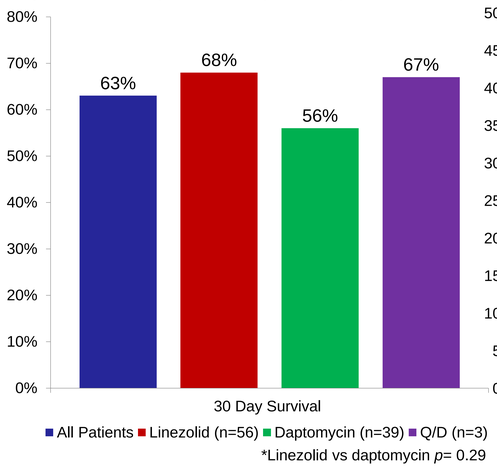
RESULTS

Table 1. Characteristics of Patients with VRE-BSI by Primary Treatment

Characteristic	All Patients n=98	Linezolid n=56	Daptomycin† n=39	Q/D n=3	*p*-value*
Median Age, years (range)	58 (21 – 86)	59 (21 – 86)	58 (27 – 82)	64 (28 – 73)	0.47
Median Weight, kg (range)	78 (37 – 145)	79 (37 – 145)	77 (40 – 140)	62 (62 – 131)	0.20
Median Pitt Bacteremia Score (range)	7 (0 – 14)	8 (0 – 13)	6 (0 – 12)	2 (2)	0.81
Prior VRE isolation, n (%)	77 (75)	45 (80)	27 (69)	3 (100)	0.23
Prior non-rectal VRE, n (%)	33 (34)	23 (41)	8 (21)	2 (67)	**0.045**
Surgery within 90 days, n (%)	56 (57)	35 (63)	19 (49)	2 (67)	0.21
Renal Replacement, n (%)	42 (43)	20 (36)	21 (54)	1 (33)	0.09
ICU at bacteremia onset, n (%)	72 (73)	42 (75)	29 (74)	1 (33)	1.00
Mechanical Ventilation, n (%)	55 (56)	33 (59)	21 (54)	1 (33)	0.68
Immunosuppressed, n (%)	61 (62)	33 (59)	26 (67)	2 (67)	0.52
Intra-abdominal Infection, n (%)	33 (34)	22 (39)	12 (31)	2 (67)	0.51
Line Infection, n (%)	34 (35)	13 (23)	22 (59)	1 (33)	**0.002**
30 Day Prior Exposure, n (%)					
Linezolid	11 (11)	8 (14)	3 (8)	0 (0)	0.51
Daptomycin	1 (1)	1 (2)	0 (0)	0 (0)	1.00
Tigecycline	8 (8)	5 (9)	2 (5)	1 (33)	0.70
Vancomycin IV	44 (45)	24 (43)	18 (46)	2 (67)	0.83
Vancomycin PO	12 (12)	7 (13)	3 (8)	2 (67)	0.51
Metronidazole	34 (35)	21 (38)	11 (38)	2 (67)	0.38
E. faecium* Susceptibility*					
Daptomycin NS, n (%)	22 (22)	18 (32)	2 (5)	2 (67)	**0.002**
Linezolid NS, n (%)	2 (2)	2 (4)	0 (0)	0 (0)	0.51

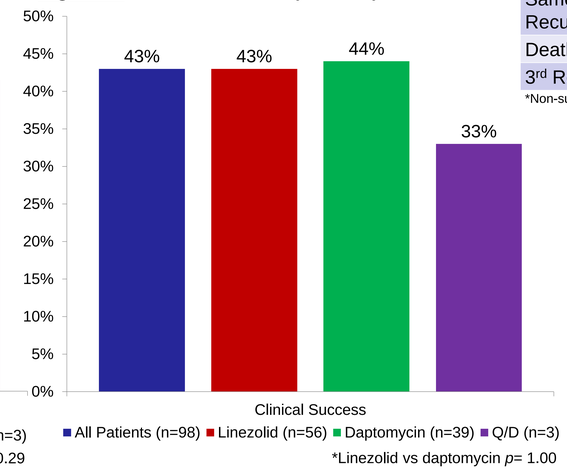
*Linezolid vs daptomycin
**Susceptibility determined via automated system (MicroScan) or Etest methods
†Median Daptomycin dose, mg/kg/day (range): 7.9 (4.7 – 13.7)

Figure 1: 30-Day Survival by Primary Treatment



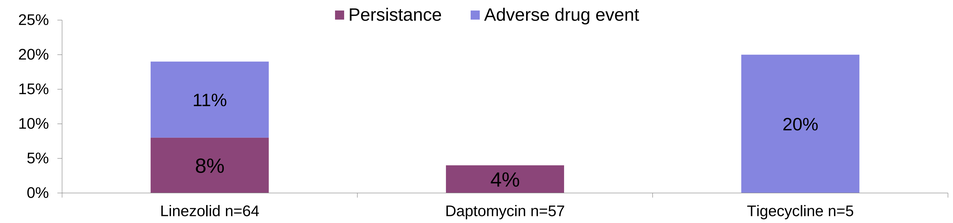
*Linezolid vs daptomycin *p*= 0.29

Figure 2: Clinical Success by Primary Treatment



*Linezolid vs daptomycin *p*= 1.00

Figure 3: Reasons for Early Treatment Discontinuation



*Linezolid vs daptomycin *p*=0.04
**No therapy change for Q/D

Table 2: Risk factors for Clinical Failure

Characteristic	Clinical Success (n=42)	Clinical Failure (n=56)	Univariate *p*=value	Multivariate *p*=value
Median Age (range)	59 (26 – 86)	58 (21 – 84)	0.54	
Residence in ICU at onset of bacteremia, n (%)	32 (76)	40 (71)	0.65	
Polymicrobial bloodstream infection, n (%)	15 (36)	16 (29)	0.51	
Abdominal surgery within 90 days, n (%)	9 (21)	19 (34)	0.26	
Immunosuppressed, n (%)	22 (52)	39 (70)	0.095	0.065
Median Pitt Bacteremia Score (range)	6 (0 – 10)	7.5 (0 – 13)	0.31	0.073

- 8% (8/98) of patients had recurrent bloodstream infections within 90 days
  - 25% (2/8) of these patients died following recurrent bloodstream infections

Table 3: Recurrent VRE-BSI Within 90 Days if Index Infection

Characteristic	Primary Agent: Linezolid (n=5)	Primary Agent: Daptomycin (n=3)
New Daptomycin NS* at Recurrence, n (%)	5 (100)	0 (0)
New Linezolid NS* at Recurrence, n (%)	0 (0)	0
Same Antimicrobial Agent Prescribed for Recurrent Episode, n (%)	3 (60)	2 (67)
Death at Recurrence, n (%)	1 (20)	1 (33)
3rd Recurrent VRE-BSI Within 90 Days, n (%)	0 (0)	2 (67)

*Non-susceptible according to Clinical and Laboratory Standards Institute (CLSI) M100-S26

CONCLUSIONS

- Clinical success was achieved in a minority of patients treated for VRE BSI despite the use of agents that were active *in vitro*
- There was no difference in survival or clinical success among patients who received daptomycin or linezolid for VRE bacteremia in this cohort
- Recurrent VRE BSI were more likely to both be associated with daptomycin resistance and to be treated with the same antimicrobial agent as the index VRE BSI
- Daptomycin resistance was seen more frequently than linezolid; however, susceptibility testing methods should be considered (see poster #1997)

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