Characteristics and Outcomes of Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections in Patients with Cancer Treated with Vancomycin: 9-Year Experience at a Comprehensive Cancer Center

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Key Words. Methicillin-resistant *Staphylococcus aureus* • Bacteremia • Bloodstream infections • Vancomycin

Disclosures: Kenneth V. Rolston: Cubist, Astellas (RF); Issam I. Raad: American Medical Systems, Cook, Cook Urological, Medline, TyRx (IP); Astellas Pharma, Merck Pharma (RF); ECP, Great Lakes Pharma, Inventive Protocol (OI); Roy F. Chemaly: Cubist (RF, H). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

ABSTRACT

Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSIs) can cause significant morbidity and mortality in patients with cancer. However, data on outcomes of patients treated with vancomycin are lacking.

Methods. We identified 223 patients with cancer who developed MRSA BSIs between January 2001 and June 2009 and were treated with vancomycin. Treatment failure was defined as death within 60 days of infection, persistent bacteremia ≥ 5 days, fever ≥ 4 days, recurrence or relapse, and secondary MRSA infection.

Results. The treatment failure rate was 52% (116 of 223 patients). These patients were more likely to have been hospitalized, been treated with steroids within the previous 3 months, developed acute respiratory distress syndrome, required mechanical ventilation, required intensive care unit care, and community-onset infections (all $p < .05$). Risk factors for MRSA-associated mortality (27 of 223 pa-

tients; 12%) included hematologic malignancy and hematopoietic stem cell transplantation, community-onset infection, secondary BSI, MRSA with minimum inhibitory concentration (MIC) ≥ 2.0 $\mu\text{g/mL}$, mechanical ventilation, and a late switch to an alternative therapy (≥ 4 days after treatment failure; all $p < .05$). On multivariate analysis, mechanical ventilation and recent hospitalization were identified as independent predictors of vancomycin failure, and community-onset infection, secondary BSIs, and MIC ≥ 2 $\mu\text{g/mL}$ were identified as significant predictors of MRSA-associated mortality.

Conclusions. We found a high treatment failure rate for vancomycin in patients with cancer and MRSA BSIs, as well as a higher mortality. A vancomycin MIC ≥ 2 $\mu\text{g/mL}$ was an independent predictor of MRSA-associated mortality. An early switch to an alternative therapy at the earliest sign of failure may improve outcome. *The Oncologist* 2012; 17:1329–1336

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INTRODUCTION

Staphylococcus aureus is known to cause serious infections that can involve the skin, soft tissues, lungs, cardiac valves, and bloodstream. It is a major cause of community-onset and hospital-acquired bloodstream infections (BSIs) globally [1–3]. Its ability to produce metastatic or secondary infections such as endocarditis, osteomyelitis, and septic arthritis has been documented in myriad studies [4–7]. The emergence and global spread of methicillin-resistant *S. aureus* (MRSA) constitutes one of the most serious contemporary challenges in the treatment of community- and health care-acquired infections. Of all MRSA infections, pneumonia and BSIs may be the most aggressive and difficult to treat; they are usually associated with significant morbidity and mortality.

Until recently, the mainstay therapy for MRSA infections was vancomycin, administered at the dosage necessary to achieve serum trough concentrations of 15–20 $\mu\text{g/mL}$ [8]. However, many studies reported treatment failures of vancomycin for infections caused by MRSA strains, mainly in immunocompetent patients, with apparent in vitro susceptibility but with a minimum inhibitory concentration (MIC) of 2 $\mu\text{g/mL}$ [9, 10] and despite the achievement of the recommended serum trough concentrations [11, 12]. As per the Infectious Disease Society of American (IDSA) 2011 recommendations [13], for isolates with a vancomycin MIC ≤ 2 $\mu\text{g/mL}$, clinical response should be used to determine whether vancomycin use should continue. Alternative therapy has been recommended when the vancomycin MIC is >2 $\mu\text{g/mL}$ [13]. On the other hand, the European Congress of Clinical Microbiology and Infectious Diseases guidelines recommend alternative therapy when the MIC is >1.5 $\mu\text{g/mL}$ [14]. Furthermore, favorable outcomes have emerged for the use of daptomycin and linezolid for MRSA BSIs and hospital-acquired pneumonia, respectively [15, 16]; thus, initial therapy with these agents for the above indications may be contemplated.

S. aureus infections such as BSIs, endocarditis, and surgical site infections can cause significant morbidity [17] and mortality in patients with cancer [18–21]. In addition, factors such as sepsis and comorbid conditions have been associated with increased MRSA-associated mortality in patients with cancer [22]. On the other hand, scarce data exist on vancomycin treatment outcomes or risk factors for treatment failure and MRSA-associated mortality in patients with cancer and MRSA BSIs. Thus, in this study, we determined the characteristics and outcomes of MRSA BSIs in patients with cancer who were treated with vancomycin over 9 years at a single institution.

PATIENTS AND METHODS

In this retrospective study, we searched the infection control database at The University of Texas MD Anderson Cancer Center in Houston, Texas, to identify all patients with cancer who were diagnosed with MRSA BSIs from January 1, 2001 to June 30, 2009. The predetermined inclusion criteria were as follows: (a) treatment for any type of malignancy at MD Anderson; (b) MRSA isolated from blood cultures between Jan-

uary 1, 2001 and June 30, 2009; and (c) treatment with vancomycin for more than 72 hours.

A waiver of informed consent and a waiver of authorization were requested because the study used retrospective data review that involved no diagnostic or therapeutic intervention, as well as no direct patient contact. The institutional review board approved the request and the protocol.

All definitions were developed before the initiation of the study. Treatment failure was defined as any of the following: (a) death within 60 days of infection and treatment for MRSA BSI (in-hospital mortality); (b) fever ≥ 4 days during therapy; (c) persistent bacteremia ≥ 5 days; (d) relapse or recurrence of MRSA BSI within 30 days of discontinuation of primary therapy; (e) secondary MRSA infection after bacteremia; or (f) early discontinuation or switch to an alternative therapy because of relapse, recurrence, or grade 3 or 4 adverse events. If patients met more than one criterion, the outcome was classified as one failure.

Sepsis was defined as any two of the following: (a) heart rate >90 beats per minute; (b) respiratory rate >20 per minute; (c) temperature $>38^\circ\text{C}$ or $<36^\circ\text{C}$; and (d) white blood cell count $>12,000/\mu\text{L}$, $<4,000/\mu\text{L}$, or $>10\%$ bands. Severe sepsis was defined as presence of hypotension responsive to fluid resuscitation in patients with sepsis. Relapse was defined as MRSA BSI within 1 month after therapy. Recurrence was defined as recurrent MRSA BSI while on therapy and after documentation of negative blood cultures.

A catheter-related BSI was defined as a BSI in patients with intravascular catheters and at least one positive blood culture for MRSA obtained from a peripheral vein, a clinical manifestation of infection (i.e., fever, chills, or hypotension), and no apparent source of the BSI except the catheter. In addition, one of the following was required: a positive semiquantitative (>15 colony-forming units [CFUs]/catheter segment) or quantitative ($>10^2$ CFUs/catheter segment) culture in which the same organism (species and antibiogram) was isolated from the catheter segment and peripheral blood; simultaneous quantitative blood cultures with a $\geq 3:1$ ratio for catheter versus peripheral blood; or a differential period of catheter culture versus peripheral blood culture positivity of >2 hours [23].

Clinical treatment success was defined as negative blood cultures for MRSA and resolution of signs and symptoms of infection by day 60, as assessed by the principal investigator.

Data Collection

Information was collected for several variables, including demographics (age, sex, and ethnicity), underlying cancer, risk factors for MRSA BSI (i.e., prior hospitalization, antibiotic exposure within 3 months of therapy, history of methicillin-sensitive *S. aureus* or MRSA infection within 1 year, comorbidities such as diabetes, chronic obstructive pulmonary disease), microbiological data, immune function (i.e., neutrophil count), neutropenia duration, concomitant immunosuppressive medications, antimicrobial therapy, and clinical and microbiological outcomes. In addition, we recorded the dates and times of blood cultures and the Etest (bioMérieux, Inc.,

Figure 1. Distribution of minimum inhibitory concentrations over time for the clinical isolates of methicillin-resistant *Staphylococcus aureus* bloodstream infections. Abbreviation: MIC, minimum inhibitory concentration.

Durham, NC) was used to determine vancomycin MICs, as per the manufacturer's instructions.

Statistical Analysis

Descriptive statistics were provided for relevant demographic, clinical, and therapeutic variables. Vancomycin treatment success and failure were compared, with regards to the distribution of each variable, using the χ^2 test or Fisher's exact test, where appropriate. Statistical significance was set at $p \leq .05$. To determine the independent predictors of vancomycin failure, we performed a backward stepwise logistic regression analysis. The variables considered for model inclusion a priori were those associated with vancomycin failure on univariate analysis, with $p < .1$.

In the mortality analysis, we calculated treatment response and mortality rates. We compared MRSA-associated death and MRSA survival with respect to each variable. A p value $< .05$ was considered to be statistically significant. A multivariate logistic regression analysis was used to identify the demographic, clinical, and therapeutic factors associated with MRSA-associated mortality. The variables selected for the regression models included all variables with $p < .1$ on univariate analysis. A backward stepwise logistic regression analysis was performed, using the significant variables to identify the independent predictors of MRSA-associated mortality. A comparison of Kaplan-Meier survival of patients with MRSA BSIs was performed using the log-rank statistic. This analysis was stratified by MIC ≥ 2 µg/mL and MIC < 2 µg/mL. A Kaplan-Meier survival curve was plotted. All calculations were computed using STATA 10 statistical software (Statacorp, College Station, TX).

RESULTS

We identified 250 patients with MRSA BSIs. Twenty-seven were excluded because of nonevaluable outcome. Discrete

vancomycin MIC values were available for all MRSA isolates during the study period because our microbiology laboratory uses the Etest to determine MICs for isolates cultured from sterile sites (Fig. 1).

Figure 2 shows a yearwise distribution of the 223 patients in the study population on the basis of underlying cancer type: 100 solid tumors (45%) versus 123 hematologic malignancies (55%). More patients were seen in 2003 and 2004 than in 2001, 2002, or 2005–2009.

Patients' characteristics are shown in Table 1. Median age was 59 years (range, 1 month to 86 years); 138 (62%) were male and 147 (66%) were non-Hispanic white. Steroid and chemotherapy use within 1 month of infection was noted for 137 (61%) and 178 (80%) patients, respectively.

A total of 139 (62%) patients had community-onset MRSA BSIs; 141 (63%) cases were catheter related. In all, 196 patients (88%) presented with sepsis-like symptoms and 90 patients (40%) had severe neutropenia.

Vancomycin Treatment Outcome

More than half of the patients experienced failure to initial vancomycin therapy (116 patients; 52%). The reasons for failure are shown in Table 2. Secondary MRSA infections were seen in 86 patients (74%) and included pneumonia (14 patients), septic thrombophlebitis (20 patients), infective endocarditis (6 patients), and deep tissue abscesses (11 patients). Persistent fever occurred in 41 patients (35%) and discontinuation of vancomycin because of adverse events occurred in 33 patients (29%). Adverse events, as documented in Table 1, included nephrotoxicity (14 patients), thrombocytopenia (9), red man syndrome/rash (6), leukopenia (3) and others (4). Few patients had more than one adverse event.

Patients who did not experience a response to vancomycin were more likely to have hematologic malignancies, community-onset BSI, or acute respiratory distress syndrome; have re-

Figure 2. Yearwise distribution of methicillin-resistant *Staphylococcus aureus* bloodstream infections in patients with solid tumors versus hematologic malignancies from 2001 to 2009. *Cases between January 1, 2009 and June 30, 2009. **Includes patients with lymphoma or leukemia, as well as hematopoietic stem cell transplant recipients.

ceived steroids within 1 month of diagnosis or vancomycin within 3 months of diagnosis; have been hospitalized within 3 months of diagnosis; had needed mechanical ventilation during therapy; or had been in the intensive care unit (ICU) during therapy (all $p < .05$; Table 3). Furthermore, the MRSA-associated mortality rate within 60 days of diagnosis was much higher in patients who did not experience a response to initial vancomycin therapy (23% vs. 0%; $p < .01$).

A multivariate logistic regression model revealed the joint effects of covariates as predictors of vancomycin treatment failure. Mechanical ventilation (odds ratio [OR] = 5.7, confidence interval [CI] = 1.92–20; $p = .02$) and hospitalization within 3 months of BSI (OR = 2.1, CI = 1.13–3.85; $p = .03$) were found to be significantly associated with vancomycin failure.

Switch to Alternative Antibiotics

Of the 116 patients who did not experience a response to vancomycin, 43 (37%) were switched to other antibiotics, including monotherapy with daptomycin (18), linezolid (10), and tigecycline (8) or in different combination of these antibiotics (7). All MRSA isolates were susceptible to these antibiotics. Among these patients, an early switch (≥ 4 days) was associated with no MRSA-associated mortality versus a 22% mortality rate for patients who were switched late (> 4 days; $p < .001$). There were similar proportions of MRSA isolates with MIC ≥ 2 $\mu\text{g/mL}$ between the two groups. Interestingly, variations in vancomycin MIC were minimal (± 0.5 $\mu\text{g/mL}$) for patients who had MRSA isolates recovered while undergoing vancomycin therapy or for patients who had relapsed or recurrent MRSA infections and received alternative therapy.

MRSA-Associated Mortality

In all, 27 patients died with MRSA infections (12%; Table 4). Underlying hematologic malignancies, hospitalization within 3 months of diagnosis, community-onset BSI, secondary BSI,

ICU stay, mechanical ventilation, acute respiratory distress syndrome, vancomycin MIC ≥ 2 $\mu\text{g/mL}$, and high vancomycin failure rates were associated with MRSA-associated death (all $p < .05$). A multivariate logistic regression model revealed the joint effects of covariates as predictors of MRSA-associated mortality: community-onset infection (OR = 3.3; CI = 1.12–9.09; $p = .04$), secondary BSI (OR = 3.2, CI = 1.32–7.2; $p = .03$), and vancomycin MIC ≥ 2 $\mu\text{g/mL}$ (OR = 2.7, CI = 1.02–7.09; $p = .05$) were significantly associated with mortality within 60 days of diagnosis. A vancomycin MIC of ≥ 2 $\mu\text{g/mL}$ was also associated with prior vancomycin exposure and sepsis at diagnosis ($p = .04$ and $.05$, respectively).

Survival Analysis of Patients with MRSA BSIs

Figure 3 depicts the Kaplan-Meier survival curve for patients with MRSA BSIs, stratified by MIC values (MIC ≥ 2 $\mu\text{g/mL}$ vs. < 2 $\mu\text{g/mL}$). More deaths were seen in patients with MIC values of ≥ 2 $\mu\text{g/mL}$ (log-rank test value, $p = .02$). We found no statistical difference in the median survival durations of these populations. We attribute this finding to a bimodal temporal mortality distribution in patients with MIC ≥ 2 $\mu\text{g/mL}$ versus a uniform distribution in patients with MIC < 2 $\mu\text{g/mL}$.

DISCUSSION

To our knowledge, this is the first study to evaluate, in depth, the characteristics and outcomes of patients with cancer and MRSA BSIs, with a focus on clinical outcomes after vancomycin therapy. Our study, which included 223 patients treated at a single institution over the span of 9 years, yielded important findings: (a) a high rate of vancomycin treatment failure in patients with cancer as based on predetermined definitions of failure; (b) a significant association exists between mortality rates and a vancomycin MIC of ≥ 2 $\mu\text{g/mL}$; and (c) switching to an alternative therapy ≤ 4 days after vancomycin treatment failure is associated with a higher survival rate.

Vancomycin treatment failure was observed in 52% of pa-

Table 1. Characteristics of 223 patients with cancer and methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections

Characteristic	Result
Age, median yrs (range)	59 (<1–86)
Male sex	138 (62)
Non-Hispanic white	147 (66)
Solid tumor	100 (45)
Hematologic malignancy and hematopoietic stem cell transplantation	123 (55)
Progressive cancer	157 (70)
Steroids within 1 month	137 (61)
Chemotherapy within 1 month	178 (80)
Hospitalization within 3 months	154 (69)
Intensive care unit stay within 3 months	15 (7)
Antibiotic exposure within 3 months	200 (90)
Vancomycin use within 3 months	48 (22)
Community onset	139 (62)
Catheter-related infection	141 (63)
Vancomycin minimum inhibitory concentration ≥ 2 $\mu\text{g/mL}$	115 (52)
With sepsis at diagnosis	96 (85)
With prior vancomycin exposure	36 (31)
Severe neutropenia	90 (40)
Vancomycin trough ^a	
≥ 15 $\mu\text{g/mL}$	103 (53)
> 20 $\mu\text{g/mL}$	70 (36)
Sepsis during antibiotic therapy	155 (79)
Severe sepsis	19 (9)
Septic shock	22 (10)
Acute respiratory distress syndrome	22 (10)
Mechanical ventilation	25 (11)
Intensive care unit stay	63 (28)
Median length of stay, days (range)	7 (1–45)
Vancomycin outcome	
Success	107 (48)
Failure	116 (52)
Most common adverse events related to vancomycin therapy	
Nephrotoxicity	14 (6)
Thrombocytopenia	9 (4)
Leukopenia	3 (1)
Rash/red man syndrome	6 (3)
MRSA-associated mortality at 60 days	27 (12)

Data are *n* (%) unless noted.
^aFor 196 patients with trough data available.

Table 2. Reasons for vancomycin treatment failure

Cause of failure	<i>n</i> (%)
<i>n</i> of patients	116
Persistent fever (>4 days)	41 (35)
Persistent bacteremia (≥ 5 days)	34 (30)
Secondary infections	86 (74)
Discontinued because of adverse events	33 (29)
MRSA-associated mortality	27 (23)
Recurrence	4 (3)
Relapse	22 (19)

Abbreviation: MRSA, methicillin-resistant *Staphylococcus aureus*.

tients in our study. A similar failure rate was reported in a recent retrospective single-center study of 320 patients [24] with documented MRSA BSIs who were initially treated with vancomycin between 2005 and 2010. However, the authors defined vancomycin failure as 30-day mortality or persistent signs and symptoms of infection after therapy and persistent BSI ≥ 7 days. Furthermore, in a logistic regression model, they identified infective endocarditis, nosocomially acquired infection, initial vancomycin trough < 15 $\mu\text{g/mL}$, and vancomycin MIC of > 1 $\mu\text{g/mL}$, as determined by an Etest, as predictors of treatment failure. In comparison, an MIC > 1 $\mu\text{g/mL}$ was not a significant predictor of treatment failure in our study. On the other hand, with a lack of standardized definitions for success and failure in these kinds of studies, comparisons of outcomes and even risk factors or predictors may be inappropriate.

In a recent cohort study by Lubin et al. [25], the variables associated with a vancomycin MIC of ≥ 2 $\mu\text{g/mL}$ included age > 50 years, prior vancomycin exposure, MRSA BSI history, chronic liver disease history, and nontunneled central venous catheter use. In our study, MRSA with a vancomycin MIC ≥ 2 $\mu\text{g/mL}$ was associated with prior vancomycin exposure and sepsis at diagnosis. In addition, our data showed that an MIC of ≥ 2 $\mu\text{g/mL}$ was associated with an increase in MRSA-associated mortality but not with vancomycin treatment failure. These findings are consistent with those of studies by Sorieno et al [2] and Lodise et al., [26] except in those studies, a high MIC (≥ 2 $\mu\text{g/mL}$) was associated with treatment failure. Several other recent studies have demonstrated poor outcomes (in terms of mortality) in patients with MRSA infections and vancomycin MIC ≥ 2 $\mu\text{g/mL}$. [27–29] The high failure rate and mortality in these patients may be due to the presence of unsuspected heteroresistant vancomycin *S. aureus*, which can be prevalent in MRSA isolates with MIC ≥ 2 $\mu\text{g/mL}$ [27, 28]. Another important factor that may affect mortality is the presence of the *panton valentine leukocidin* gene. However, in a recent study at our institution, the presence of this gene was not associated with a poor outcome in patients with cancer and MRSA infections [30].

On the basis of our findings, an alternative agent to vancomycin should be considered for MRSA with vancomycin MIC

Table 3. Characteristics of patients who did and did not experience a response to initial vancomycin therapy

Variable	Success	Failure	<i>p</i> value
<i>n</i> of patients	107	116	
Age, mean yrs (range)	53 (>1–82)	57 (1–86)	NS
Hematologic malignancy	51 (48)	72 (62)	.04
Steroids within 1 month	65 (61)	88 (76)	.02
Hospitalization in prior 3 months	59 (55)	81 (70)	.03
Community onset	61 (57)	83 (72)	.03
Therapy within 24 hours	88 (82)	105 (91)	.06
Acute respiratory distress syndrome	0 (0)	12 (10)	.001
Mechanical ventilation during therapy	4 (4)	21 (18)	.001
Vancomycin in prior 3 months	19 (18)	33 (28)	.05
ICU stay during therapy	20 (19)	41 (35)	.01
Minimum inhibitory concentration ≥ 2 $\mu\text{g/mL}$	56 (52)	59 (51)	NS
60-day MRSA-associated mortality	0 (0)	27 (23)	<.01

Data are *n* (%) unless noted.

Abbreviations: ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*; NS, not significant.

Table 4. Patient characteristics and risk factors for MRSA-associated mortality

Variable	Mortality	Survival	<i>p</i> value
<i>n</i> of patients	27	196	
Age, mean yrs	59	55	NS
Hematological cancer	19 (70)	104 (53)	.01
Hospitalization in prior 3 months	22 (81)	118 (60)	.001
Community-onset infection	22 (81)	122 (62)	.01
Non-catheter-related infection (secondary bacteremia)	16 (59)	67 (34)	<.001
Minimum inhibitory concentration ≥ 2 $\mu\text{g/mL}$	21 (78)	104 (53)	<.01
Vancomycin trough >15 $\mu\text{g/mL}$	17 (63)	87 (44)	.01
Acute respiratory distress syndrome	9 (33)	3 (2)	<.01
Mechanical ventilation	14 (52)	11 (6)	<.01
Intensive care unit stay	20 (74)	41 (21)	.01
Vancomycin failure	27 (100)	89 (40)	<.01

Data are *n* (%) unless noted.

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; NS, not significant.

≥ 2 $\mu\text{g/mL}$. Moreover, the IDSA 2011 recommendations for vancomycin MIC > 2 $\mu\text{g/mL}$ include the use of appropriate alternative therapy [13]. Previous studies have made similar recommendations, but with MIC values of > 1 $\mu\text{g/mL}$ and a target vancomycin trough serum value of > 10 $\mu\text{g/mL}$ [2, 9, 10]. In a prospective cohort study by Hidayat et al [12], 95 patients with MRSA with a vancomycin MIC ≥ 2 $\mu\text{g/mL}$ had a lower clinical response rate than did those with an MIC of < 2 $\mu\text{g/mL}$, after controlling for the targeted trough.

Interestingly and similar to our findings, Holmes et al. [31] found that higher vancomycin MIC was associated with increased mortality; however, it was regardless of the usage of vancomycin or flucloxacillin. The authors theorized that treat-

ment outcome might have been affected by additional unrecognized host or pathogen factors. The design of our study precluded this kind of comparison because we included only patients who received vancomycin as initial therapy for MRSA BSI and excluded patients with MSSA bacteremia.

As highlighted by Holland and Fowler [32], various studies showed some relationship between vancomycin MIC and high failure rate or mortality, but the link between the two is probably not causal. Although the guidelines may differ regarding at which level of MICs an alternative therapy should be considered and for which MRSA infections (and despite the limitations of our findings), we recommend the cautious use of vancomycin in severe (life-threatening) staphylococcal dis-

Figure 3. Survival curves of patients with methicillin-resistant *Staphylococcus aureus* bloodstream infections stratified by minimum inhibitory concentrations $\geq 2 \mu\text{g/mL}$ versus $p = .02$. Abbreviation: MIC, minimum inhibitory concentration.

eases as recommended by others as well [33]; alternative therapy should be considered if the vancomycin MIC is $\geq 2 \mu\text{g/mL}$, particularly in immunocompromised patients.

Patients who were switched earlier to an alternative anti-MRSA agent (within 4 days) because they did not experience a response to vancomycin had much lower mortality rates, indicating the crucial timing of empiric “optimal” therapy for serious infections in immunocompromised patients in particular. Various studies have found that daptomycin, linezolid, and tigecycline are important substitutes for vancomycin, depend-

ing on the site of infection [15, 34–37]. In one study, daptomycin and linezolid were recommended for managing severe community- or hospital-acquired infections [38].

Our study has some inherent limitations, including its retrospective nature. However, it includes a large number of patients treated with the same initial antibiotic over the span of 9 years. Furthermore, relevant cofounders could have been overlooked, and the complexity of our immunocompromised patients may make the determination of causality difficult.

In summary, we found a high failure rate for vancomycin in MRSA BSI in patients with cancer, with increased morbidity and mortality. Switching to an alternative therapy at the earliest sign of failure (≤ 4 days) may improve outcome. We also recommend alternative anti-MRSA therapy in patients with cancer with serious MRSA infections with a vancomycin MIC of $\geq 2 \mu\text{g/mL}$.

ACKNOWLEDGMENTS

This work was supported by Cubist Pharmaceuticals. We thank Ann M. Sutton from the University of Texas MD Anderson Cancer Center for editorial support.

AUTHOR CONTRIBUTIONS

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