



Incidence of Bacteremia and Associated Mortality after Allogeneic Stem Cell Transplantation during Two Different Prophylactic Strategies: A 12-Year Experience at Memorial Sloan-Kettering Cancer Center (MSKCC)

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Introduction

Bacteremia is a frequent complication of allogeneic stem cell transplantation (HSCT). At MSKCC during 1999-2004, the rate of pre-engraftment bacteremia was 22%. Viridans streptococcal bacteremia (VSB) comprised 30% of all early bacteremias. In a retrospective study we showed that vancomycin pre-engraftment was associated with a decrease in VSB. Since Dec 2005, we instituted vancomycin prophylaxis in HSCT patients undergoing myeloablative conditioning. In 2006, we implemented fluoroquinolone (FQ) prophylaxis in selected patient groups. Information regarding the effect of prophylaxis antibiotics among patients undergoing HSCT is scanty.

Objectives

- To study trends in the rate of bacteremia occurring from Day -7 to Day +100 post transplant in adult SCT during 2000 to 2011
- To study the impact of antibiotic prophylactic strategies on:
 - Overall rate of pre-engraftment bacteremia
 - Rate of bacteremia caused by specific organism
 - Antibiotic resistance
- To analyze risk factors associated with pre-engraftment bacteremia

Methods & Materials

Retrospective review of 1,138 consecutive adult allogeneic HSCT between January 1, 2000 and December 31, 2011. Figure 1 summarizes antibiotic prophylaxis strategies during the study period. Bacteremia was defined as isolation of a bacterial pathogen from ≥1 blood culture or ≥2 consecutive for coagulase negative staphylococci (CoNS) and other skin contaminants. Bacteremic episodes from Day -7 through Day+100 were extracted from the BMT database. To assess the effect of prophylaxis antibiotics, we compared the etiology of pre-engraftment bacteremia during the study period. Risk factors of pre-engraftment bacteremia were also assessed. Figure 1 summarizes antibiotic prophylaxis strategies throughout the study period.

Results

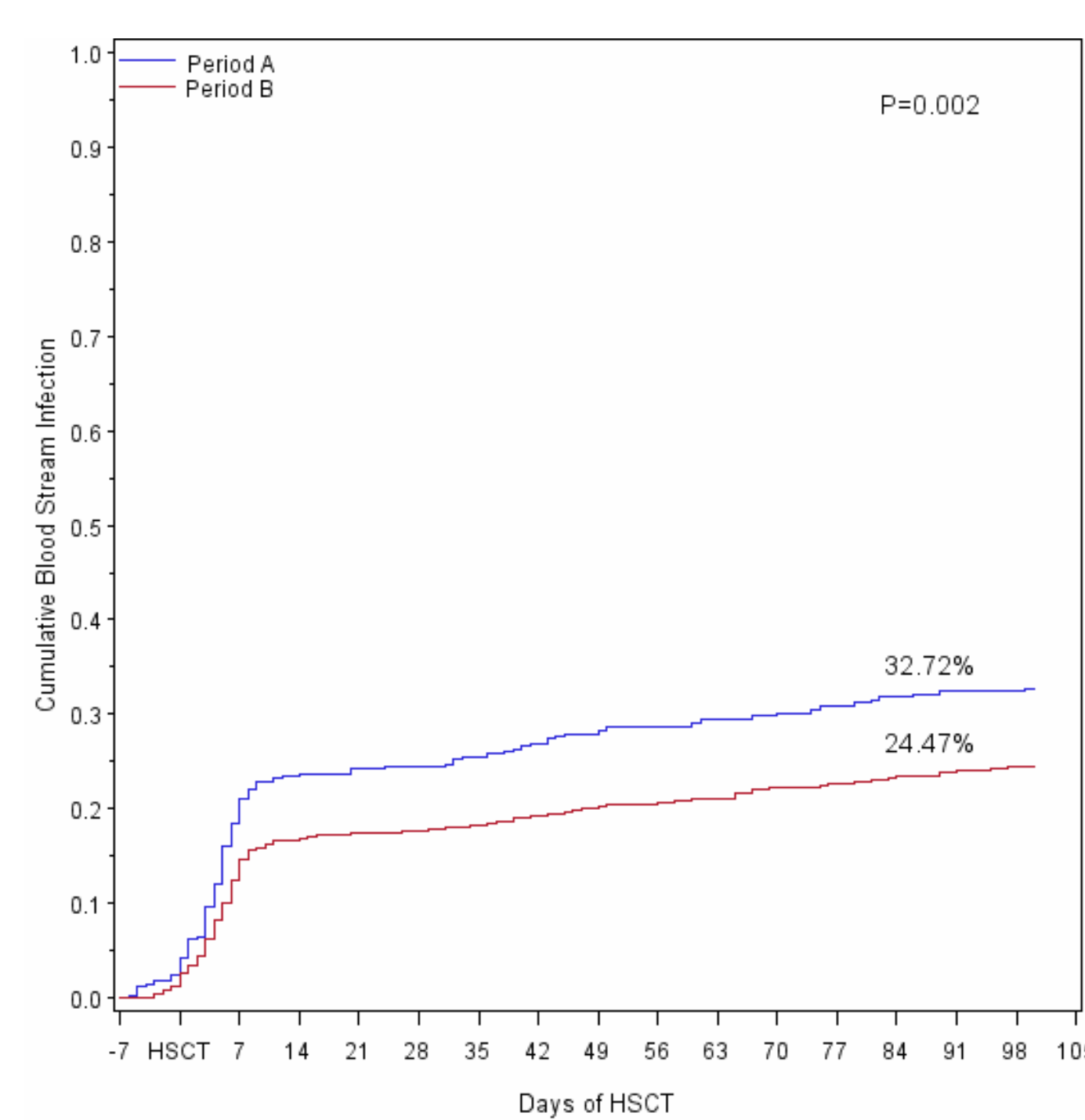
27% of patients developed 361 bacteremic episodes; 70.6% had pre-engraftment bacteremia.

Baseline characteristics

Variable	2000-2005 (%) N = 397	2006-2011 (%) N = 741	P-value
Age, median	46	52	<0.001
Male	223 (56)	443 (60)	NS
Stem cell source			<0.001
- PBSC	274 (69)	595 (80)	
- bone marrow	122 (31)	36 (5)	
- umbilical cord blood	1	110 (15)	
Conditioning regimen			0.005
-MA/RIC	311 (78)	521 (70)	
-NMA	86 (22)	220 (30)	
T-cell depletion	131 (33)	378 (51)	<0.001
Antibiotic prophylaxis			<0.001
- None	179 (45)	44 (6)	
- Vancomycin only	143 (36)	370 (50)	
- FQ only	12 (3)	67 (9)	
- FQ + vancomycin	60 (15)	259 (35)	

Abbreviations: PBSC = peripheral blood stem cell; MA = myeloablative; NMA = non-myeloablative; RIC = reduced intensity conditioning; FQ = fluoroquinolones.

Cumulative incidence of bacteremia

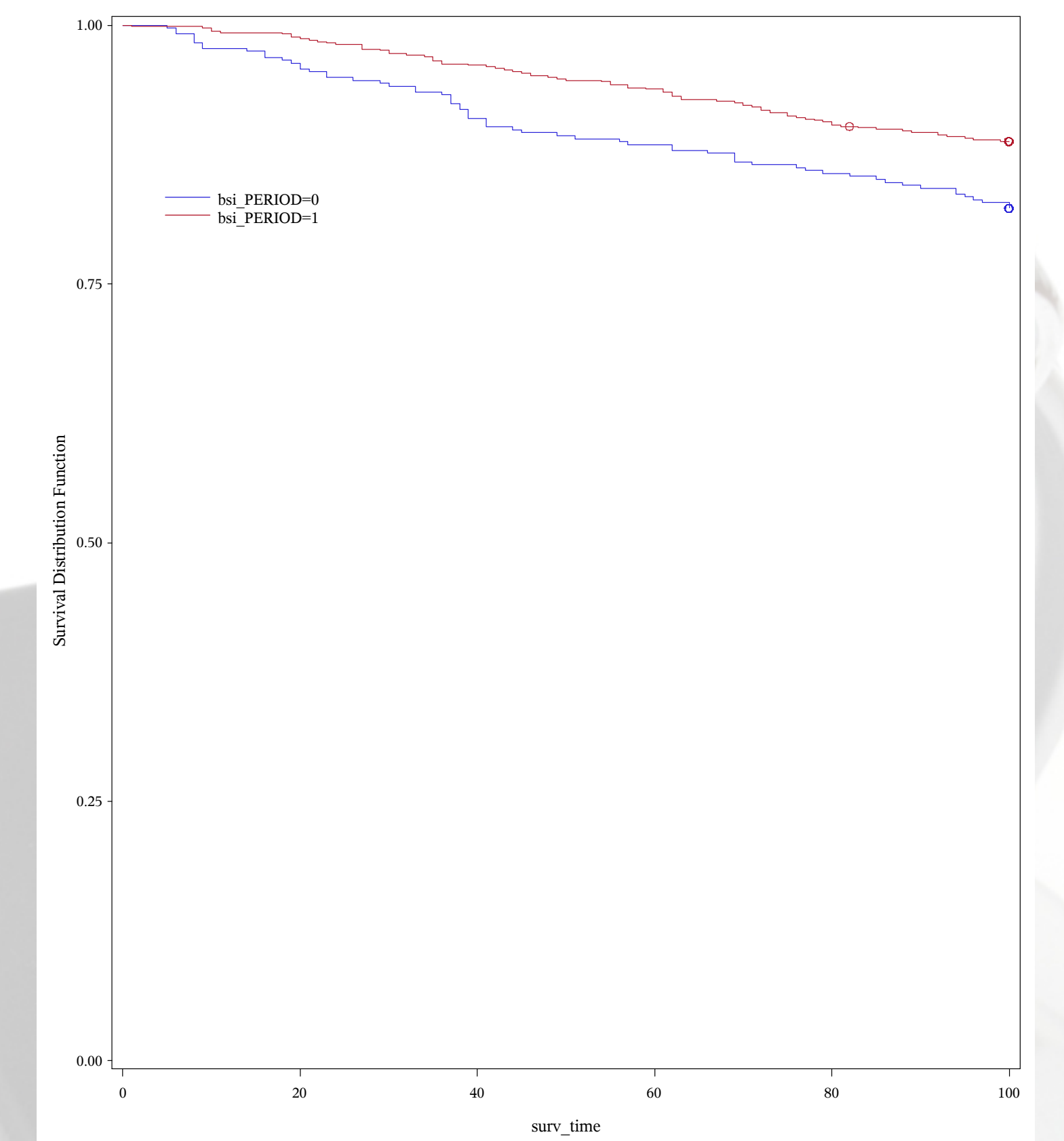


Antibiotic resistance

- Vancomycin-resistant enterococci comprised the majority of enterococcal isolates (81% in period A and 90% in period B, P = NS).
- Among GNR, the rate of FQ resistance was 39% and was unchanged between the two periods.
- Resistance to carbapenem and ESBL-producer were also similar in both time periods.

Overall survival at day 100.

Infection-related mortality was significantly higher in period A (7% in period A vs 2% in period B, P=0.002).



Multivariate analyses of risk factors for pre-engraftment bacteremia

Variable	Hazard ratio (95% CI)	P-value
Stem cell source		0.0009
- PBSC	1.0	
- bone marrow	0.97 (0.6-1.6)	
- umbilical cord blood	3.4 (1.5-7.9)	
T-cell depletion	2.9 (1.8-4.5)	<0.0001
Antibiotic prophylaxis		0.0001
- None	1.0	
- Vancomycin only	0.5 (0.3-0.7)	
- FQ only	0.7 (0.4-1.1)	
- FQ + vancomycin	0.3 (0.2-0.5)	
Transplant period B	1.0 (0.6-1.5)	0.99

Trends in Causative organisms

Rates of pre-engraftment bacteremia per 1,000 HSCT days

Organisms	Period A	Period B	P-value
<i>S. viridans</i>	7.1	0.3	<0.001
<i>Enterococcus</i> spp.	7.1	6.3	0.92
<i>Staphylococcus</i> spp.	2.9	1.5	0.2
Gram-negative bacteria	6.6	7.8	0.66
Other	1.8	0.4	0.23

Figure 1. Antibiotic prophylaxis during the study period

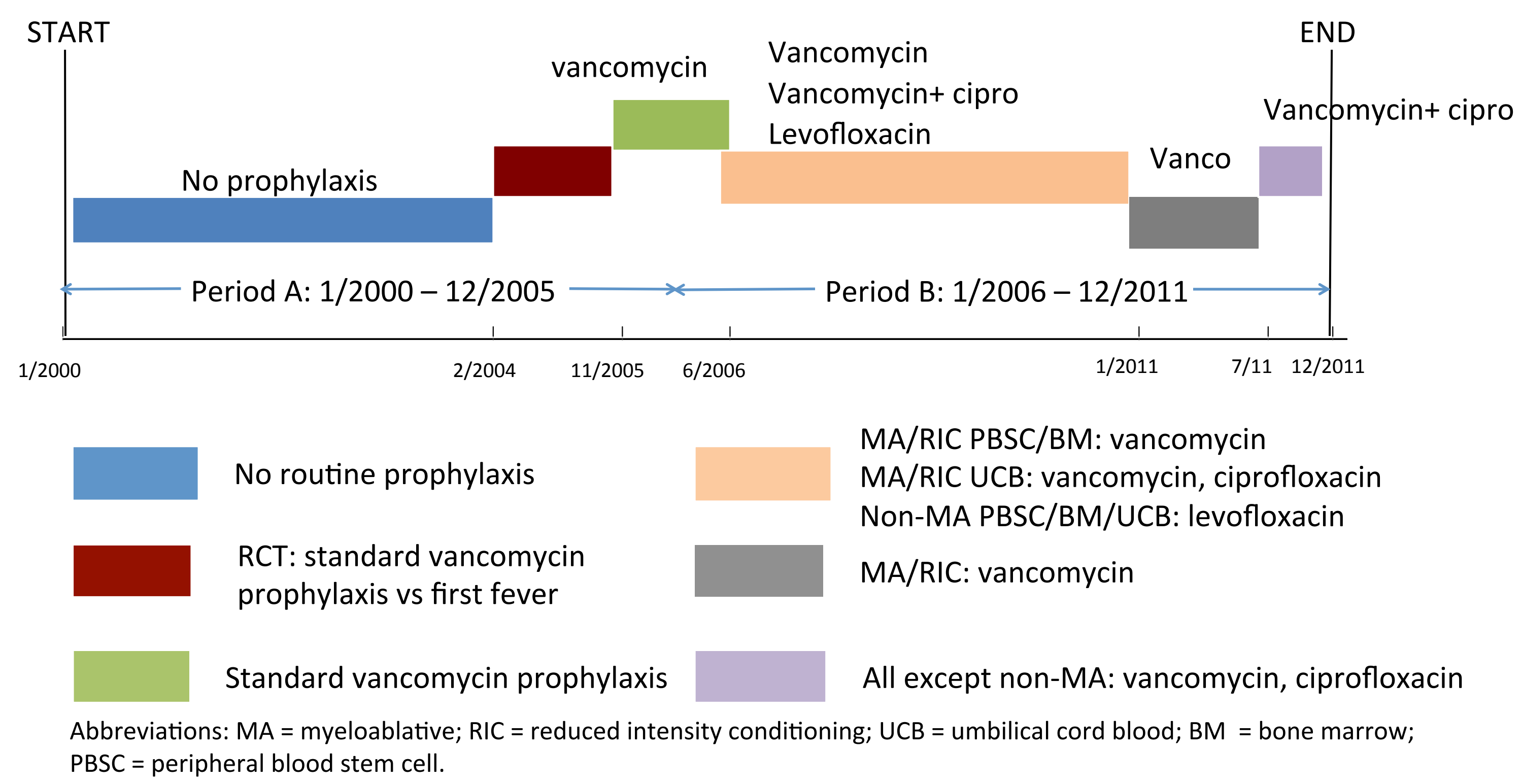
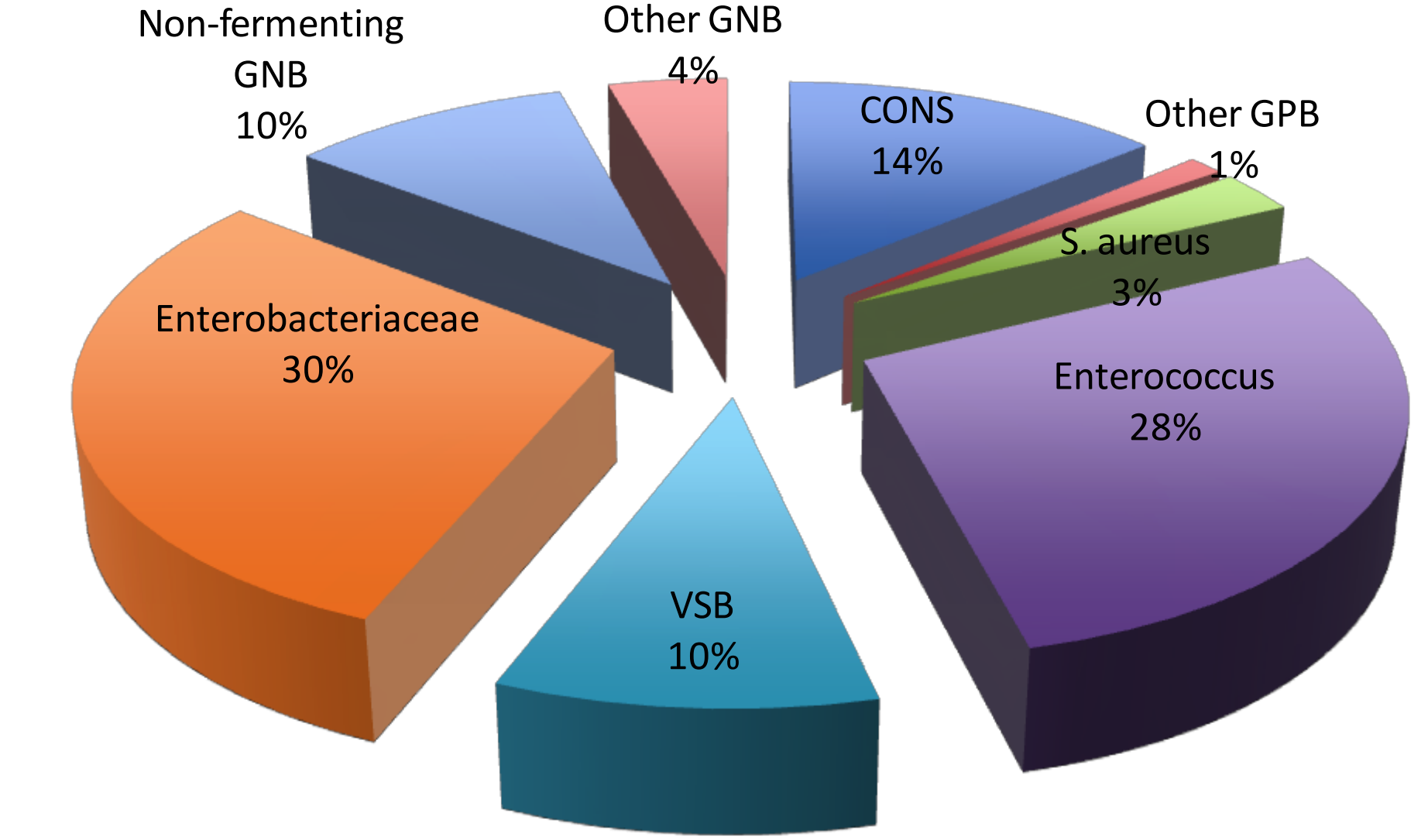


Figure 2. Causative organisms



Abbreviations: GNB = gram negative bacteria; GPB = gram-positive bacteria

Summary

- Vancomycin prophylaxis was associated with decreased incidences of pre-engraftment bacteremia, mainly due to the dramatic decrease of VSB.
- Infection-related mortality was also reduced during the prophylactic period.

References

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