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## ABSTRACT (modified from original submission)

**Background:** Few contemporary studies have evaluated the role of antibacterial prophylaxis during neutropenia in patients with lymphoma undergoing autologous hematopoietic stem cell transplantation (HSCT).

**Methods:** At our center, levofloxacin prophylaxis was initiated during neutropenia in February 2012 in autologous HSCT recipients with lymphoma. We compared the incidence of bloodstream infection (BSI) and fever and neutropenia (FN) within 30 days of transplantation before (February 2008-January 2012) and after (February 2012-October 2015) the initiation of levofloxacin prophylaxis. A multivariable logistic regression model was constructed to determine whether levofloxacin prophylaxis was independently associated with these outcomes. Finally, we compared rates of BSI due to multidrug-resistant (MDR) bacteria (e.g., methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, levofloxacin-resistant or ceftriaxone-resistant Enterobacteriaceae) and the rate of *Clostridium difficile* infection within 90 days of transplantation before and after this intervention.

**Results:** After initiation of levofloxacin prophylaxis, the rate of BSI decreased from 40% (40/101) to 18% (18/87;  $P = 0.001$ ). This decline was largely due to decreases in the rates of Gram-negative bacteremia (29% vs. 5%,  $P < 0.001$ ) and bacteremia caused by Enterobacteriaceae (22% vs. 3%,  $P < 0.001$ ). There was a non-significant decrease in the rate of Gram-positive bacteremia from 21% to 14% ( $P = 0.15$ ). Levofloxacin prophylaxis was independently associated with decreased odds of BSI (odds ratio 0.33; 95% confidence interval, 0.17-0.76;  $P = 0.002$ ) in multivariable analysis. There was no change in the rate of BSI due to MDR bacteria (11% vs. 8%), *C. difficile* infection (9% vs. 7%), or 30-day mortality (5% vs. 1%) between study periods. On the other hand, there was only a non-significant trend towards a decreased rate of febrile neutropenia before and after the initiation of levofloxacin prophylaxis (91% vs. 83%;  $P = 0.09$ ).

**Conclusion:** Levofloxacin prophylaxis is associated with a decreased risk of BSI in patients with lymphoma undergoing autologous HSCT, without a concurrent increased risk of BSI caused by MDR bacteria or *C. difficile* infection.

## INTRODUCTION

- IDSA recommends consideration of prophylactic antibiotics in patients with anticipated chemotherapy induced neutropenia of at least 7 days.<sup>1</sup>
- Past studies have demonstrated reductions in rates of FN and BSI among patients with chemotherapy-induced neutropenia who received fluoroquinolone prophylaxis.<sup>2,3</sup>
- Previously published data from our center demonstrated reductions in rates of FN and BSI among autologous HSCT-recipients with multiple myeloma who received levofloxacin prophylaxis.<sup>4</sup>

## METHODS

**Design:** Single center, retrospective cohort study.

**Study Population:** Adult ( $\geq 18$  years of age) patients with lymphoma who received autologous HSCT at New York Presbyterian Hospital/Weill Cornell Medical Center between February 2008 and October 2015.

- Period 1: Feb 2008 – Jan 2012 (no antibacterial prophylaxis)
- Period 2: Feb 2012 – Oct 2015 (**levofloxacin prophylaxis**)
  - 500 mg daily starting one day prior to HSCT until fever and neutropenia or resolution of neutropenia.

## Primary Outcomes:

1. BSI within 30 days of transplant
2. Febrile neutropenia (FN) within 30 days transplant

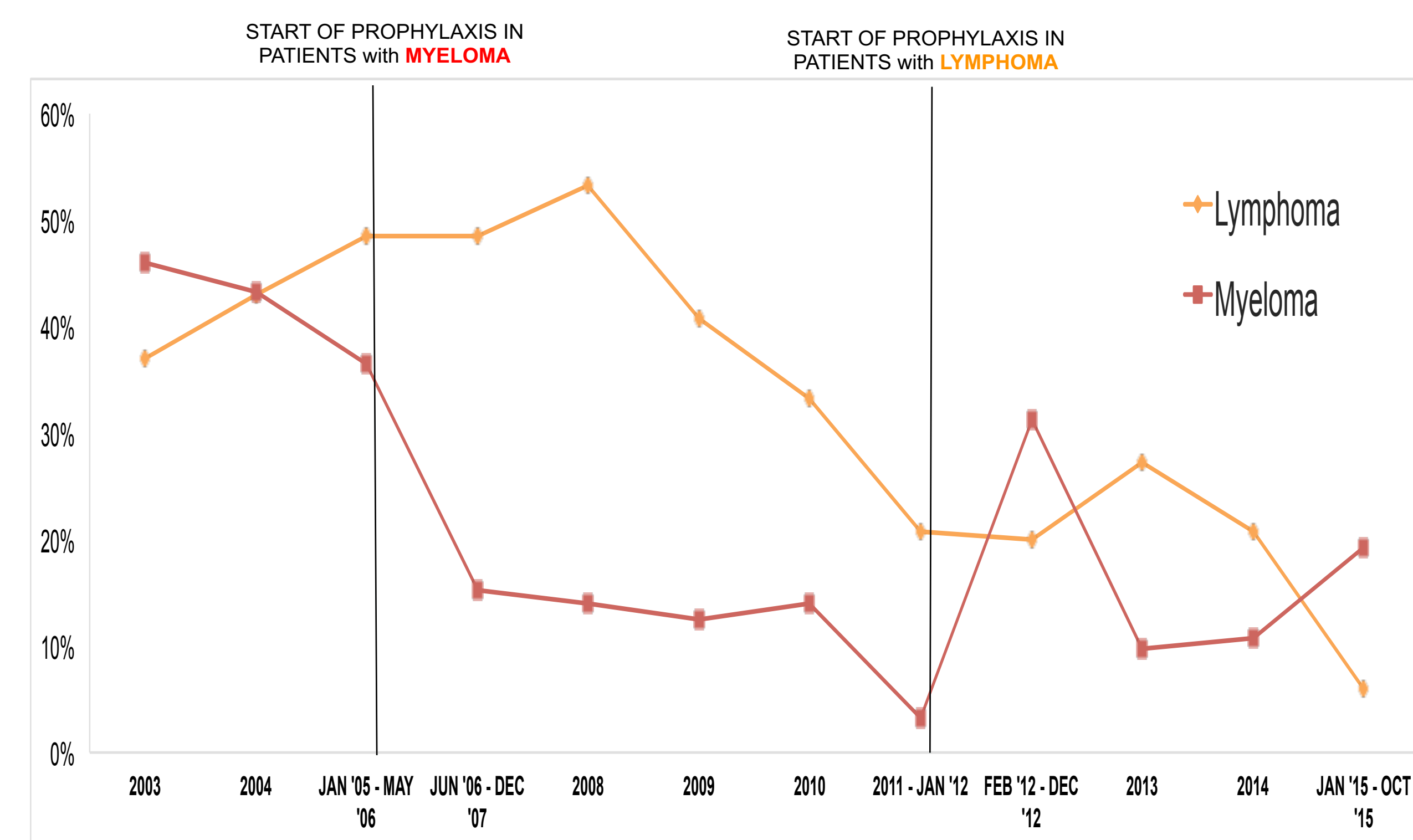
## Secondary Outcomes:

- BSI due to specific MDR-pathogens
  - VRE, MRSA, levofloxacin or ceftriaxone-resistant Enterobacteriaceae
  - *Clostridium difficile* infection within 90-days of transplant
- BSI associated with:
  - Severe sepsis
  - ICU admission
- Readmission within 90 days of transplant
- Mortality within 90 days of transplantation.

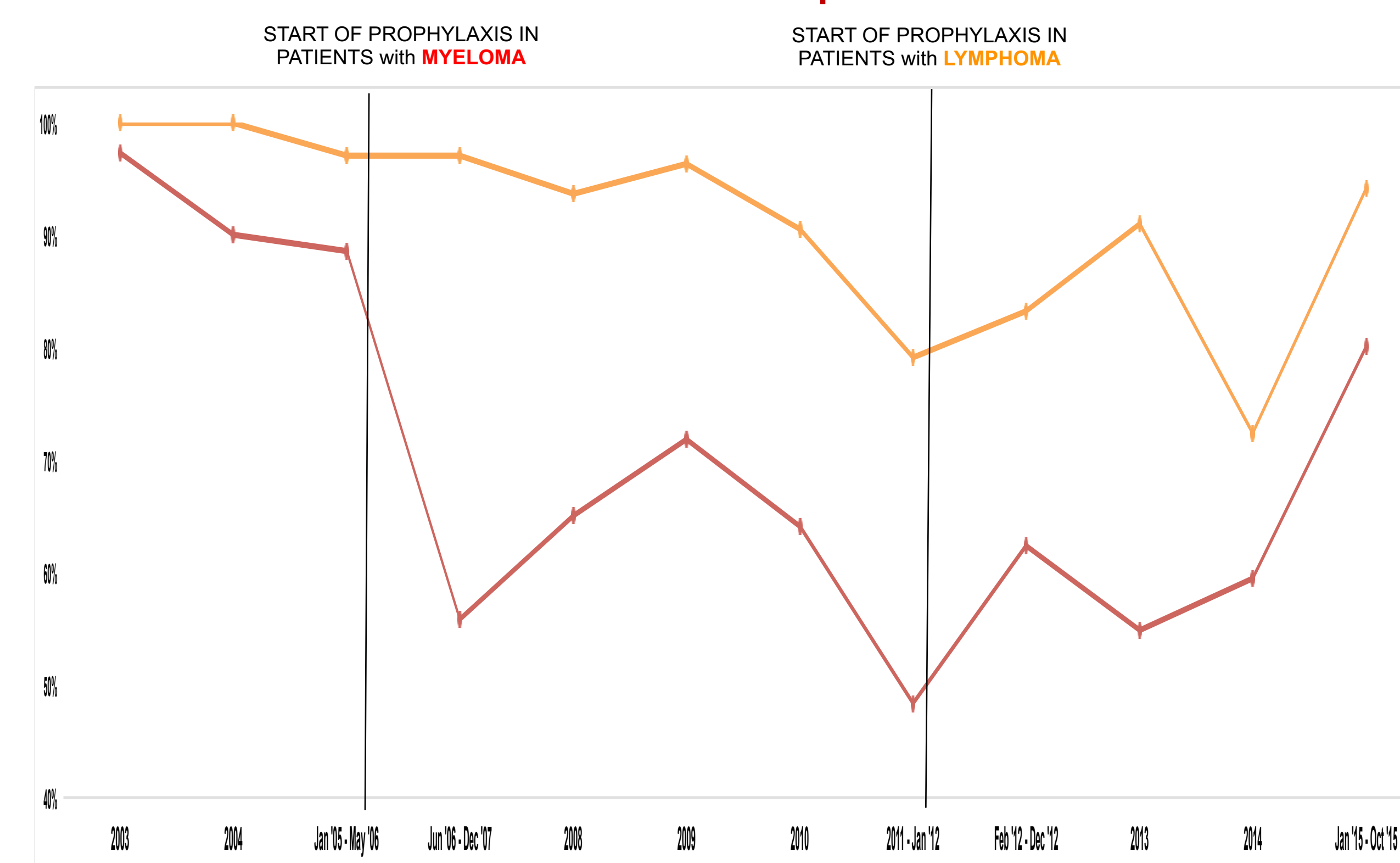
**Neutropenia:** absolute neutrophil count  $\leq 500$  cells/ $\mu$ L.

## RESULTS

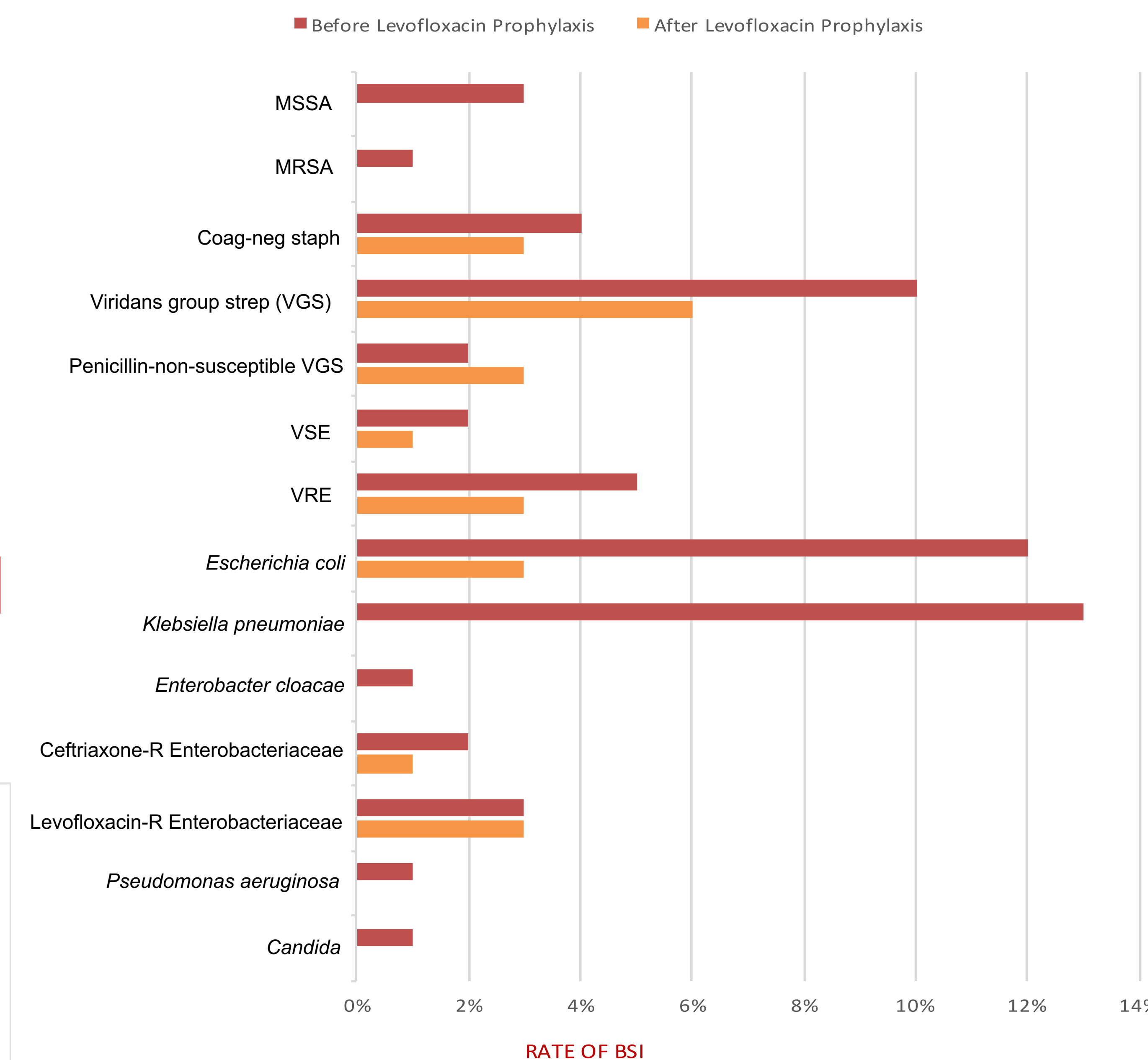
### Rates of BSI within 30 days Over Time



### Rates of Febrile Neutropenia Over Time



## Rates of BSI by Organism in Autologous HSCT Recipients with Lymphoma Before and After the Initiation of Levofloxacin Prophylaxis



## Outcomes in Patients with Lymphoma Who Received and Did Not Receive Prophylactic Levofloxacin during Neutropenia after HSCT

Outcomes	No Levofloxacin Prophylaxis (n = 101) N (%)	Levofloxacin Prophylaxis (n = 87) N (%)	P
Febrile neutropenia	92 (91)	73 (83)	0.09
<b>BSI</b> (within 30d of transplant)	40 (40)	16 (18)	<b>0.001</b>
Gram-positive BSI	22 (22)	12 (14)	0.15
<b>Gram-negative BSI</b>	29 (29)	4 (5)	<b>&lt;0.001</b>
BSI associated with severe sepsis	11 (11)	6 (7)	0.33
BSI associated with ICU admission	5 (5)	2 (2)	0.33
<i>Clostridium difficile</i> infection within 90d of transplant	4 (9)*	6 (7)	0.59
Readmission within 90d of transplantation	16 (16)	10 (11)	0.37
<b>Mortality within 90d of transplantation</b>	8 (8)	1 (1)	<b>0.04</b>

\*Excluded patients before 2010 because PCR-based testing for *C. diff* started in Jan 2010

## Multivariable Analysis

### Factors Associated with Developing BSI and FN

Variable	BSI Odds Ratio (95% CI)	P	FN Odds Ratio (95% CI)	P
Age, per year	1.03 (1.00-1.05)	0.05	1.01 (0.99-1.05)	0.24
Diabetes	Not in model		0.26 (0.05-1.33)	0.11
Baseline creatinine, per mg/dL increase	3.30 (0.7-15.2)	0.13	0.08 (0.01-0.62)	0.015
<b>Levofloxacin prophylaxis</b>	<b>0.33 (0.17-0.66)</b>	<b>0.002</b>	<b>0.44 (0.17-1.13)</b>	<b>0.09</b>

## CONCLUSIONS

- In patients with lymphoma undergoing autologous HSCT, levofloxacin prophylaxis is associated with:
  - Decrease in rate of BSI, mostly because of a decrease in Gram-negative bacteremia
    - This association persisted in a multivariable analysis
  - Non-significant decrease in rate of febrile neutropenia
- There was no significant increase in rates of BSI caused by MDR bacteria or *C. difficile* infection.
- There was an association with decreased 90-day mortality, but unclear whether this is related to the intervention of levofloxacin prophylaxis

## References:

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- <sup>4</sup>Satlin, M.J., et al. Impact of Prophylactic Levofloxacin on Rates of Bloodstream Infection and Fever in Neutropenic Patients with Multiple Myeloma Undergoing Autologous Hematopoietic Stem Cell Transplantation. Biol Blood Marrow Transplant, 2015. 21(10), pp. 1808-1814.