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Fluoroquinolone prophylaxis is highly effective for the prevention of central line-associated bloodstream infections in autologous stem cell transplant patients

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Abstract

Objectives: Patients undergoing stem cell transplant (SCT) for the treatment of hematologic malignancy are at increased risk for central line-associated bloodstream infections (CLABSIs). The use of prophylactic antibiotics to prevent CLABSIs in the setting of autologous SCT is of unclear benefit. We aimed to evaluate the impact of levofloxacin prophylaxis on reducing CLABSIs in this high-risk population.

Methods: Patients undergoing autologous SCT at a tertiary-care hospital received levofloxacin prophylaxis from January 13, 2016 to January 12, 2017. Levofloxacin was administered from autologous SCT (day 0) until day 13, absolute neutrophil count > 500/mm^3, or neutropenic fever, whichever occurred first. Clinical outcomes were compared to a baseline group who underwent autologous SCT but did not receive antibacterial prophylaxis during the previous year. The primary endpoint was incidence of CLABSIs assessed using Cox proportional hazards regression.

Results: A total of 324 patients underwent autologous SCT during the entire study period, with 150 receiving levofloxacin prophylaxis during the intervention period. The rate of CLABSIs was reduced from 18.4% during the baseline period to 6.0% during the intervention period. On multivariable analysis, levofloxacin prophylaxis significantly reduced CLABSI incidence (hazard ratio (HR) 0.33; 95% confidence interval (CI) 0.16–0.69; P=0.003). There was also a reduction in the risk of neutropenic fever (odds ratio (OR) 0.23; 95% CI 0.14–0.39; P<0.001) and a trend

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toward a reduction in intensive-care unit transfer for sepsis (OR 0.33; 95% CI 0.09–1.24; *P*=0.10) in patients receiving levofloxacin prophylaxis. Notably, there was no increase in *Clostridium difficile* infection in the levofloxacin group (OR 0.66, 95% CI 0.29–1.49, *P*=0.32).

Conclusions: Levofloxacin prophylaxis was effective in reducing CLABSIs and neutropenic fever in patients undergoing autologous SCT. Further studies are needed to identify specific patient groups who will benefit most from antibiotic prophylaxis.

INTRODUCTION

Over the past decade, rates of central line-associated bloodstream infections (CLABSIs) have been reduced by over 50% among hospitalized patients through the implementation of standardized infection prevention strategies[1,2]. However, CLABSIs remain common in patients with hematologic malignancy and are associated with significant morbidity and mortality, including an increased risk of acute graft-versus host disease (GVHD), prolonged lengths of stay, and up to a 7-fold increased risk of death[3–8]. In patients undergoing autologous stem cell transplant (SCT), rates of CLABSIs have been estimated to be as high as 20–40%[6,9].

Patients undergoing SCT are at increased risk of infection due to their underlying malignancy, frequent hospitalizations, chemotherapy-induced immune suppression, and neutropenia. The majority of patients require prolonged use of central venous access devices for the receipt of chemotherapy and transfusion of blood products. In addition, myeloablative regimens prior to SCT result in neutropenia of days to weeks and typically result in mucosal barrier injury in the gastrointestinal tract[10]. Translocation of gut bacteria can then result in primary bloodstream infections, an infection termed mucosal barrier injury laboratory confirmed bloodstream infection (MBI-LCBI) for surveillance purposes by Centers for Disease Control and Preventions (CDC)'s National Healthcare Safety Network (NHSN)[11]. Importantly, these MBI-CLABSI events may not be preventable with common infection prevention strategies such as aseptic catheter insertion, chlorhexidine gluconate bathing, and optimal central line care[12]. However, MBI-CLABSIs are associated with similar morbidity and mortality as CLABSIs associated with typical, non-MBI pathogens and as such, represent a critical target for prevention in hospitalized patients[5,11].

Two randomized trials of levofloxacin prophylaxis among cancer patients conducted more than a decade ago demonstrated conflicting results for the prevention of bloodstream infections and were limited by inclusion of patients with both solid and hematologic malignancy and varied timing and duration of prophylaxis regimens[13–15]. Since these studies, the utility of antibiotic prophylaxis has become less clear, due in part to increasing rates of fluoroquinolone resistance and the risk of *Clostridium difficile* infection associated with these agents[16–18]. Additionally, the complexity of these patients and delivery of care (e.g., chemotherapy regimens) have significantly increased. Given the paucity of evidence for the impact of routine antibiotic prophylaxis in patients undergoing autologous SCT, there has been a lack of standardized recommendations from hematology oncology society guidelines, as well as significant variation in application by cancer treatment programs[19–21]. Thus, we aimed to investigate not only the benefit of levofloxacin prophylaxis for the

prevention of CLABSIs, but also potential risks in a current group of patients undergoing autologous SCT at a tertiary care center.

METHODS

Study design and setting.

We performed a retrospective cohort study of autologous SCT patients admitted to the Hospital of the University of Pennsylvania (HUP) from January 13, 2015 to January 12, 2017. HUP is a 776-bed tertiary care medical center and a National Cancer Institute Comprehensive Cancer Care designated center.

Study population.

Levofloxacin prophylaxis in patients undergoing autologous SCT was initiated on January 13, 2016 as an infection prevention initiative. Prior to January 13, 2016 no routine antibiotic prophylaxis was provided to these patients. With the initiation of levofloxacin prophylaxis, patients undergoing autologous SCT were prescribed levofloxacin 500 mg oral daily (with dosing adjustments made based on creatinine clearance), from the date of SCT (day 0) until day 13, engraftment (absolute neutrophil count (ANC) >500 cells/mm^3), or neutropenic fever (ANC<500 cells/mm^3 with oral temperature >100.4˚ F), whichever occurred earliest. With the onset of neutropenic fever, patients were switched to cefepime or meropenem as per institutional neutropenic fever guidelines. No alternative antibiotics were provided for prophylaxis in the setting of an allergy or contraindication to fluoroquinolones (e.g., prolonged QT interval). During the entire study period, there was also an ongoing infection prevention educational campaign to improve adherence to daily chlorhexidine gluconate (CHG) bathing. There were no additional co-occurring interventions targeted towards the reduction of CLABSIs during the study period. Additionally, no routine surveillance cultures were performed. The group of patients who received levofloxacin prophylaxis during the year after initiation of this intervention (January 13, 2016 to January 12, 2017) were compared to those who did not receive prophylaxis in the previous year (January 13, 2015 to January 12, 2016). Therefore, the exposure of interest for this cohort study was the receipt of levofloxacin prophylaxis. The study was reviewed and approved by the University of Pennsylvania institutional review board (IRB).

Data collection.

Clinical data were collected via electronic medical record review, including demographics and comorbidities. Specific oncology data were ascertained, including type of malignancy, history of relapsed or recurrent primary malignancy, the chemotherapy regimen received during autologous SCT, duration of neutropenia, development of mucositis, inpatient medications, and adherence to CHG bathing. CHG bathing adherence was measured as the number of days with documented completion in the nursing flowsheet during the day of SCT and the following seven days (day 0 to day 7).

Study outcomes.

The primary outcome of interest was incidence of CLABSI, including both MBI and non-MBI primary bloodstream infection events. CLABSI events had been previously ascertained

by standardized review by the Department of Healthcare Epidemiology and Infection Prevention utilizing NHSN surveillance criteria[11], defined as a primary BSI with the presence of a central venous catheter. Within the definition of CLABSI, these events may be classified as either MBI or non-MBI depending on the pathogen (i.e. intestinal organisms) and clinical characteristics of the patient (e.g. neutropenia, diarrhea, or GVHD of the gut). Secondary BSIs were attributed when there was a known primary site of infection (e.g., pneumonia). Secondary outcomes included in-hospital mortality, requirement for medical intensive care unit (ICU) transfer, *C. difficile* infection, bloodstream infection other than primary CLABSI, neutropenic fever, and broad-spectrum antibiotic utilization, all within 30 days of SCT. Inpatient antibiotics were reviewed from patient charts and recorded as days of therapy (DOT). Additional outcomes included total length of stay following SCT and readmission to any University of Pennsylvania Health System hospital within 30 days from discharge.

All blood cultures were performed in the Hospital of the University of Pennsylvania Clinical Microbiology Laboratory using the BACTEC™ FX system (Becton Dickinson, Franklin Lakes, NJ), organism identification using the Vitek MS Matrix Assisted Laser Desorption/ Ionization (MALDI-TOF) (bioMérieux, Durham, NC), and antibiotic susceptibilities using the Vitek 2 automated platform (bioMérieux, Durham, NC) with Clinical and Laboratory Standards Institute (CLSI) breakpoints[22]. *C. difficile* testing was performed using a commercial EIA for detection of toxin A, B, and glutamate dehydrogenase (GDH) (C Diff Quik Check Complete, Alere, Waltham, MA). Samples negative for toxin A and B but positive for GDH were subsequently tested using PCR for toxin genes (BD MAX Cdiff Assay, Becton Dickinson, Franklin Lakes, NJ).

Statistical analysis.

Primary outcome analysis was conducted using survival analysis to determine the association between levofloxacin prophylaxis and time to development of a CLABSI. Time zero for all patients was defined as the day of SCT (day 0). The failure event was defined as development of CLABSI. Patients who did not develop a CLABSI were censored at death, discharge, or day 30 of hospital stay. Evaluation of the time to development of CLABSI was assessed with the Kaplan-Meier product-limit survival curve estimates and the log-rank statistic for comparison of multiple hazard ratios (HRs) for unadjusted comparison of groups and Cox-proportional hazards regression covariate adjustment. Multivariable Cox-proportional hazards regression analysis was performed to determine the adjusted association between levofloxacin prophylaxis and time to development of CLABSI. This multivariable model was developed beginning with the primary risk factor of interest, admission during the time period following routine antibiotic prophylaxis with levofloxacin. A manual stepwise selection procedure was used, with variables with a P value of <0.25 on bivariable analysis considered as candidate variables and maintained in the final model if their inclusion was statistically significant on likelihood ratio testing. Underlying malignancy was *a priori* selected for inclusion in the model regardless of significance on bivariable analysis due to its clinical importance. The proportional hazards assumption was assessed visually using a log-log plot and by plotting Kaplan-Meier survival against predicted survival. Primary analysis was performed per protocol and an intention-to-treat

analysis was performed as a secondary analysis. Additionally, subanalysis was performed using a bivariable Cox proportional hazard regression model to evaluate the differential impact of levofloxacin prophylaxis on MBI-CLABSIs vs non-MBI CLABSIs. In this subanalysis, all patients were censored at time of CLABSI, with separate failure events of MBI-CLABSI and non-MBI-CLABSI. Two tailed *P* values <0.05 were considered statistically significant.

Categorical secondary outcomes were analyzed using logistic regression. To determine the strength of the association between receipt of levofloxacin and the categorical secondary outcomes, an odds ratio (OR) and 95% confidence interval (CI) were calculated. The association between receipt of levofloxacin and the continuous secondary outcomes, length of stay and antibiotic duration, was assessed using linear regression. All analyses were performed using STATA v.14.2 (StataCorp, College Station, Texas).

RESULTS

Study population.

A total of 324 patients received an autologous SCT during the 2-year study period, with 174 patients included in the baseline group, and 150 patients in the levofloxacin prophylaxis group. Baseline characteristics were similar in both groups (Table 1). In the total population, the median age was 59 years (interquartile range (IQR), 52–65), 194 (60%) were male, and 83 (26%) were categorized as non-white race. Comorbidities were common in the study population, with 83 (26%) of patients with acute kidney injury, and 207 (64%) of patients with mucositis.

There was a greater proportion of patients with multiple myeloma in the levofloxacin prophylaxis group (n=121; 81%) compared to the baseline group that did not receive antibiotic prophylaxis (n=126; 72%) (*P*=0.01). Rates of relapsed or recurrent hematologic malignancy were similar between the levofloxacin and the baseline group, 22 (13%) and 15 (10%), respectively (*P*=0.46). Adherence to CHG bathing was lower in the baseline group, with 140 (80%) patients receiving CHG on <50% of days, compared to 71 (47%) in the levofloxacin group (*P*<0.001).

Primary outcome.

The incidence of CLABSI was 18.4% (32 episodes) in the baseline group and 6.0% in the levofloxacin group (9 episodes). MBI-CLABSI represented 67% of all CLABSIs in the baseline group and 56% in the intervention group. On bivariable analysis, receipt of levofloxacin prophylaxis was associated with a significant reduction in the hazard of CLABSI (HR 0.30, 95% CI 0.14–0.62, *P* <0.001) (Table 2). CLABSI-free survival from autologous SCT is shown in Figure 1. On multivariable analysis adjusting for age, and underlying malignancy, receipt of levofloxacin significantly decreased the hazard of CLABSI with an adjusted HR of 0.33 (95% CI 0.16–0.69, *P* =0.003) (Table 2). On subanalysis, receipt of levofloxacin prophylaxis was associated with a significant reduction in MBI-CLABSI (HR 0.24, 95% CI 0.09–0.64, *P*=0.004) but not non-MBI-CLABSI (HR 0.42, 95% CI 0.13–1.37, *P*=0.15).

On intention-to-treat analysis, an additional eight patients were included who did not receive levofloxacin during the intervention period. Reasons for withholding levofloxacin prophylaxis included reported levofloxacin allergy (n=2), prolonged QT interval at baseline (n=2), history of tendon injury (n=1), history of foot drop (n=1), and ongoing treatment with broad-spectrum gram-negative antibiotics (n=2). On intention-to-treat analysis, there was a similar reduction in hazard of CLABSI with levofloxacin on multivariable analysis, with a HR of 0.34 (95% CI 0.17–0.70, P=0.003).

Secondary outcomes.

Receipt of levofloxacin was associated with a significant reduction in neutropenic fever (OR 0.23, 95% CI 0.14–0.39, P<0.001) and a trend towards a significant reduction in ICU transfer for sepsis (OR 0.33, 95% CI 0.09–1.234, P=0.10) (Table 3). There was no significant association of levofloxacin prophylaxis with in-hospital mortality, hospital readmission, or *C. difficile* infection.

Of the primary and secondary BSIs, there were a total of 61 organisms identified among 50 infections in both groups; 33 (67%) were gram-negative organisms and 16 (33%) were gram-positive organisms in the baseline group compared to 4 (33%) and 8 (67%) respectively in the levofloxacin group. Among gram-negative organisms, the susceptibility rate to levofloxacin was 94% in the baseline group compared to 0% in the levofloxacin group. In the baseline group, the majority of blood culture isolates were levofloxacin-susceptible *Klebsiella* species (35%), *Pseudomonas aeruginosa* (12%), and *Escherichia coli* (12%). In the levofloxacin prophylaxis group, most isolates were levofloxacin-resistant or non-susceptible organisms including *Escherichia coli* (33%) and *Enterococci* (25%).

Mean total days of levofloxacin therapy was greater in the levofloxacin group versus the baseline group (mean 9.2 vs 0.9 days, respectively; P<0.001). However, the levofloxacin group compared to the baseline group demonstrated significant reductions in the use of cefepime (mean 3.1 vs 4.7 days, respectively; P<0.001), and piperacillin-tazobactam (mean 0.1 vs 0.8 days, respectively; P=0.001) (Table 4). There was also a trend toward a decrease in the use of aminoglycosides (mean 0.2 vs 0.4 days, P=0.07) and intravenous vancomycin (mean 1.1 vs 1.7 days, P=0.06) in the levofloxacin prophylaxis group.

DISCUSSION

In this study, we demonstrated that receipt of levofloxacin prophylaxis was associated with a significant reduction in the incidence of CLABSI in patients undergoing autologous SCT. Additionally, the use of levofloxacin resulted in a reduction in neutropenic fever and a trend toward reduced ICU transfers for sepsis, without an increase in rates of *C. difficile* infection. These findings suggest that the use of routine levofloxacin prophylaxis in autologous SCT patients may be beneficial in certain settings where rates of CLABSIs are particularly high. The results of our study are strengthened by a large sample size, use of a current cohort, and detailed collection of both patient characteristics and concomitant interventions (e.g., CHG bathing) that may have impacted the risk of CLABSI.

CLABSIs are associated with significant morbidity and mortality in patients with hematologic malignancy[5]. Our study demonstrated a 67% reduction in hazard of CLABSI with receipt of levofloxacin prophylaxis. To our knowledge, our study is only the second to date to investigate the utility of antibiotic prophylaxis in patients undergoing autologous SCT, and the first to include patients receiving autologous SCT for all malignancy diagnoses[9]. A previous study also found a reduction in bloodstream infections (BSIs) with the use of levofloxacin prophylaxis (41.2% to 14.7%), but was restricted to autologous SCT patients with multiple myeloma and focused on a composite outcome of primary and secondary BSIs[9]. We were primarily interested in the ability of antibiotic prophylaxis to prevent CLABSIs due to high rates in this population and prior studies demonstrating increased mortality with these infections[5,23,24]. We demonstrated that the greatest reduction in BSI with levofloxacin prophylaxis was the prevention of MBI-CLABSI. This distinction is important because it suggests that antibiotic prophylaxis, in concert with traditional methods to reduce CLABSI such as central line care and CHG bathing, may be a particularly beneficial strategy in institutions that provide care for oncology populations.

Our study also demonstrated a substantial reduction of 77% in the odds of neutropenic fever with the use of routine levofloxacin prophylaxis. Neutropenic fever results in prolonged lengths of stay and cost, with an average length of stay of 20 days and a cost of $38,000 per episode[25–27]. Thus, strategies for the prevention of neutropenic fever are important in this population independent of reductions in bloodstream infections. Additionally, prior studies have demonstrated that episodes of neutropenic fever result in over three weeks of antibiotic use per patient[28]. Exposure to broad-spectrum antibiotics, including vancomycin and aminoglycosides, increase the risk of antibiotic resistance, *C. difficile*, and other antibiotic-associated adverse events (e.g. renal failure) which could potentially be limited by use of prophylactic antibiotic therapy. While levofloxacin use increased in our intervention, there was a corresponding reduction in the exposure to broad-spectrum antibiotic therapy, as well as a trend towards decreased transfers to the ICU for neutropenic sepsis. Antibiotic stewardship programs will need to balance the potential benefits of levofloxacin prophylaxis with other factors such as local antibiotic resistance patterns and ongoing interventions that may restrict fluoroquinolone use.

In patients with hematologic malignancy, gut microbiome diversity has been associated with important clinical outcomes including mortality[29]. Prior studies have shown a differential impact of antibiotic classes on microbiome measures, and that the impact of fluoroquinolones is of shorter duration and less severity than beta-lactam antibiotics[30–34]. Thus, it possible that exposure to fluoroquinolone prophylaxis may result in less disruption of the gut microbiome if patients are spared subsequent broad-spectrum beta-lactam antibiotic exposure for neutropenic fever. Further studies are needed to investigate the impact of prophylactic antibiotics versus those administered for the treatment of neutropenic fever on the gut microbiome in this population.

The use of fluoroquinolones has previously been associated with an over two-fold increased risk of *C. difficile* infection among hospitalized adult patients[35–37]. However, we found no increase in the rate of *C. difficile* in among autologous SCT patients receiving levofloxacin prophylaxis. These results are similar to a previous study evaluating fluoroquinolone

prophylaxis in multiple myeloma patients undergoing autologous SCT, where rates of *C. difficile* were 7% and 3% in the intervention versus baseline groups, respectively (P=0.75)[9]. It is likely that our intervention did not result in an increase in *C. difficile* rates due to the reduction in broad-spectrum antibiotics used for neutropenic fever, which have also been implicated in *C. difficile* infection[38].

Not surprisingly, in our study, we saw an overall shift in the proportion of levofloxacin-resistant gram-negative organisms isolated from blood cultures with receipt of levofloxacin prophylaxis. However, the absolute increase was small (2 isolates in the baseline group versus 4 in the levofloxacin group). This is similar to the prior study in this population where the investigators found an increase in the rate of BSIs due to levofloxacin-resistant Enterobacteriaceae from 1% to 5% with the introduction of levofloxacin prophylaxis[9]. These findings suggest a relatively low rate of levofloxacin-resistant bloodstream infections in our population. However, rates of levofloxacin resistant gram-negative organisms should be systematically monitored in institutions where levofloxacin prophylaxis is used. Future studies should also focus on rates of gastrointestinal colonization with fluoroquinolone-resistant Enterobacteriaceae with the introduction of fluoroquinolone prophylaxis.

There are potential limitations to our study. First, a retrospective study design was used, which can lead to greater misclassification of variables. However, we performed detailed medical record review of patient factors including comorbidities, medications, and laboratory results, rather than utilizing diagnostic or billing codes. Second, while the impact of antibiotic prophylaxis on rates of detection of *C. difficile* was assessed, we were unable to ascertain if positive *C. difficile* tests represented colonization or active infection, as approximately 65% of cases were associated only with a positive molecular assay for toxin gene and not with detectable *C. difficile* toxin in the stool specimen. However, colonization with toxigenic *C. difficile* remains a clinically important outcome as colonization with *C. difficile* increases the risk of infection and contributes to transmission in the hospital setting[18,39]. Third, while rates of fluoroquinolone resistance were tracked in bloodstream isolates, we did not perform patient screening for gastrointestinal colonization with fluoroquinolone-resistant gram-negative organisms. Fourth, while we were powered to detect a difference in our primary outcome, we may not have had sufficient power to detect a difference in our less common secondary outcomes, including ICU transfer for sepsis. Finally, this study was conducted in a tertiary care center, and may not be generalizable to other centers performing autologous SCT that may have different patient characteristics, prevention practices, or risk of *C.difficile* infection.

In conclusion, we found that levofloxacin prophylaxis significantly reduced rates of CLABSI and neutropenic fever in patients undergoing autologous SCT. Further studies are needed to identify individual patient factors, and patient groups, at highest risk of MBI-CLABSI who would benefit most from antibiotic prophylaxis.

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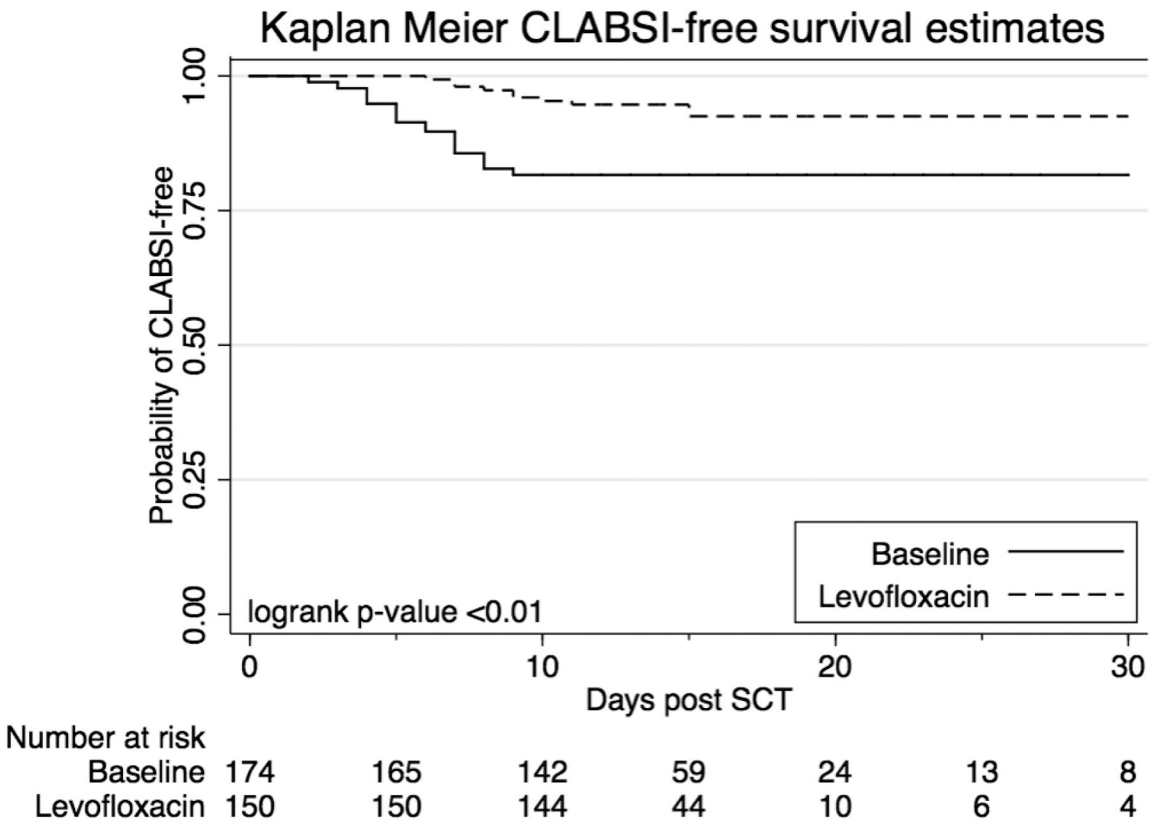

Figure 1.

Kaplan Meier CLABSI-free survival estimates comparing those who received levofloxacin prophylaxis to those who did not

TABLE 1.

Characteristics of patients undergoing autologous stem cell transplant, comparing the baseline group to those who received levofloxacin prophylaxis.

Characteristics	Total Population[a] n = 324	Baseline Group[a] n = 174	Levofloxacin Group[a] n = 150	*P* Value
Age, median years (IQR)	59 (52–65)[b]	59 (52–66)[b]	59 (52–64)[b]	0.72
Male sex	194 (60)	102 (59)	92 (61)	0.62
Non-white race	83 (26)	36 (26)	37 (25)	0.72
Malignancy				
Multiple myeloma	247 (76)	126 (72)	121 (81)	0.01
Non-Hodgkin's lymphoma	41 (13)	30 (17)	11 (7)	
Hodgkin's lymphoma	16 (5)	11 (6)	5 (3)	
Other	20 (6)	7 (4)	13 (9)	
Recurrent disease[c]	37 (11)	22 (13)	15 (10)	0.46
Chemotherapy				
Melphalan 200mg/m^2	204 (63)	97 (56)	107 (71)	0.002
Melphalan, reduced dose	47 (14)	33 (19)	14 (9)	
BCV	45 (14)	30 (17)	15 (10)	
BEAM	16 (5)	11 (6)	5 (3)	
Other	12 (4)	3 (2)	9 (6)	
Neutropenia[d]	6 (5–7)[b]	6 (5–7)[b]	6 (5–7)[b]	0.45
CHG compliance[e]				<0.001
<50%	211 (65)	140 (80)	71 (47)	
50–75%	99 (31)	32 (18)	67 (45)	
>75%	14 (4)	2 (1)	12 (8)	
Comorbidities				
Chronic liver disease[f]	8 (2)	2 (1)	6 (4)	0.10
Chronic lung disease[g]	17 (5)	9 (5)	8 (5)	0.95
Chronic kidney disease	58 (18)	28 (16)	30 (20)	0.36
Acute kidney injury	83 (26)	47 (27)	36 (24)	0.54
Coronary artery disease	32 (10)	17 (10)	15 (10)	0.94
Congestive heart failure	13 (4)	7 (4)	6 (4)	0.99
Diabetes mellitus	31 (10)	12 (7)	19 (13)	0.08
Mucositis[h]	207 (64)	112 (64)	95 (63)	0.85

NOTE. BCV, busalfan, cyclophosphamide, and etoposide; BEAM, caramustine, etoposide, cytarabine, and melphalan; CHG, chlorhexidine gluconate.

[a] Unless noted otherwise, n (%)

[b] Median, inter-quartile range (IQR)

[c] History of same hematologic malignancy with relapsed disease

[d] Days of absolute neutrophil count (ANC) <500 cells/mm3

[e] Days of documented CHG bathing from date of stem cell transplant to day 7

[f] Chronic liver disease includes cirrhosis and chronic viral hepatitis

[g] Chronic lung disease includes chronic obstructive pulmonary disease (COPD), emphysema, asthma, and pulmonary fibrosis

[h] Mucositis of any grade

TABLE 2.

Survival analysis for time to development of central line-associated bloodstream infection in patients undergoing autologous stem cell transplant

Variable	Bivariable HR (95% CI)	*P* Value	Multivariable HR (95% CI)	*P* Value
Levofloxacin prophylaxis	0.30 (0.14–0.63)	<0.001	0.33 (0.16–0.69)	0.003
Age	1.02 (0.99–1.05)	0.22	1.03 (1.00–1.06)	0.05
Male sex	1.33 (0.70–2.54)	0.38		
Non-white race	0.93 (0.47–1.86)	0.84		
Multiple myeloma	0.42 (0.23–0.79)	0.005	0.36 (0.19–0.69)	0.002
Recurrent disease[a]	1.65 (0.73–3.73)	0.22		
Neutropenia[b]	1.18 (1.07–1.29)	<0.001		
CHG compliance <50%[c]	1.99 (0.95–4.17)	0.06		
Chronic liver disease[d]	2.11 (0.51–8.74)	0.29		
Chronic lung disease[e]	0.42 (0.06–3.12)	0.39		
Chronic kidney disease	1.25 (0.60–2.63)	0.54		
Acute kidney disease	1.90 (1.01–3.56)	0.04		
Coronary disease	1.56 (0.66–3.71)	0.31		
Congestive heart failure	0.56 (0.08–4.10)	0.56		
Diabetes mellitus	0.74 (0.23–2.40)	0.61		
Mucositis	1.22 (0.63–2.36)	0.55		

NOTE. CHG, chlorhexidine gluconate

[a]History of same hematologic malignancy with relapsed disease

[b]Days of absolute neutrophil count (ANC) <500 cells/mm^3

[c]Days of documented CHG bathing from date of stem cell transplant to day 7

[d]Chronic liver disease includes cirrhosis and chronic viral hepatitis

[e]Chronic lung disease includes chronic obstructive pulmonary disease (COPD), emphysema, asthma, and pulmonary fibrosis

TABLE 3.

Comparison of secondary outcomes between the baseline group and the levofloxacin prophylaxis group in patients undergoing autologous stem cell transplant

Outcome	Baseline Group No. (%) n = 174	Levofloxacin Group No. (%) n = 150	Odds Ratio (95% CI)	*P* Value
Secondary BSI	7 (4)	2 (1)	0.32 (0.07–1.58)	0.16
Neutropenic fever	143 (82)	78 (52)	0.23 (0.14–0.39)	<0.001
ICU transfer[a]	12 (7)	8 (5)	0.76 (0.30–1.91)	0.56
ICU transfer for sepsis	10 (6)	3 (2)	0.33 (0.09–1.24)	0.10
C.difficile[a]	17 (10)	10 (7)	0.66 (0.29–1.49)	0.32
Mortality[a]	2 (1)	2 (1)	1.16 (0.16–8.35)	0.88
Length of stay[b]	14 (12–16)	14 (13–15)	0.20 (−1.07–1.48)	0.75
Readmission[a]	18 (10)	18 (12)	1.18 (0.59–2.36)	0.64

NOTE. CLABSI, central line-associated bloodstream infection; MBI, mucosal barrier injury BSI, bloodstream infection; ICU, intensive care unit, IQR; inter-quartile range

[a]Within 30 days of stem cell transplant

[b]Median days, inter-quartile range (IQR)

TABLE 4.

Antibiotic use in days of therapy in patients undergoing autologous stem cell transplant

Antibiotic	Baseline Group Mean (SD)	Levofloxacin Group Mean (SD)	*P*-Value
Levofloxacin	0.9 (2.2)	9.2 (2.9)	<0.001
Cefepime	4.7 (3.9)	3.1 (3.6)	<0.001
Meropenem	1.1 (2.9)	1.5 (2.9)	0.22
Piperacillin-tazobactam	0.8 (2.5)	0.1 (0.7)	0.001
Aminoglycosides	0.4 (1.3)	0.2 (0.8)	0.07
Vancomycin, intravenous	1.7 (2.9)	1.1 (2.7)	0.06