Primary Prophylaxis with Oral Vancomycin to Prevent *Clostridioides difficile* Infection in Recipients of Allogeneic Hematopoietic Stem Cell Transplantation

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BACKGROUND

Patients undergoing allogeneic hematopoietic stem cell transplant (alloHSCT) are at an increased risk of *Clostridiodes difficile* infection (CDI), with a reported prevalence greater than 30%. Exposure to broad-spectrum antimicrobials, prolonged neutropenia, chemotherapy-induced mucosal damage, and extended hospitalizations likely contribute to this increased rate.

Previous literature has shown that alloHSCT recipients who develop CDI are three times more likely to develop acute graft-versus-host disease (aGVHD), specifically gastrointestinal GVHD. This may be related to the tissue inflammation and activation of the immune system caused by CDI. GVHD is the leading cause of non-relapse mortality in alloHSCT recipients.

A small body of literature supports the use of oral vancomycin prophylaxis for prevention of CDI in an aloHSCT population without adversely impacting post-transplant outcomes. However, this practice has not been universally accepted and is not currently incorporated into national infectious disease or alloHSCT guidelines. Additional investigation is needed to confirm these findings.

OBJECTIVES

Primarily, to investigate the association between prophylactic oral vancomycin and the development of CDI within 30 days of alloHSCT.
Secondarily, to investigate rates of CDI at any time point, all GVHD, GI GVHD, development of vancomycin-resistant Enterococcus (VRE) bacteremia, hospital length of stay, 30-day survival, and overall survival.

METHODS

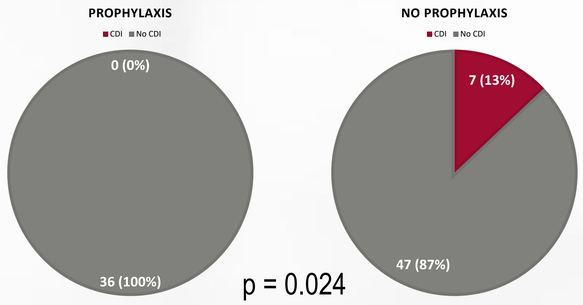
Retrospective chart review of patients 18 years and older who received an alloHSCT at UAMS between June 1, 2020, to June 30, 2022. Per provider preference, patients either received CDI prophylaxis with oral vancomycin 125 mg twice daily (starting from the day of alloHSCT admission and continued until discharge) or no prophylaxis. CDI was defined as having both positive PCR (Cepheid®) as well as toxin and antigen production (TechLab®).

BASELINE CHARACTERISTICS

Characteristic	Prophylaxis (n = 36)	No Prophylaxis (n = 54)	p-value
Mean age, years	58	51.7	0.042
Male sex, n (%)	21 (58)	33 (61)	0.792
Oncology diagnosis, n (%)			
Acute myeloid leukemia	22 (61)	16 (30)	0.006
Myelodysplastic syndrome	6 (17)	17 (32)	0.114
Acute lymphoblastic leukemia	2 (6)	9 (17)	0.115
Other	6 (17)	12 (22)	0.348
Use of post-transplant cyclophosphamide, n (%)	33 (92)	28 (52)	<0.001
Prior history of CDI, n (%)	6 (17)	0 (0)	0.027
Abx exposure 30 days prior			
Gram-negative	34 (94)	54 (100)	0.157
Gram-positive	6 (17)	14 (26)	0.301
Abx exposure 30 days post			
Gram-negative	36 (100)	54 (100)	1
Gram-positive	28 (78)	50 (93)	0.087

RESULTS

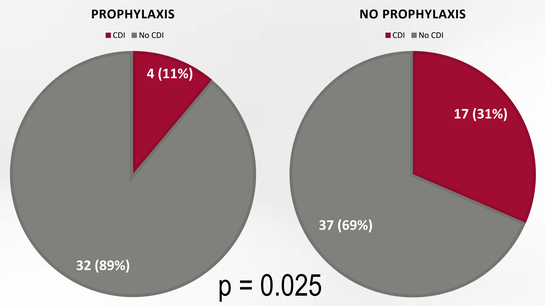
CDI Rates 30 Days Post AlloHSCT



p = 0.024

RESULTS

CDI Rates Any Time Post AlloHSCT



p = 0.025

Outcome	Prophylaxis (n = 36)	No Prophylaxis (n = 54)	p-value
Any GVHD, n (%)	19 (53)	22 (41)	0.261
Grade 3-4 GVHD, n (%)	2 (6)	5 (9)	0.520
Any GI GVHD, n (%)	4 (11)	11 (20)	0.248
Grade 3-4 GI GVHD, n (%)	1 (3)	5 (9)	0.227
VRE bacteremia within 180 days of HSCT, n (%)	2 (6)	13 (24)	0.021
Length of hospital stay post alloHSCT, days	23.4	27.8	0.053
30-day survival, n (%)	35 (97)	50 (93)	0.348
Overall survival, n (%)	22 (61)	31 (57)	0.726

CONCLUSIONS

Oral vancomycin prophylaxis given throughout hospitalization for alloHSCT was effective at preventing CDI. We did not see a significant impact on rates of GVHD, but our study was underpowered for this outcome. When CDI prophylaxis was used, trends towards lower rates of severe GI GVHD and decreased length of hospital stay were noted. The lower rates of VRE bacteremia seen in our prophylaxis group may be related to the decreased rates of CDI seen. We theorize that less GI mucosa disruption may lead to less bacterial translocation, but further investigation is warranted.