Background: Patients colonized by multidrug-resistant bacteria (MDR) have high risk for infection after hematopoietic stem cell transplantation (HSCT). Probiotic is a strategy that can be used to decolonize patients. Our aim was to describe the impact of use of *Lactobacillus plantarum* (LP) on decolonization, MDR infections and intestinal microbiome (IM) of autologous HSCT patients colonized by vancomycin-resistant *Enterococcus* (VRE) and carbapenem-resistant Gram-negative (CRGN).

Methods: A prospective study was conducted at Hospital das Clinicas of University of Sao Paulo Brazil from 2017 to 2018. Candidates for auto-HSCT colonized by MDR received LP in capsules, 5×10^9 CFU twice daily until neutropenia (NP). Rectal swabs were performed and cultured using selective media as well as PCR for carbapenemases, *van*A and *van*B. Stool samples for IM analysis were collected weekly as baseline (before LB use) until the NP. The V4 region of 16S rDNA gene were sequenced by Ion Torrent PGM and analyzed using alpha and β diversities by Qiime. Demographic and clinical data including previous antibiotics use were evaluated; CDC criteria was applied for colonization and infection.

Results: All of seven patients were colonized by VRE and CRGN (Table 1). Only one patient remained colonized by CRGN after 61 days of LP. Four patients developed seven bloodstream infections (BSI) during the NP, two of them by CRGN. There was no infection caused by VRE neither by LP. One patient, with low adherence to LP use (66%), died due to MDR *K. pneumoniae* BSI. We observed a decrease of Clostridia, Verrucomicrobiae, *Blautia* and an increase of Enterobacteriaceae. Baseline samples from patients who used TMP/SMX had higher concentrations of Bacteroidetes when compared with those who had not use it. The Shannon index in controls ranged 1.98–5.55 and during NP 1.15–5.99. The β diversity analysis showed no clear patterns between patients.

Conclusion: We observed a heterogeneity among IM of auto-HSCT patients prior and after LP. It was not possible to establish an IM pattern, probably, because of small number of patients. Although, clinical infections by CRGN occurred despite of LP use, no cases of colonization and infection by VRE were identified. Thus, it seems that LP is a good and safe strategy to decolonized HSCT.
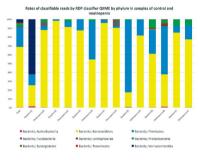

Rates of classifiable reads by RDP classifier QIIME by phylum in samples of control and neutropenia

Table 1. Demographic, clinical characteristics and IM of seven auto-HSCT.

Characteristics	n	%
Diagnosis		
Multiple Myeloma	2	29%
Hodgkin's lymphoma	4	57%
Acute Myeloid Leukemia	1	14%
Age		
≥60 years	3	43%
18 - 59 years	4	57%
Gender		
Women	4	57%
MDR Colonization		
VRE	7	100%
K. pneumoniae	4	57%
A. baumannii	3	43%
Conditioning Therapy		
BEAM (carmustine, etoposide, aracytin and melphalan)	3	43%
Bu Cy (busulfan and cyclophosphamide)	1	14%
Bu Mel (busulfan and melphalan)	1	14%
Use of ATB in collection of samples		
Baseline	5	71%
Neutropenia	5	71%
ATB class used by number of patients		
baseline		
Beta lactam + inhibitor	1	14%
Tuberculostatic	1	14%
Fluoroquinolone	3	43%
Sulfonamide	4	57%
Antifungal	0	0%
Antiviral	2	29%
neutropenia		
Beta lactam + inhibitor	1	14%
Fluoroquinolone	1	14%
Polymyxin	1	14%
Carbapenem	1	14%
Oxazolidinone	1	14%
Sulfonamide	2	29%
Aminoglycoside	1	14%
Antifungal	1	14%
Antiviral	7	100%
BSI in HSCT		
Yes	4	71%
No	3	29%
Adherence to LP (mean 84%)		
≤50%	0	0%
50% ≤ 70%	1	14%
71% ≤ 80%	1	14%
81% ≤ 90%	3	43%
91% ≤ 100%	2	29%
LP consumption (Median 29; SD ±23)		
≤10 days	0	0%
11≤30 days	4	57%
31≤50 days	1	14%
51≤80 days	1	14%
81≤90 days	1	14%

2666. De-escalation of Broad-Spectrum Antibiotics in Hematopoietic Stem Cell Transplant Patients During Initial Episode of Febrile Neutropenia

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Background: Febrile neutropenia (FN) is a common and serious complication in patients undergoing hematopoietic stem cell transplant (HSCT). Typically, broad-spectrum antibiotics (BSA) are promptly initiated with controversy on timing of de-escalation. ECIL 2013 guidelines suggest de-escalation after 72 hours if the patient is infection free and afebrile for at least 48 hours. Conversely, the 2011 IDSA recommends continuing BSA in patients who defervesce until absolute neutrophil count (ANC) recovery. In 2014, our center's practice changed to early de-escalation and we sought to compare outcomes between the two practices.

Methods: We retrospectively analyzed patients who underwent a HSCT in 2013 and 2017 with an episode of FN and negative infectious work up. The standard care group (SCG) were continued on BSA until ANC recovery. The early de-escalation group (EDG) de-escalated to fluoroquinolone prophylaxis at least 24 hours prior to ANC recovery after the patient was fever free for 48 hours. The primary end-point was duration of BSA. Secondary endpoints included 30-day mortality, re-hospitalization and length of stay (LOS) from FN. Median values were compared with the Mann–Whitney test.

Results: Among 229 HSCT patients, 155 (68%) developed FN post-transplant and of those 97 (63%) were without infection (13 EDG and 84 SCG). Initial FN duration of BSA was less in the EDG (3.09 days vs. 4.69 days, $P = 0.069$). Total antibiotic free days to 30 day follow-up were similar (EDG 24.08 vs SCG 25.19, $P = 0.81$). Duration of neutropenia was less in the SCG with 7.99 days compared with 11.69 days in the EDG ($P = 0.007$), but duration of initial fever was less in the EDG (2.55 days vs. 3.33 days, $P = 0.023$). 30 day mortality was 0% in both groups. Rates of re-hospitalization within 30 days were approximately the same (7.1% vs. 7.6%). LOS from FN was not significantly different with 6.68 days in SCG and 7.75 days in EDG ($P = 0.140$). More new bacterial infections were identified within 30 days of FN in the SCG than the EDG (10.7% vs. 7.6%).

Conclusion: Early BSA de-escalation resulted in no significant difference in LOS from FN and fewer days of BSA with 30-day mortality and re-hospitalization rates similar. This data suggest de-escalating BSA prior to ANC recovery is likely safe and leads to less BSA exposure, but more multi-center data are needed.

2667. Does Ceftazidime–Avibactam (CAZ-AVI) Improve Short- and Long-Term Outcomes Among Solid-Organ Transplant (SOT) Recipients with Carbapenem-Resistant Enterobacteriaceae (CRE) Infections?

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Background: SOT recipients are an ideal population in which to study the impact of new antibiotics, since they are particularly dependent upon drug activity to clear infections. In 3/15, FDA approved CAZ-AVI, the first new anti-CRE agent to arrive in the clinic. Our objective was to determine whether CAZ-AVI improves short- and long-term outcomes of CRE-infected SOT recipients.

Methods: We performed a retrospective study of SOT recipients infected with CRE since 2012, who were treated with CAZ-AVI or salvage agents for ≥ 3 days.

Results: 35 CRE-infected SOT recipients (14 liver, 11 lung, 6 kidney, 3 intestine, 1 heart) with bacteremia (20), pneumonia (11), intra-abdominal abscess (3) and soft-tissue infection/osteomyelitis (1) were enrolled. 16 and 19 patients (pts) were treated with CAZ-AVI and salvage agents, respectively. Types of infection or SOT, APACHE II and McCabe scores did not differ significantly between patients treated with CAZ-AVI or salvage agents. 30- and 90-d mortality rates were significantly lower among SOT recipients treated with CAZ-AVI (0% and 6%, respectively) compared with salvage agents (26% and 37%; $P = 0.049$ and 0.047). Among patients who survived 90 days, recurrent CRE infections were diagnosed in 53% and 17% of those treated with CAZ-AVI and a salvage regimen, respectively ($P = 0.10$). Median time from end of therapy for the 1st CRE infection to recurrent infection was 116 days (max 1,242) and 361 days (max 799) for CAZ-AVI and salvage regimens, respectively. Survival and recurrence-free survival were greater for treatment with CAZ-AVI and salvage agents, respectively, as measured by Kaplan–Meier (Figures). CAZ-AVI resistance developed in 37% ($n = 3$) of patients with recurrent infections. Recurrent isolates were genetically indistinguishable from parent isolates by core genome SNP phylogeny (< 15 SNP).

Conclusion: CAZ-AVI significantly reduced short-term mortality among SOT recipients with CRE infections compared with salvage regimens, but was limited by recurrent infections and emergence of resistance. The same strains caused recurrent and initial infections, suggesting that CAZ-AVI did not eliminate CRE from GI sites that serve as sources of recurrence. Optimizing outcomes in SOT recipients with CRE infections will require new agents like CAZ-AVI, and strategies to eliminate long-term colonization.