249. Frequency of Antimicrobial Complications Following Initiation of Palliative Chemotherapy in Advanced Cancer Patients

Rupak Datta, MD PhD[1]; Margaret Doyle, MPhil[2]; Vincent Quagliarello, MD, FIDSA[1]; Tara Sanft, MD[3] and Manisha Juthani-Mehta, MD, FSHEA[1]; [1]Department of Internal Medicine, Section of Infectious Diseases, Yale School of Medicine, New Haven, Connecticut, [2]Department of Internal Medicine, Section of Geriatrics, Yale School of Medicine, New Haven, Connecticut, [3]Department of Internal Medicine, Section of Medical Oncology, Yale School of Medicine, New Haven, Connecticut

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Background. Evaluating antimicrobial complications in advanced cancer patients on palliative chemotherapy may guide clinical care and stewardship efforts.

Methods. We identified advanced cancer patients aged ≥65 years started on palliative chemotherapy from January 2016 to September 2017 at Yale New Haven Hospital. Complications with and without antimicrobials were assessed during first hospitalizations until death or March 2018. We compared differences with χ^2 tests.

Results. Of 2,680 patients started on palliative chemotherapy, 1181 had ≥1 hospitalization. Median age was 74 years (range 65–98), and 856 (72%) had solid tumors. Median time to hospitalization from starting palliative chemotherapy was 77 days (range 1–580) and length of stay was 4 days (range 1–50). During first hospitalization, 158 (13%) died or were discharged to hospice. Overall, 493 (42%) died. Palliative chemotherapy often included FOLFIRINOX ($n = 257$), FOLFOX ($n = 239$), or pembrolizumab ($n = 210$). During first hospitalizations, patients given antimicrobials more likely incurred nephrotoxicity, hepatotoxicity, or *C. difficile* infection within 7 days of use than patients not given antimicrobials (Table 1).

Conclusion. Antimicrobial complications are common in advanced cancer patients on palliative chemotherapy. Increased stewardship and alignment of infection treatment with goals of care are needed.

Table 1: Complications in Palliative Chemotherapy Patients.

Complication[a]	Definition	Antimicrobials ($N = 805$)	No Antimicrobials ($N = 376$)	P value
Cardiotoxicity	>60ms QTC rise	83 (10%)	35 (9%)	0.68
Nephrotoxicity, mg/dL	QTC > 500ms S_{CR} ≥0.5 if Cr <3.0 S_{CR} ≥1.0 if Cr ≥3.0	49 (6%)	6 (2%)	<0.001
Hematologic, /mm[3b]				
Aplastic anemia	Two of: ANC <1,500 Plt <50,000 Hg <10	9 (2%)	4 (1%)	0.78
Leukopenia	ANC <1,500	10 (2%)	4 (1%)	0.59
Thrombocytopenia	Plt <100,000	9 (2%)	6 (2%)	0.79
Hepatotoxicity, U/L	ALT ≥102 ALP ≥390	88 (12%)	26 (7%)	0.03
Electrolyte, mEq/L				
Hypokalemia	K < 3.0	45 (6%)	17 (5%)	0.49
Hyperkalemia	K > 5.5	3 (0%)	21 (6%)	<0.001
Hypomagnesemia	Mg < 1.2	10 (1%)	5 (1%)	1.00
Clostridium difficile				
	Antigen +	27 (3%)	1 (0%)	<0.001
	Toxin +	16 (2%)	1 (0%)	0.02

[a]Within 7 days of specified antimicrobials vs. entire hospitalization in those not given antimicrobials.

[b]Solid tumor patients only: antimicrobials $N = 538$; no antimicrobials $N = 318$.

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250. Antimicrobial Management in Extracorporeal Membrane Oxygenation: The AMMO study

Aditya Shah, MBBS[1]; Prabij Dhungana, MBBS[2]; Priya Sampathkumar, MD, FIDSA, FSHEA[1]; John K. Bohman, MD[3] and John C O'horo, MD[4]; [1]Infectious Diseases, Mayo Clinic, Rochester, Minnesota, [2]Department of Critical Care, Mayo Clinc, Rochester, Minnesota, [3]Anesthesiology/Critical Care Medicine, Mayo Clinc, Rochester, Minnesota, [4]Division of Infectious Diseases, Mayo Clinic, Rochester, Minnesota

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Background. The use of extracorporeal membrane oxygenation (ECMO) in critically ill adults is increasing with no guidelines for antimicrobial prophylaxis. Patients on ECMO are at a high risk for infections, 6.1% of neonates and 20.5% of adults. An Extracorporeal Life Support Organization (ELSO) Infectious Disease Task Force statement concludes that no additional antibiotic coverage is needed for patients on ECMO. Since patients on ECMO are severely ill, providers tend to prescribe empiric antibiotics. To guide rational antibiotic therapy we introduce an ECMO antimicrobial protocol on July 1, 2014 and report its impact.

Methods. We conducted a retrospective review of 294 patients on ECMO between July 1, 2011 and July 1, 2017. The ECMO antimicrobial protocol was introduced on July 1, 2014. We had a cohort of 133 patients before and 161 patients after the implementation of protocol. We evaluated days of antimicrobial use, antibiotic-free days and days of individual antimicrobial use, adjusted for APACHE scores and ECMO duration.

Results. Total days of antimicrobial use after the protocol decreased from 2,508 to 2,186 days ($P = 0.01$) with statistically significant reduction of individual antimicrobials; vancomycin (407 to 266, $P < 0.03$), cefepime (196 to 165, $P < 0.06$), along with reduced days of anidulafungin, caspofungin, fluconazole, meropenem, and daptomycin. However, when adjusted for mean days on ECMO 7 (4–14) before as compared with 5 (3–9.5) after ($P < 0.0119$), "antimicrobial free days" actually reduced after implementation of the protocol. Early trends of improved stewardship were off-set when time frame and number of patients were increased. Despite this, no difference was seen in rate of nosocomial infections, with increased rates seen for *Clostridium difficile* (0 vs. 4, $P < 0.06$).

Conclusion. "Protocolization" and standardization of antimicrobial recommendations for patients on ECMO led to reduction in the use of specific antibiotics but paradoxically increased overall antibiotic use. We are in the process of emphasizing compliance with this protocol, which will be followed by implementation of a more restrictive protocol. We will do a step wedge randomized control prospective analysis to evaluate compliance differences between the medical and surgical critical care services, and the impact on patient outcomes.

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251. Overuse of Antimicrobials in the End-of-life Care: Factors Influencing Physicians' Prescribing Behaviors in Treating Patients With an Advanced Stage of Illnesses in the Robust Era of Antimicrobial Stewardship

Kanae Kawahara, MD; Yasuaki Tagashira, MD; Akane Takamatsu, MD and Hitoshi Honda, MD, PhD; Infectious Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan

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Background. Antimicrobials are frequently administered to patients with an advanced stage of illnesses. Understanding current practice of antimicrobial use at the end of life and factors influencing physicians' prescribing behavior is necessary to provide an effective antimicrobial stewardship program and the best end-of-life care in terminally ill patients.

Methods. The current study was a 1-year retrospective cohort study of patients with an advanced stage of illnesses and was conducted at a 790-bed, public, tertiary care center in Japan. Patterns in current antimicrobial use in the last 14 days of the life of terminally ill patients and the factors influencing physicians' prescribing behaviors were analyzed.

Results. Of the 260 patients, 192 (73.8%) had an advanced stage malignancy, 136 (52.3%) received antimicrobial therapy in the last 14 days of their life, of whom 60 (44.1%) received antimicrobials for symptom relief. Overall antimicrobial use in the last 14 days of their life was 421.9 days of therapy per 1,000 patient-days. Factors associated with antimicrobial use in this period included a history of antimicrobial use prior to the last 14 days of life during index hospitalization (adjusted odds ratio [aOR]: 4.86; 95% confidence interval [CI]: 2.67–8.84), antipyretic use in the last 14 days of life (aOR: 4.19 95%; CI: 2.01–8.71), and the Charlson comorbidity index ≤ 5 (aOR: 2.18 95%; CI: 1.06–4.53).

Conclusion. Approximately half of the patients hospitalized with an advanced stage of illnesses received antimicrobials in the last 14 days of their life. Antimicrobials were commonly prescribed and their overall consumption was significant despite their limited efficacy. The factors associated with antimicrobial use at the end-of-life in this study are likely to explain physicians' prescribing behaviors. In the era of robust antimicrobial stewardship, reconsidering antimicrobial use in terminally ill patients is necessary.

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252. Relative Use of Carbapenems in Immunocompromised Patients

Jacob Pierce, MD[1]; Kimberly Lee, PharmD[2]; John Markley, DO[3]; Amy Pakyz, PharmD, MS, PhD[4]; Michelle Doll, MD, MPH[5]; Andrew Kirk, BS[6]; Gonzalo Bearman, MD, MPH, FSHEA[3]; Oveimar De La Cruz, MD[3] and Michael Stevens, MD, MPH[3]; [1]Internal Medicine, VCU Commonwealth Health System, Richmond, Virginia, [2]Virginia Commonwealth University Health System, Richmond, Virginia, [3]Infectious Diseases, Virginia Commonwealth University Health System, Richmond, Virginia, [4]Department of Pharmacotherapy and Outcomes Science, Virginia Commonwealth University, Richmond, Virginia, [5]VCU Medical Center, Richmond, Virginia, [6]Virginia Commonwealth University School of Medicine, Richmond, Virginia

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Background. Gram-negative bacterial infections are associated with high mortality in immunocompromised hosts, and the presence of drug resistance further increases mortality. Antibiotic consumption is a key outcome measure for Antimicrobial

Stewardship Programs. Proper utilization of antibiotics can help limit the development of antimicrobial resistance. Resistance in Gram-negative organisms such as *Pseudomonas*, *Enterobacter*, and *Acinetobacter* is a major issue given the paucity of new drugs in the antibiotic pipeline for these organisms. A novel relative carbapenem consumption metric (the Proportion of Carbapenem Consumption, or PoCC) was recently described in US academic medical centers. The PoCC is calculated as follows: PoCC = [(meropenem Days of therapy(DOT)/1,000 patient-days (PDs))/(meropenem DOT/1,000 PDs + cefepime DOT/1,000 PDs + piperacillin–tazobactam DOT/1,000 PDs)]. The regional mean PoCC for the South Atlantic region has previously been approximated at 17%.

Methods. We examined the PoCC for the Bone Marrow Transplant (BMT) and dedicated Hematology/Oncology (H/O) inpatient wards at an academic medical center from August 2012 to June 2017.

Results.

Table 1: Average Use of Antibiotics Expressed in DOT/1,000 PDs.

Ward	Piperacillin–Tazobactam	Cefepime	Meropenem	Total	PoCC
Hematology/oncology	105.1	134.4	76.6	316.1	0.24
Bone marrow transplant	34.3	201.0	127.4	362.7	0.35
National means[a]	76.2	60.2	30.7	b	0.18

[a]As described by Markley et al. Infect Control Hosp Epidemiol 2018;39:229–232.
[b]Data unavailable.

PoCC Aug. 2012-June 2017

Mean Antibiotic usage
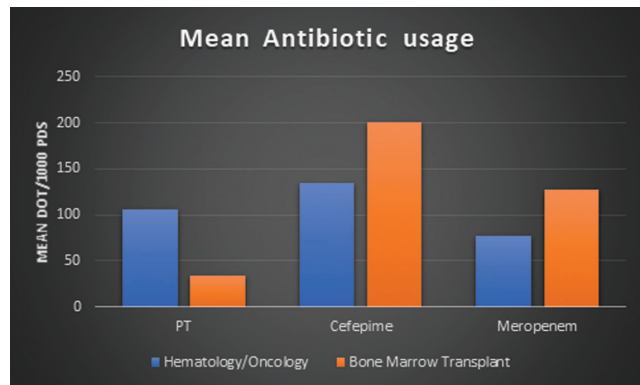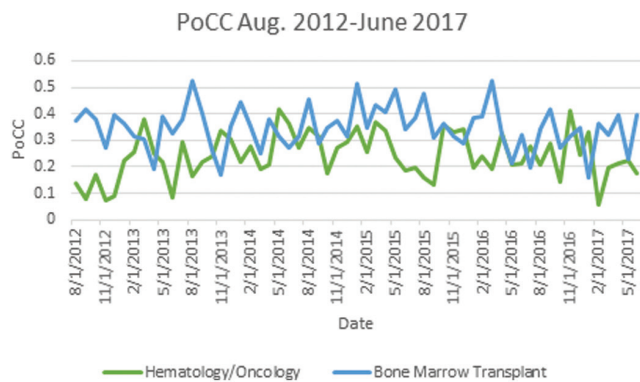
Conclusion. This is the first description of the PoCC metric for dedicated Hematology/Oncology and Bone Marrow Transplant wards. When compared with national and regional mean PoCC scores for academic medical centers, the PoCC for these units was higher. More research is needed to determine the optimal PoCC scores for these types of units. The PoCC can contextualize relative carbapenem use and may be a useful antibiotic consumption metric. However, it does not provide data on absolute consumption. Further studies are needed to determine the best use of the PoCC metric by Antimicrobial Stewardship Programs for Hematology/Oncology and Bone Marrow Transplant wards.

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253. Febrile Neutropenia Antibiotic De-escalation Study in Acute Myeloid Leukemia Patients With Prolonged Neutropenia

William Alegria, PharmD[1]; Bernard L. Marini, PharmD, BCOP[2]; Anthony J. Perissinotti, PharmD, BCOP[2]; Dale Bixby, MD[3]; Kevin Gregg, MD[4] and Jerod Nagel, PharmD, BCPS[1]; [1]Department of Pharmacy, Michigan Medicine, Ann Arbor, Michigan, [2]Michigan Medicine, Ann Arbor, Michigan, [3]Department of Internal Medicine, Division of Hematology/Oncology, Michigan Medicine, Ann Arbor, Michigan, [4]Department of Internal Medicine, Division of Infectious Diseases, Michigan Medicine, Ann Arbor, Michigan

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Background. The IDSA and NCCN guidelines recommend continuing IV anti-pseudomonal (IVPSA) therapy until neutrophil recovery (i.e., an ANC > 500 cells/mm^{3}) in high-risk acute myeloid leukemia (AML) patients with febrile neutropenia (FN). This recommendation is based on expert opinion and the current practice should be re-evaluated given the emergence of multi-drug-resistant organisms and high rates of *Clostridium difficile* infection (CDI) in this population. The purpose of this study was to evaluate whether IVPSA antibiotics could be safely de-escalated or discontinued in high-risk AML patients with FN following implementation of a guideline.

Methods. This single-center, pre–post quasi-experimental study included patients with AML receiving induction chemotherapy hospitalized between September 2015 to February 2018. Patients in the intervention group were compared with a historical cohort of patients admitted before implementation of the guideline. The primary outcome was the incidence of suspected or documented bacterial infection after antibiotic de-escalation in the intervention group (or meeting criteria for de-escalation in the historical control group). Secondary outcomes included the incidence of CDI, IVPSA Days of Therapy (DOTs), hospital length of stay (LOS), and mortality. Patients in the intervention group were evaluated for antibiotic de-escalation on day 5 of FN and antibiotics were discontinued if patients were afebrile, hemodynamically stable, and without evidence of infection irrespective of their ANC (or de-escalated to fluoroquinolone prophylaxis in relapsed/refractory disease). In clinically stable patients with suspected or documented bacterial infection, antibiotics were continued for a defined duration per indication as outlined in the guideline.

Results. A total of 93 patients were included in the analysis. Baseline demographics were similar between the two groups with the exception of more relapsed/refractory patients in the intervention group. Patients in the intervention group had similar clinical outcomes and lower rates of CDI and IVPSA DOTs (see Figure 1).

Conclusion. In high-risk AML patients with FN, an antibiotic de-escalation guideline reduced the incidence of CDI and IVPSA antibiotic DOTs without adversely affecting clinical outcomes.

Figure 1: Outcomes in High-risk AML Patients with Febrile Neutropenia

Endpoint	Historical Group (n=40)	Intervention Group (n=53)	P-value
Suspected or documented bacterial infection after antibiotic de-escalation[1], n (%)	18 (45%)	18 (34%)	0.292
De-escalated IVPSA antibiotics while neutropenic, n (%)	3 (7.5%)	38 (71.7%)	<0.001
Incidence of CDI, n (%)	11 (27.5%)	3 (5.7%)	0.007
Hospital LOS, median (IQR)	29 (24-37)	27 (24-39)	0.467
All-cause mortality, n (%)	6 (15%)	6 (11%)	0.757
IVPSA antibiotic DOTs, median (IQR)	25 (17-33)	14 (9-24)	<0.001

[1]In the historical group, outcomes were evaluated after day 5 of FN once patients met clinical criteria for de-escalation as stated in the guideline

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254. Antimicrobial Use in Hospitalized Older Patients with Advanced Cancer

Mojun Zhu, MD[1]; Rupak Datta, MD PhD[2]; Vincent Quagliarello, MD, FIDSA[2] and Manisha Juthani-Mehta, MD, FIDSA, FSHEA[2]; [1]Department of Internal Medicine, Yale School of Medicine, New Haven, Connecticut, [2]Department of Internal Medicine, Section of Infectious Diseases, Yale School of Medicine, New Haven, Connecticut

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Background. Antimicrobial use may prolong hospitalization and suffering in patients with advanced cancer whose goals of care transition to comfort measures only (CMO).

Methods. We conducted a retrospective study of all patients aged ≥65 years with stage III–IV solid tumors, stage III–IV lymphomas, or acute, refractory or active liquid tumors requiring chemotherapy or targeted therapies who were transitioned to CMO during hospitalization at Yale New Haven Hospital between July 2014 and November 2016. We performed chart review, determined antimicrobial use (including antibiotics, antifungal and antiviral agents) around CMO, and evaluated the association between antibiotic density (use of oral and IV antibiotics by calendar days) and length of stay (LOS) using multivariable linear regression.

Results. We identified 461 patients. Median age was 74 years (range 65–99), 49% (*n* = 226) were female, and 79.4% (*n* = 366) had solid tumors. Overall, 113 patients (group 1) did not receive antimicrobials within 1 calendar day of CMO transition. Of the 343 patients who did, antimicrobials were continued after CMO in 20% (*n* = 70, group 2) and discontinued in 80% (*n* = 273, group 3). Patients who had antimicrobials continued after transition to CMO spent 1 more day inpatient until discharge compared with those who did not (group 2 vs. 3 in Figure 1). Five patients (group 4) started antimicrobials after CMO transition. In the multivariable model, antibiotic density remained associated with LOS (β = 1.2, 95% CI 1.1, 1.3; *P* < 0.0001) (Table 1).

Conclusion. During their terminal hospitalization, most older adults with advanced cancer received antimicrobials, and increased antibiotic density was associated with prolonged LOS. Antimicrobial stewardship efforts should be focused on this population to optimize utilization and facilitate transitions of care.