



# IDWeek Highlights: Antibacterials and Antifungals



November 11th, 2020

# IDSA non-TB Mycobacterial Guideline Update

Mostly clarification of drug regimens:

- Macrolides continue to be cornerstone to therapy for MAC; azithro 250mg ~clarithro
- Intermittent vs. Daily Therapy?
  - Cavitory disease -> Daily
  - Non-cavitory -> Intermittent
- Toxicity counseling important
  - Don't wait until next visit for visual acuity, hearing issues!
- Amikacin resistance marker for poor outcomes
- Liposomal amikacin (Arikayce) inhaled only studied in refractory cases so far

Clinical Infectious Diseases

IDSA FEATURES



## Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline

Charles L. Daley,<sup>1,2,3</sup> Jonathan M. Iaccarino,<sup>2</sup> Christoph Lange,<sup>3,5,6,7,8</sup> Emmanuelle Cambau,<sup>8,9</sup> Richard J. Wallace, Jr.,<sup>8,9</sup> Claire Andrejak,<sup>10,11</sup> Erik C. Böttger,<sup>12</sup> Jan Brozek,<sup>13</sup> David E. Griffith,<sup>14</sup> Lorenzo Guglielmetti,<sup>8,15</sup> Gwen A. Huit,<sup>12</sup> Shandra L. Knight,<sup>16</sup> Philip Leiman,<sup>17</sup> Theodore K. Marras,<sup>18</sup> Kenneth N. Olivier,<sup>19</sup> Miguel Santin,<sup>20</sup> Jason E. Stout,<sup>21</sup> Enrico Tortoli,<sup>22</sup> Jakko van Ingen,<sup>23</sup> Dirk Wagner,<sup>24</sup> and Kevin L. Winthrop<sup>25</sup>

**Table 6. Common Adverse Drug Reactions and Monitoring Recommendations<sup>a</sup>**

Drug	Adverse Reactions	Monitoring
Azithromycin	Gastrointestinal	Clinical monitoring
	Tinnitus/hearing loss	Audiogram
	Hepatotoxicity	Liver function tests
	Prolonged QTc	ECG (QTc)
Clarithromycin	Gastrointestinal	Clinical monitoring
	Tinnitus/hearing loss	Audiogram
	Hepatotoxicity	Liver function tests
	Prolonged QTc	ECG (QTc)
Clofazimine	Tanning of skin and dryness	Clinical monitoring
	Hepatotoxicity	Liver function tests
	Prolonged QTc	ECG (QTc)
Doxycycline	GI upset	Clinical monitoring
	Photosensitivity	Clinical monitoring
	Tinnitus/vertigo	Clinical monitoring
Ethambutol	Ocular toxicity	Visual acuity and color discrimination
	Neuropathy	Clinical monitoring
Isoniazid	Hepatitis	Liver function tests
	Peripheral neuropathy	Clinical monitoring
Linezolid	Peripheral neuropathy	Clinical monitoring
	Optic neuritis	Visual acuity and color discrimination

Daley CL et al. . Clin Infect Dis. 2020;71(4):e1–e36



# IDSA *C. Difficile* Update

Last Update in 2018 occurred just as Fidaxomicin and Bezlotuxumab being approved

- Fidaxomicin associated with reduced CDI recurrence, especially in some higher-risk subgroups

- Bezlotuxumab, as adjunctive, associated with decreased CDI recurrence

Upcoming update will carve out indications for these drugs

Clinical Infectious Diseases

IDSA GUIDELINE

IDSA  
Infectious Diseases Society of America

hivma  
hiv medicine association

OXFORD

## Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

L. Clifford McDonald,<sup>1</sup> Dale N. Gerding,<sup>2</sup> Stuart Johnson,<sup>3,4</sup> Johan S. Bakken,<sup>5</sup> Karen C. Carroll,<sup>6</sup> Susan E. Coffin,<sup>7</sup> Erik R. Dubberke,<sup>8</sup> Kevin W. Garey,<sup>9</sup> Carolyn V. Gould,<sup>1</sup> Ciaran Kelly,<sup>1</sup> Vivian Loo,<sup>10</sup> Julia Shaklee Sammons,<sup>1</sup> Thomas J. Sandora,<sup>11</sup> and Mark H. Wilcox<sup>12</sup>

<sup>1</sup>Centers for Disease Control and Prevention, Atlanta, Georgia; <sup>2</sup>Edward Hines Jr Veterans Administration Hospital, Hines, and <sup>3</sup>Loyola University Medical Center, Maywood, Illinois; <sup>4</sup>St Luke's Hospital, Duluth, Minnesota; <sup>5</sup>Johns Hopkins University School of Medicine, Baltimore, Maryland; <sup>6</sup>Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; <sup>7</sup>Washington University School of Medicine, St Louis, Missouri; <sup>8</sup>University of Houston College of Pharmacy, Texas; <sup>9</sup>Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts; <sup>10</sup>McGill University Health Centre, McGill University, Montreal, Quebec, Canada; <sup>11</sup>Boston Children's Hospital, Massachusetts; and <sup>12</sup>Leeds Teaching Hospitals NHS Trust, United Kingdom

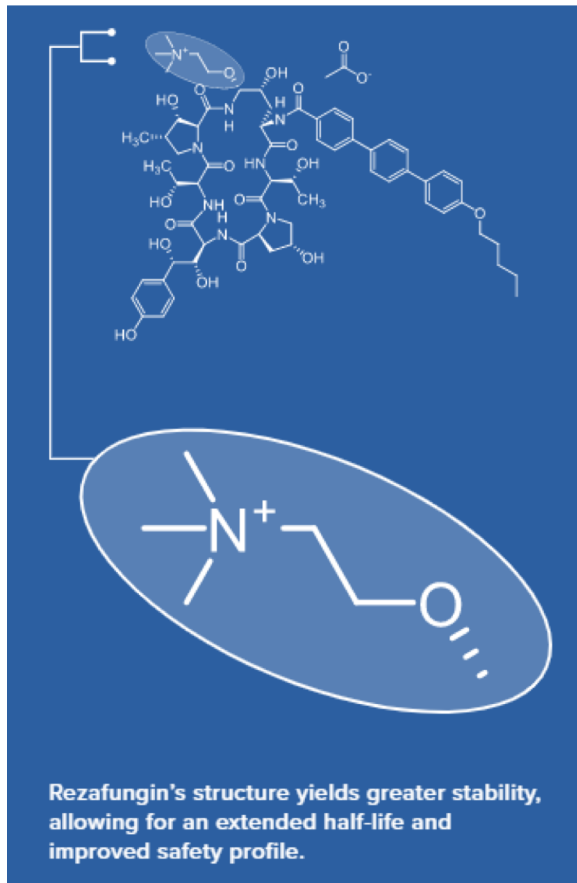
Table 1. Recommendations for the Treatment of *Clostridium difficile* Infection in Adults

Clinical Definition	Supportive Clinical Data	Recommended Treatment <sup>a</sup>	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	Leukocytosis with a white blood cell count of <15000 cells/mL and a serum creatinine level <1.5 mg/dL	<ul style="list-style-type: none"> <li>VAN 125 mg given 4 times daily for 10 days, OR</li> <li>FDX 200 mg given twice daily for 10 days</li> <li>Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days</li> </ul>	Strong/High Strong/High Weak/High
Initial episode, severe <sup>b</sup>	Leukocytosis with a white blood cell count of ≥15000 cells/mL or a serum creatinine level >1.5 mg/dL	<ul style="list-style-type: none"> <li>VAN, 125 mg 4 times per day by mouth for 10 days, OR</li> <li>FDX 200 mg given twice daily for 10 days</li> </ul>	Strong/High Strong/High
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	<ul style="list-style-type: none"> <li>VAN, 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present.</li> </ul>	Strong/Moderate (oral VAN); Weak/Low (rectal VAN); Strong/Moderate (intravenous metronidazole)
First recurrence	---	<ul style="list-style-type: none"> <li>VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR</li> <li>Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR</li> <li>FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode</li> </ul>	Weak/Low Weak/Low Weak/Moderate
Second or subsequent recurrence	---	<ul style="list-style-type: none"> <li>VAN in a tapered and pulsed regimen, OR</li> <li>VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR</li> <li>FDX 200 mg given twice daily for 10 days, OR</li> <li>Fecal microbiota transplantation<sup>c</sup></li> </ul>	Weak/Low Weak/Low Weak/Low Strong/Moderate

McDonald LC et.al. ClinInfectDis. 2018;66(7):e1–e48



# Rezafungin - The Long Acting Echinocandin



To date, data demonstrate that rezafungin has potent antifungal activity against representative strains of *Candida* spp., *Aspergillus* spp., *Pneumocystis* spp. and dermatophytes. In addition, rezafungin has potent activity against fungal pathogens designated as Urgent and Serious Threats by the CDC.

Pathogen	CDC Threat Level	Rezafungin
<i>Candida auris</i>	Urgent Threat	✓
Drug resistant <i>Candida</i>	Serious Threat	✓
Azole-resistant <i>Aspergillus fumigatus</i>	Watch List	✓

Source: CDC, Report on Antibiotic Resistant Threats. Updated Dec 2019.

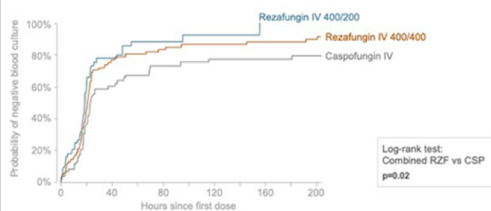
<https://www.cidara.com/rezafungin/>



# Rezafungin - The Long Acting Echinocandin

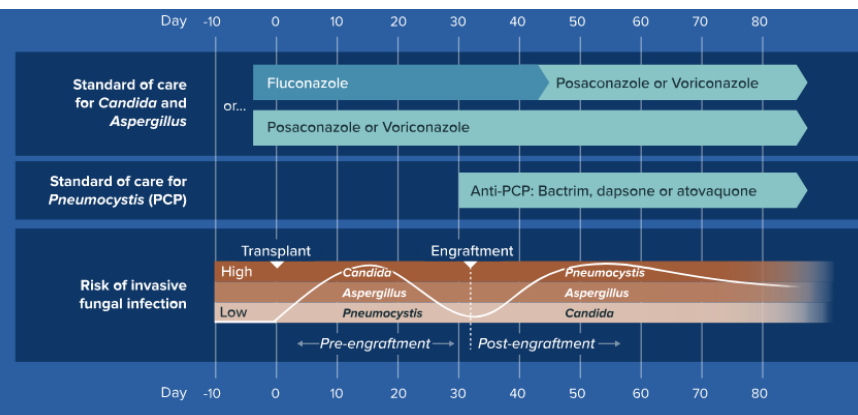
Phase 2 STRIVE trial data showed that rezafungin met all of its objectives for safety, efficacy and tolerability in the treatment of patients with candidemia and/or invasive candidiasis.

Time to negative blood culture  
(mITT population)



REFERENCE: RICA 2019, Invited Presentation

Current  
prophylaxis  
requires multiple  
drugs



Cidara's ReSPECT trial (NCT04368559) is a global, randomized, double-blind, controlled, pivotal Phase 3 trial of rezafungin versus the standard antimicrobial regimen to prevent invasive fungal disease due to *Candida*, *Aspergillus* and *Pneumocystis* in subjects undergoing allogeneic BMT. Rezafungin, dosed once-weekly, will be compared to a daily regimen containing multiple drugs including fluconazole or posaconazole, and trimethoprim-sulfamethoxazole, also known as Bactrim, for 90 days, at which time fungal-free survival will be measured as the primary efficacy outcome. The trial will enroll approximately 462 adults with underlying conditions, such as acute myeloid leukemia, acute lymphoblastic leukemia, chronic myelogenous leukemia, myelodysplastic syndrome(s), lymphoma and aplastic anemia, across approximately 30 BMT centers.

<https://www.cidara.com/rezafungin/>



# Ibrexafungerp – First Triterpenoid

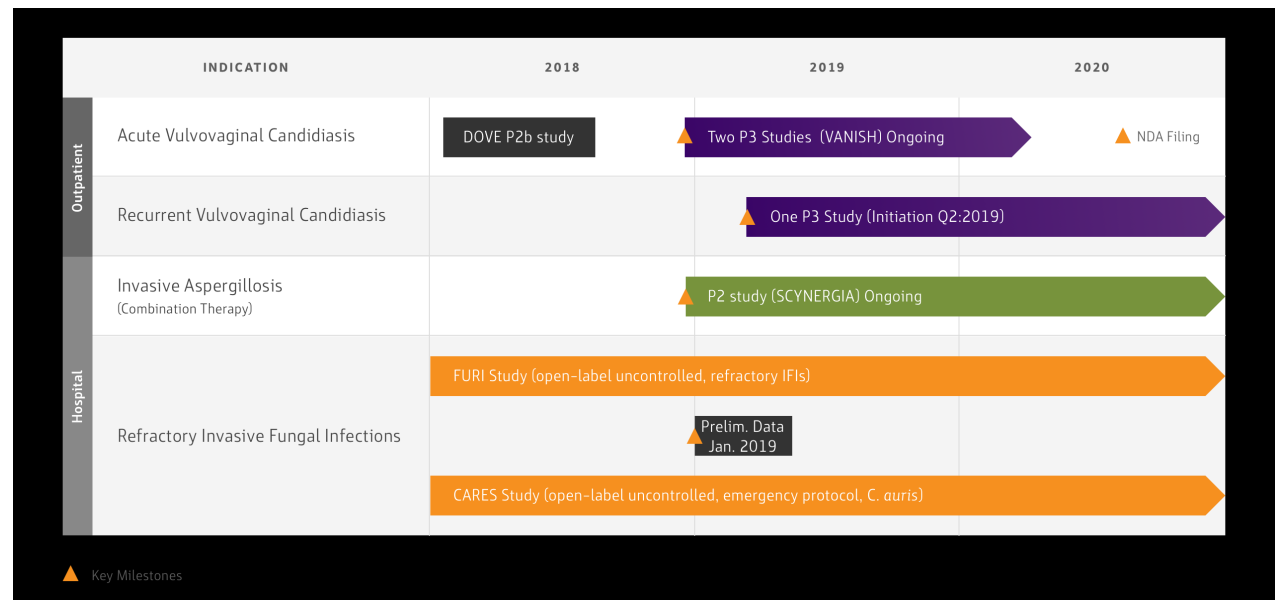
Ibrexafungerp is a glucan synthase inhibitor

Activity against:

- *Candida spp.*
- *Aspergillus spp.*
- *Pneumocystis jiroveci*

Oral and IV formulations

Active against isolates with current antifungal resistance



<https://www.scynexis.com/pipeline>



# Ibrexafungerp – First Triterpenoid

## Efficacy and Safety of Oral Ibrexafungerp in 41 Patients with Refractory Fungal Diseases, Interim Analysis of a Phase 3 Open-label Study (FURI)

BD Alexander<sup>3</sup>, OA Cornely<sup>1</sup>, PG Pappas<sup>2</sup>, R Miller<sup>3</sup>, M Johnson<sup>3</sup>, J Vazquez<sup>4</sup>, L Ostrosky-Zeichner<sup>5</sup>, A Spec<sup>6</sup>, R Rautemaa-Richardson<sup>7</sup>, R Krause<sup>8</sup>, GR Thompson<sup>9</sup>, TJ Walsh<sup>10</sup>, CG Morse<sup>11</sup>, JW Sanders<sup>11</sup>, D Andes<sup>12</sup>, GM Lyon<sup>13</sup>, FM Marty<sup>14</sup>, MH Miceli<sup>15</sup>, TF Patterson<sup>16</sup>, M Hoenig<sup>17</sup>, N Azie<sup>18</sup>, DA Angulo<sup>18</sup>

<sup>1</sup>University of Cologne, <sup>2</sup>University of Alabama Birmingham, <sup>3</sup>Duke University, <sup>4</sup>Augusta University, <sup>5</sup>University of Texas Houston, <sup>6</sup>Washington University St. Louis, <sup>7</sup>University of Manchester, <sup>8</sup>Medical University of Graz, <sup>9</sup>UC Davis, <sup>10</sup>Cornell University, <sup>11</sup>Wake Forest University, <sup>12</sup>University of Wisconsin, <sup>13</sup>Emory University, <sup>14</sup>Brigham and Women's Hospital, <sup>15</sup>University of Michigan, <sup>16</sup>UT Health and STVHCS San Antonio, <sup>17</sup>University of California at San Diego, <sup>18</sup>SCYNEXIS, Inc.

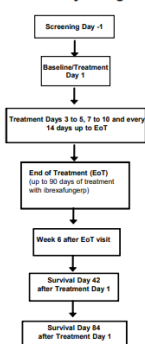


### BACKGROUND

Ibrexafungerp is a novel class triterpenoid antifungal with activity against *Candida*, *Aspergillus*, and *Pneumocystis* species, including azole- and echinocandin-resistant strains. A Phase 3 open-label, single-arm study of oral ibrexafungerp (FURI) (ClinicalTrials.gov NCT03059992) is ongoing for the treatment of patients (≥18 years) with fungal diseases who are intolerant of or refractory to standard antifungal therapies.

### METHODS

#### Study Design



An independent Data Review Committee (DRC) provided an assessment of treatment response for 41 patients who completed therapy by October 2019. Patients were enrolled in 22 centers from six countries. Patients were eligible for enrollment if they had proven or probable, invasive or severe mucocutaneous candidiasis and documented evidence of failure of, intolerance to, or toxicity related to a currently approved standard-of-care antifungal treatment or could not receive approved oral antifungal options (e.g., susceptibility of the organism) and a continued IV antifungal therapy was undesirable or unfeasible due to clinical or logistical circumstances.

### Demographics

Per Table 1, of the 41 patients analyzed, 22 (54%) were enrolled with invasive candidiasis/candidemia and 19 (46%) with mucocutaneous candidiasis infections; 70% of patients were immunocompromised.

Table 1: FURI Study Patient Demographics

Demographics	Ibrexafungerp
Patients (No.)	41
Mean Days of Therapy	37.2
Site of infection	# of Patients
Intraabdominal candidiasis	7
Intraabdominal + candidemia	1
Candidemia*	6
Hepato-splenic	2
Osteoarticular	3
Endocarditis, Mediastinitis, Cystitis	1 (each)
Oropharyngeal	8
Esophageal	7
Chronic mucocutaneous	2
Wound infection	2

\*One patient with candidemia had UTI

### CONCLUSIONS

Preliminary analysis of these 41 cases indicate that oral ibrexafungerp provides a favorable therapeutic response in the majority of patients with difficult to treat *Candida* spp. infections, including those caused by non-*albicans* *Candida* species.

### RESULTS

#### Outcomes

Of the 41 patients analyzed, oral ibrexafungerp showed clinical benefit in 34 patients (83%), including patients with a complete or partial response and patients who maintained stable disease. Six patients (15%) did not respond to the ibrexafungerp treatment (one patient was considered indeterminate).

Table 2: FURI Study Outcomes

	Complete/Partial Response	Stable Disease	Progression of Disease	Indeterminate
All Patients (41)	23 (56%)	11 (27%)	6 (15%)	1 (2%)

*Candida glabrata* was the most common pathogen isolated, representing 54% of the 46 *Candida* species recovered from these patients. 32 patients were infected with one species while two species were isolated in 7 (18%) patients.

Table 3: FURI Study Outcomes by Pathogen

Pathogen (n)	Complete/Partial Response	Stable Disease	Progression of Disease
<i>C. glabrata</i> (17)	9	5	3
<i>C. albicans</i> (7)	5	2	
<i>C. krusei</i> (5)	2	3	
<i>C. parapsilosis</i> (3)	3		
Two Pathogens			
<i>C. glabrata/C. albicans</i> (4)	2		2
<i>C. krusei/C. albicans</i> (1)	1		
<i>C. tropicalis/C. albicans</i> (1)		1	
<i>C. glabrata/C. dubliniensis</i> (1)			1

1 patient outcome indeterminate, 1 patient's organism not identified

#### Safety

Ibrexafungerp was well-tolerated with the most common treatment-related adverse events being of gastrointestinal origin. No deaths due to progressive fungal disease were reported.



# Variation in Clinical Practice and Attitudes in the Management of Fever and Neutropenia in Patients with Hematologic Malignancy: A Survey of Cancer Centers Across the United States

Samuel L. Aitken, PharmD, MPH<sup>1</sup>; Jason N. Barreto, PharmD<sup>2</sup>; Jerod L. Nagel, PharmD<sup>3</sup>; Susan K. Seo, MD<sup>4</sup>; Catherine Liu, MD<sup>5</sup>

on behalf of the Antimicrobial Stewardship in Cancer Consortium (ASCC)

<sup>1</sup>Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, TX; <sup>2</sup>Department of Pharmacy, Mayo Clinic, Rochester, MN; <sup>3</sup>Department of Pharmacy Service, Michigan Medicine, Ann Arbor, MI; <sup>4</sup>Infectious Diseases Service, Memorial Sloan-Kettering Cancer Center, New York, NY; <sup>5</sup>Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA

## Contact Information:

Samuel L. Aitken, PharmD, MPH  
slaitken@mdanderson.org

Catherine Liu, MD  
Catherine.liu@fredhutch.org

## ABOUT ASCC

The Antimicrobial Stewardship in Cancer Consortium (ASCC) is a group of pharmacists and physicians practicing at cancer centers nationwide who are dedicated to advancing the science and practice of antimicrobial stewardship in patients with cancer.

## BACKGROUND

- Guidelines from multiple organizations exist for the management of neutropenic fever among patients with cancer
- Recent publications suggest alternative approaches to traditional guideline recommendations for to the management of fever and neutropenia (e.g., continuation of empiric antimicrobial therapy until resolution of neutropenia, use of fluoroquinolone prophylaxis) may not be applicable
- No contemporary information on management of fever and neutropenia in a representative sample of cancer centers is available
- The purpose of this study was to survey cancer centers in the U.S. to gauge current practices for fever and neutropenia in patients with hematologic malignancy and hematopoietic cell transplant (HCT) recipients

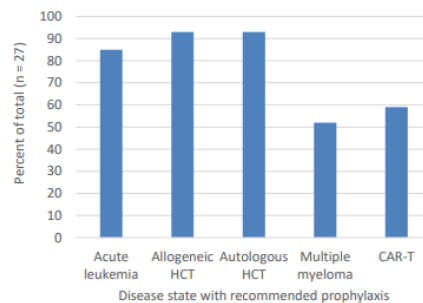
## METHODS

- In order to identify high-volume cancer centers with a large number of patients with hematologic malignancy, we identified all centers performing  $\geq 20$  allogeneic HCTs annually from the National Marrow Donor Program's "Be the Match" registry
- Infectious Diseases (ID) physicians, pharmacists, and others involved in the antimicrobial stewardship program and/or care of immunocompromised patients at each institution were identified by the authors via a manual review of publicly available information sources and personal contacts
- A survey assessing institutional standards and practices was distributed via email using Qualtrics software between 11/7 and 12/12/2019; survey reminders were sent every two weeks
- Duplicate surveys at the hospital level were removed and only complete responses were assessed using a 5-point Likert scale ranging from "Strongly Agree" to "Strongly Disagree"

- 34/148 (24%) individuals responded from 31/86 hospitals (36%)

Characteristic	No. (%) of individuals
Profession (n = 34)	
ID / AMS pharmacist	17 (50)
ID physician	12 (35)
Other	5 (15)
Years in practice (n = 29)	
<5	9 (31)
5 – 9	8 (28)
$\geq 10$	12 (41)
Type of practice (n = 34)	
Academic	30 (88)
Other	4 (12)

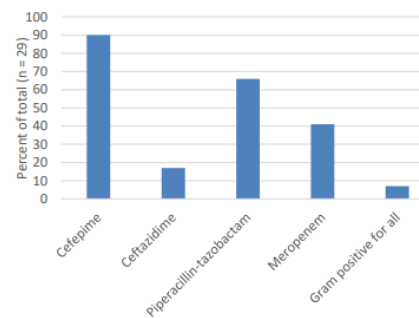
Figure 1. Disease states where antibacterial prophylaxis is recommended



- 27 / 31 (87%) centers recommend antibiotic prophylaxis
- Levofloxacin was the most commonly recommended antibiotic in centers recommending prophylaxis

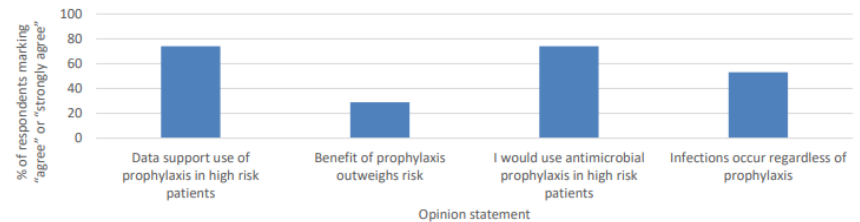
## RESULTS

Figure 2. Recommendations for empiric therapy for undifferentiated neutropenic fever



- 18/29 (62%) specifically provided recommendations on the de-escalation of Gram-negative therapy
- 8/18 (44%) at neutrophil recovery, 7/18 (39%) after 48 - >72 hours being afebrile

Figure 3. Individual attitudes on prophylaxis for fever and neutropenia



## SURVEY INSTRUMENT



## DISCUSSION

- Administration of prophylaxis and empiric antimicrobial therapy appears to be consistent with national guideline recommendations
- Over 1/3 of respondents do not provide specific guidance on antibiotic de-escalation; among those who provide recommendations, significant heterogeneity in de-escalation approaches were observed
- Prescriber attitudes on antibiotic prophylaxis in patients at high risk for fever and neutropenia indicate uncertainty over the benefit of the practice, yet antibiotic prophylaxis is widely recommended and widely used
- Factors compelling the discordant perceptions surrounding the antibacterial prophylaxis risk/benefit ratio and approach to antibiotic de-escalation requires further exploration.



# A hematology/oncology unit-specific antibiogram emphasizes the need for intensified local stewardship

Poster number:  
192

Rachel Bartash MD<sup>1</sup>, Margaret E McCort MD MS<sup>1</sup>, Kelsie Cowman MPH<sup>1</sup>, Erika Orner PhD<sup>2</sup>, Wendy Szymczak PhD<sup>2</sup>, and Priya Nori MD<sup>1</sup>

<sup>1</sup>Department of Medicine, Division of Infectious Diseases, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY;

<sup>2</sup>Microbiology Laboratory, Montefiore Medical Center, Bronx NY

3411 Wayne Avenue, 4H  
Bronx, NY 10467  
Phone: 718-920-7700  
[rbartash@montefiore.org](mailto:rbartash@montefiore.org)

## BACKGROUND

- Appropriate empiric antibiotics are key for patients with hematologic malignancies (HM) and bone marrow transplants (BMT) with febrile neutropenia
- Patients with HM and BMTs are at risk for multidrug resistant organisms
  - Prior antibiotic use and prolonged hospital exposures
- Hospital wide antibiograms (AB) may not accurately reflect resistance pattern
- We hypothesized that a **unit-specific AB** would have decreased susceptibilities compared to our hospital-wide AB

## METHODS

Reviewed **positive cultures with antimicrobial susceptibilities** on a closed 32-bed hematology-oncology unit (7/2016-6/2019)

Organisms with **≥ 30 isolates** were included in AB per the Clinical and Laboratory Standards Institute standards

Susceptibilities **compared to hospital-wide AB** from 7/2016-6/2019 using Fisher's exact test.

Figure 1: % of *E. coli* susceptible isolates

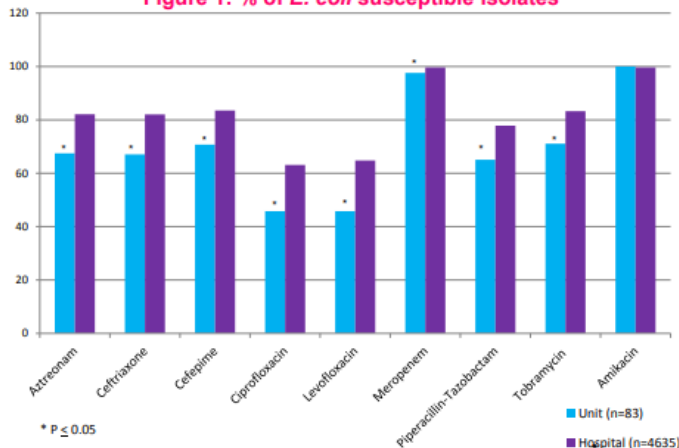
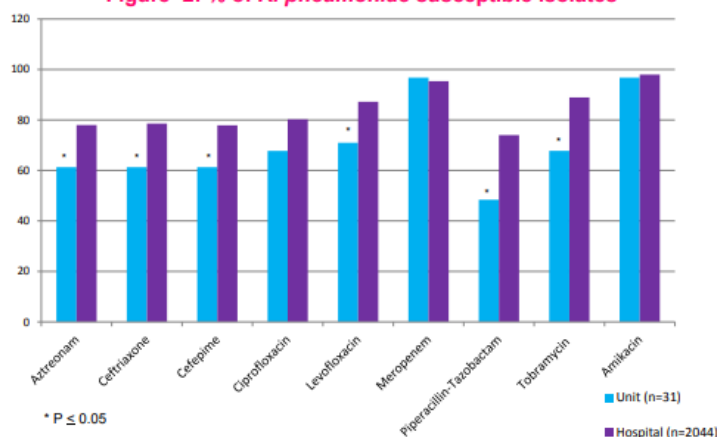


Figure 2: % of *K. pneumoniae* susceptible isolates



## RESULTS

- Two organisms met CLSI criteria:
  - *Escherichia coli* (n=83)
    - Unit isolates had lower susceptibilities to all tested antibiotics, except amikacin (Figure 1)
  - *Klebsiella pneumoniae* (n=31)
    - Unit isolates had lower susceptibilities to aztreonam, ceftriaxone, cefepime, levofloxacin, piperacillin-tazobactam and tobramycin (Figure 2)

## CONCLUSIONS

- A hematology-oncology unit-specific AB found **higher resistance in *Escherichia Coli* and *Klebsiella pneumoniae* isolates** compared with the hospital-wide AB.
- Findings can help guide appropriate empiric antibiotic therapy
- Results suggest a need for intensified stewardship measures to prevent multi-drug resistance in this population.

## ACKNOWLEDGEMENTS

Special thanks to Dr. Liise-anne Pirofski



# Antimicrobial Stewardship for Patients at the End of Life

Olivia Kates, MD

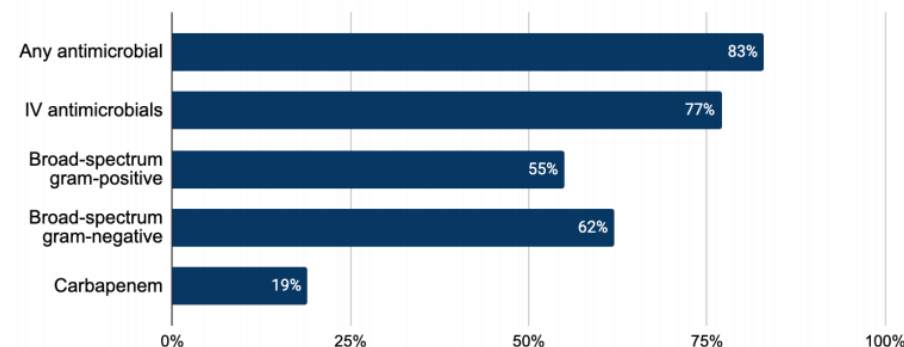
Senior Fellow, Infectious Diseases

Masters Candidate, Bioethics and Humanities

University of Washington & Fred Hutchinson Cancer Research Center



Proportion of patients receiving antimicrobials during last 30 days of life (n=1295 patients with at least 1 inpatient day during the last 30 days of life)



## Washington POLST Form: Antibiotics

### D NON-EMERGENCY MEDICAL TREATMENT PREFERENCES

#### ANTIBIOTICS:

- ☒ Use antibiotics for prolongation of life.  
☐ Do not use antibiotics except when needed for symptom management.

#### MEDICALLY ASSISTED NUTRITION:

Always offer food and liquids by mouth if feasible.

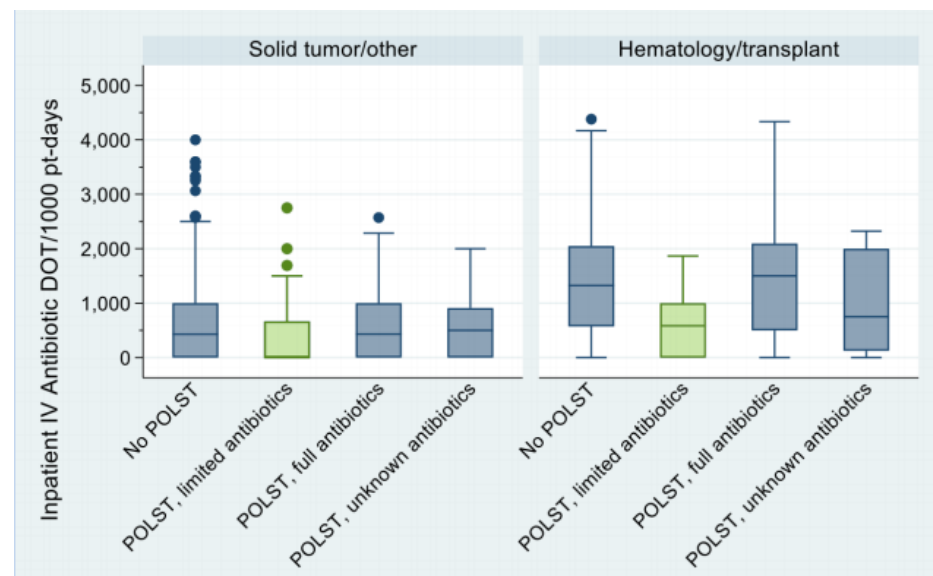
- ☐ No medically assisted nutrition by tube. ☐ Trial period of medically assisted nutrition (Goal: \_\_\_\_\_)

- ☐ Long-term medically assisted nutrition

**ADDITIONAL ORDERS:** (e.g. dialysis, blood products, implanted cardiac devices, etc. Attach additional or

☒ Physician/ARNP/PA-C Signature Date

☒ Patient or Legal Surrogate Signature Date



# Microbiome Disruption by Oral Antibiotics

Washington  
University in St. Louis  
SCHOOL OF MEDICINE

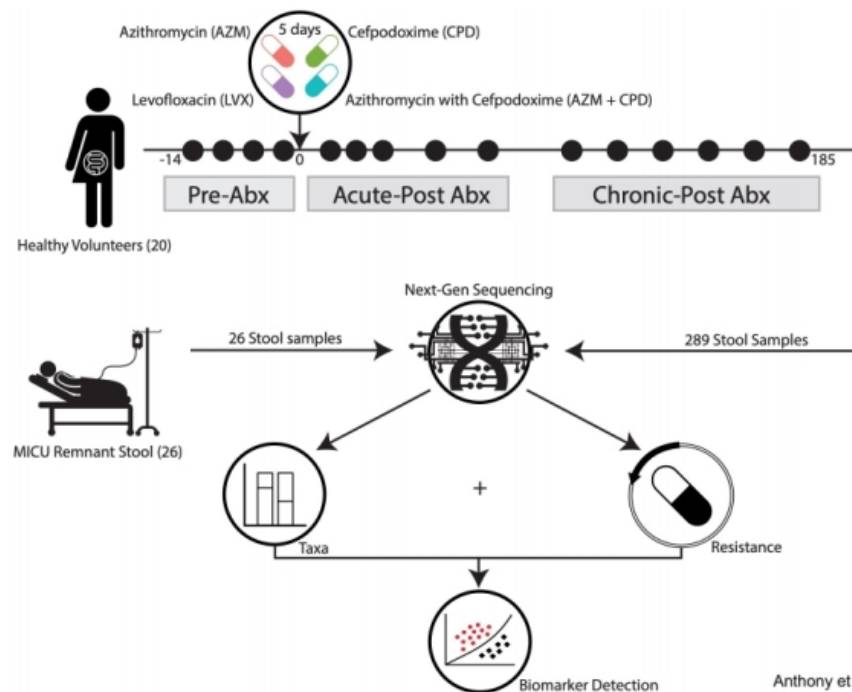
BARNESJEWISH  
Hospital  
HealthCare

## The Gut Microbiome and Resistome of Healthy Volunteers are Restructured After Short Courses of Antibiotics

Winston Anthony, BS, Bin Wang, MS, Kimberley Sukhum, PhD, Alaric W. D'Souza, PhD, Candice Cass, AA, Tiffany Hink, BA, Kimberly Reske, MPH, Sondra Seiler BA, Christopher Coon, MS, Erik R. Dubberke, MD, MSPH, Carey-Ann D. Burnham, PhD, Gautam Dantas, PhD, Jennie H. Kwon, DO, MSCI  
SHEA Decennial Top Oral Abstracts  
IDWeek 2020



 @JHKwonDO

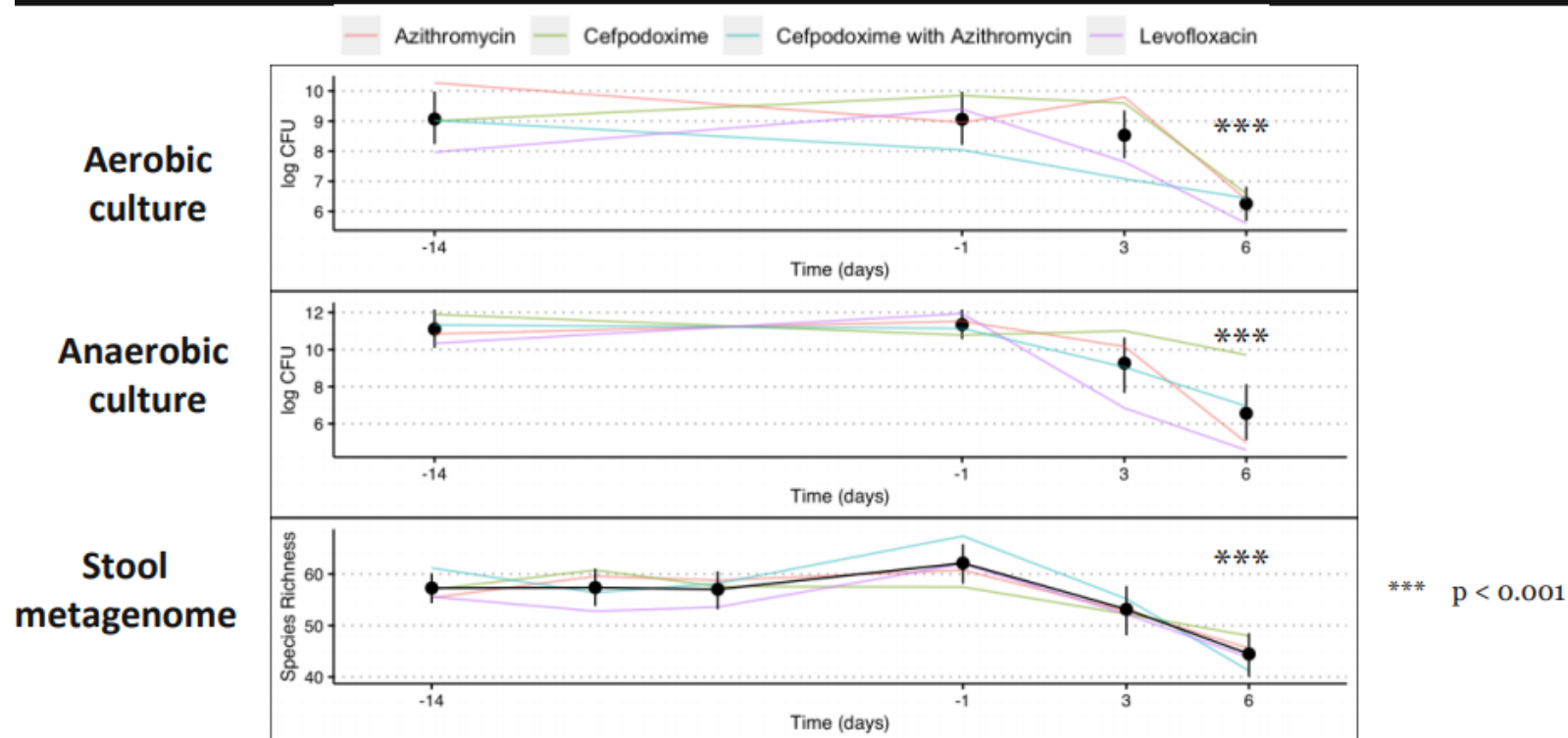


Anthony et al. *unpublished*



# Microbiome Disruption by Oral Antibiotics

Short courses of antibiotics can perturb the gut microbiome acutely



# Repurposing Older Drugs

## Retrospective study from large hospital in Israel

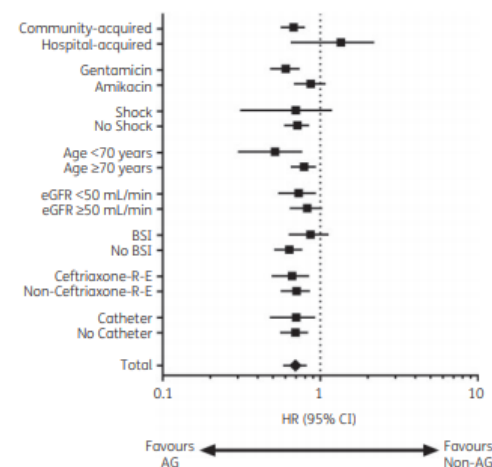
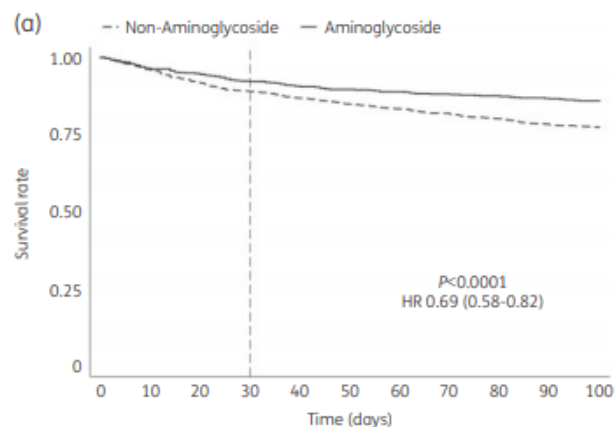
- Stewardship program promoted aminoglycosides as first-line therapy for adult pyelonephritis
  - Bacteremia included
  - Neutropenia excluded
  - Oral step down allowed
- N=2026; 715 AG, 1311 non-AG
- Median age 82
- Median duration 3 days (IQR 2-5)
- Primary endpoint, death within 30 days: 7.6 vs. 11%
- AKI occurred in 2.5% vs. 2.9%

## Effectiveness and safety of an institutional aminoglycoside-based regimen as empirical treatment of patients with pyelonephritis

Meital Elbaz<sup>1</sup>, Hila Zadka<sup>2</sup>, Ahuva Weiss-Meilik<sup>2</sup> and Ronen Ben-Ami<sup>3,4\*</sup>

<sup>1</sup>Internal Medicine, Tel Aviv Medical Center, Tel Aviv, Israel; <sup>2</sup>Data Science and Quality Division, Tel Aviv Medical Center, Tel Aviv, Israel;

<sup>3</sup>Infectious Diseases Unit, Tel Aviv Medical Center, Tel Aviv, Israel; <sup>4</sup>Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel



Elbaz M et.al. J Antimicrob Chemother 2020; 75: 2307–2313



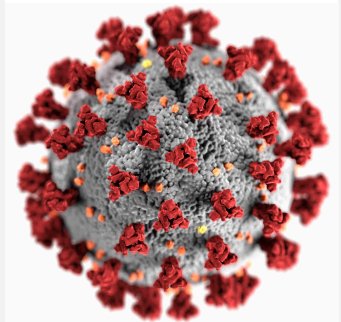


# ID WEEK 2020 IN BRIEF REVIEW

Ania Sweet, PharmD, BCOP

## OBJECTIVES

1. Review clinical presentation of COVID-19 infections and what we have learned in 2020
2. Review long term sequela of COVID-19 infections.
3. Analyze prescribing trends of oseltamivir and antibiotics in patients with laboratory confirmed influenza in an ambulatory cancer center.



# CLINICAL SPECTRUM OF COVID-19 PRESENTATIONS: FROM FLICKERS TO BLAZING INFERNOS

## Asymptomatic Infections

- Estimated 30-40% but could be higher
- Symptoms could still occur later even if asymptomatic at baseline
- Some are “pre-symptomatic”
- Even if asymptomatic can still have clinical abnormalities (CT scan of chest)
- Still can spread infection, but lower risk

## Symptomatic Infections (most are not severe)

- Mild 81%
  - No or mild pneumonia
- Severe 14%
  - Dyspnea, hypoxia, or >50% lung involvement on imaging within 24-48 hrs
- Critical 5%



Preeti Malani, MD, MSJ University of Michigan Ann Arbor

## Clinical Presentation

- Incubation
  - Median 5-6 days, up to 14 days
- Symptoms at the time of testing
  - Cough (50%)
  - Fever (43%)
  - Dyspnea (19%)
  - Headache (34%)
  - Loss of smell/taste (10%)
  - Sore throat (20%)

## Not Just Respiratory virus...

Critical illness and multiple systems

- Resp: PNA, ARDS
- CV: arrhythmias, acute cardiac injury, cardiomyopathy
- Heme: hypercoagulability/thrombotic complications: PE, CVA
- Inflammatory responses: CRS

# CLINICAL SPECTRUM OF COVID-19 PRESENTATIONS: FROM FLICKERS TO BLAZING INFERNOS



Preeti Malani, MD, MSJ University of Michigan Ann Arbor

## NEUROLOGIC DYSFUNCTION

- ▶ Contrary to some earlier reports, for most patients, anosmia does NOT appear to be permanent
- ▶ Other neurologic dysfunction, usually from cerebrovascular complications, are long lasting
- ▶ Significant burden of non-COVID related delays in care having worse outcome from delays in stroke care?

## POST ICU CARE SYNDROME

- ▶ PICS affects up to half of ICU admissions
- ▶ More likely in those treated with ventilation and with comorbidities
- ▶ Combination of pulmonary issues, physical debility and psychological impact
- ▶ Needs multidisciplinary recovery approach

## 48 DAYS AFTER DISCHARGE

- ▶ UK study found fatigue in 60.3% of admissions and 72% of ICU admissions
- ▶ Breathlessness in 42.6% inpatients and 65.6% of ICU patients
- ▶ PTSD in 23.5% of inpatients and 46.9% of ICU patients

John O'Horo, Sr., MD, MPH Mayo Clinic

## CARDIAC EFFECTS

- 78 patients who recently recovered from COVID-19, 75% had abnormal cardiac MRI
  - Long lasting effects on cardiac function?
- 26 athletes, 4 had abnormal findings on cardiac MRI suggestive of myocarditis
  - Are these reversible?



## Antiviral and Antibiotic Prescribing Among Patients at an Ambulatory Cancer Center with Laboratory-Confirmed Influenza

Woody Sorey, BA,<sup>1</sup> Elizabeth M. Krantz, MS,<sup>2</sup> Jessica Morris, MPH,<sup>2</sup> John Klaassen, BA,<sup>3</sup> Ania Sweet, PharmD,<sup>2,3</sup> Frank Tverdek, PharmD,<sup>2,3</sup> Steven A. Pergam, MD, MPH,<sup>2,3,4</sup> Catherine Liu, MD, FIDSA<sup>2,3,4</sup>

<sup>1</sup>School of Medicine, University of Washington, Seattle, WA; <sup>2</sup>Vaccine and Infectious Disease Division, Fred Hutch Cancer Research Center, Seattle, WA; <sup>3</sup>Seattle Cancer Care Alliance, Seattle, WA; <sup>4</sup>Division of Allergy and Infectious Diseases, University of Washington, Seattle, WA;

Poster #1505

Table 1. Patient Demographics and Characterist

Baseline <sup>1</sup> Characteristic	Antiviral Prescribed (n=110)	No Antiviral Prescribed (n=23)
Age (years), median (IQR)	57 (40 – 66)	47 (29 – 66)
Sex		
Male	65 (89)	8 (11)
Female	45 (75)	15 (25)
Diagnosis		
Heme Malignancy	93 (85)	16 (15)
Solid Tumor	11 (73)	4 (27)
Other	6 (67)	3 (33)
Clinical Service		
Heme	58 (83)	12 (17)
Solid Tumor	11 (65)	6 (35)
Transplant (BMT)	38 (88)	5 (11)
Other	3 (100)	0 (0)
Absolute Neutrophil Count <sup>2</sup> – median (IQR)	2.7 (1.6, 4.9)	2.9 (1.7, 5.2)

<sup>1</sup>Values are in n (%) unless otherwise specified.

<sup>2</sup>Baseline defined as date of first clinical encounter.

<sup>3</sup>ANC in units of 10<sup>3</sup> cells/μL.

Figure 1. Time from Symptom Onset to Date of First Clinical Encounter

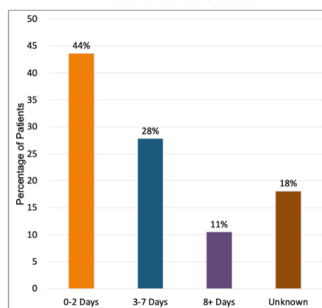
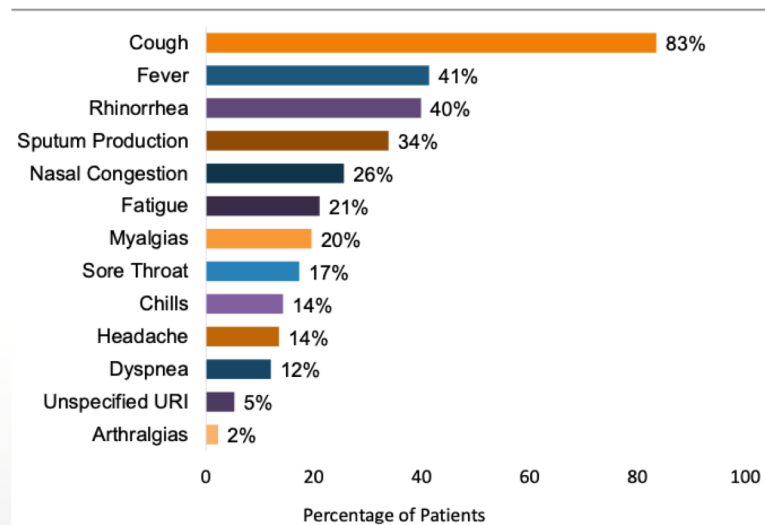
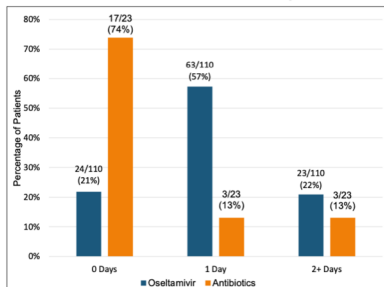


Figure 2. Symptoms Reported at First Clinical Encounter

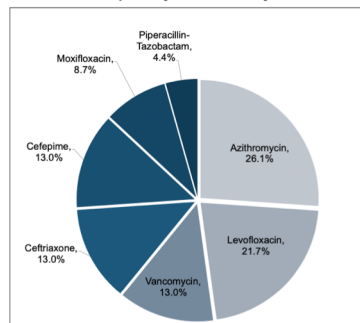


**Figure 4. Time from First Clinical Encounter to Oseltamivir and Antibiotic Prescription**



• Of 109 patients with known symptom onset date, 34 (31%) were prescribed oseltamivir within 48 hours of symptom onset

**Figure 3. Antibiotics Prescribed for Respiratory Illness on Day 0**



## Conclusions

- NAIs were frequently prescribed among cancer patients, but less than a third received treatment within 48 hours of symptom onset.
- Most were prescribed NAIs only after test results were available, while antibiotics were prescribed empirically.
- Delayed presentation to care is an obstacle to early NAI use; patient and provider education along with rapid diagnostics are needed to improve early NAI use among cancer patients with influenza.

- 23 (17.3%) received antibiotics for URI or LRTI within 7 days of first clinical encounter
- 17 (12.8%) received antibiotics for URI or LRTI on Day 0

**Table 2. Clinical Outcomes <sup>1</sup>**

Outcome	Number of Patients (%)
LRTI <sup>2</sup>	10 (7.5)
Influenza-Related ED Visit	7 (5.3)
Influenza-Related Hospitalization	11 (8.3)
Influenza-Related ICU Admission	1 (0.8)
Intubation / Mechanical Ventilation	0

<sup>1</sup>Outcomes captured from day 0 to day 14

<sup>2</sup>One microbiologically documented bacterial pneumonia (sputum culture: MSSA)



# Questions?

