Conclusion. These study data suggest that PORT Risk Class III or IV patients can be effectively managed as outpatients with 5 days of oral LEF as an alternative to fluoroquinolones for the treatment of CABP.

Table 1: Clinical Efficacy Outcomes (LEAP 2 Outpatients)

Subgroup Outcome	Lefamulin n/N (%)	Moxifloxacin n/N (%)
All Outpatients		
ECR Responder	138/151 (91.4)	142/159 (89.3)
IACR at TOC Success	138/151 (91.4)	143/159 (89.9)
PORT Risk Class III or IV Outpatients		
ECR Responder	59/66 (89.4)	56/64 (87.5)
IACR at TOC Success	60/66 (90.9)	58/64 (90.6)
CURB-65 Score 2 or 3 Outpatients		
ECR Responder	27/31 (87.1)	28/34 (82.4)
IACR at TOC Success	28/31 (90.3)	30/34 (88.2)

CURB-65=confusion, blood urea nitrogen >19 mg/dL (>6.8 mmol/L), respiratory rate ≥30 breaths/min, blood pressure <90 mmHg systolic or ≤60 mmHg diastolic, age ≥65 years; ECR=early clinical response; IACR=investigator's assessment of clinical response; PORT=pneumonia outcomes research team; TOC=test of cure

Table 2: Overall Summary of Adverse Events (LEAP 2 Outpatients)

Adverse Event	Lefamulin N=151 n (%)	Moxifloxacin N=159 n (%)
Treatment-emergent AE	52 (34.4)	48 (30.2)
Related TEAE	34 (22.5)	18 (11.3)
Serious TEAE	0	5 (3.1)
Related serious TEAE	0	0
TEAE leading to DC of study drug	4 (2.6)	4 (2.5)
Related TEAE leading to DC of study drug	2 (1.3)	2 (1.3)
TEAE leading to death	0	2 (1.3)

AE=adverse event; DC=discontinuation; TEAE=treatment-emergent adverse event

Disclosures. **All authors:** No reported disclosures.

2246. Improved Outcomes for Cancer Patients Treated With Ceftazidime–Avibactam vs. Polymyxin-Containing Regimens for Carbapenem-Resistant *Enterobacteriaceae* Bacteremia

Jovan Borjan, PharmD; Samuel A. Shelburne, MD, PhD;
Samuel A. Shelburne, MD, PhD; Micah M. Bhatti, MD, PhD;
Samuel L. Aitken, PharmD; Samuel L. Aitken, PharmD; The University of Texas MD Anderson Cancer Center, Houston, Texas

Session: 246. Clincal Outcomes of Infections with Resistant Organisms
Saturday, October 5, 2019: 12:15 PM

Background. Outcomes are improved with ceftazidime–avibactam (CZA) compared with polymyxin-based regimens (PBR) for carbapenemase-producing carbapenem-resistant *Enterobacteriaceae*. It is unclear whether this finding is true in non-carbapenemase (non-CP) producing CRE. The purpose of this study was to compare the efficacy and safety of CZA-based and PBR for CRE bacteremia in cancer patients with a high prevalence of non-CP CRE.

Methods. Adult cancer patients with first occurrence of CRE (i.e., meropenem non-susceptible) bacteremia treated with either CZA or PBR as directed therapy were included. Day 14 integrated benefit-risk outcomes based on desirability of outcome ranking (DOOR; (1) cured and discharged home, (2) cured and hospitalized, (3) cured and hospitalized with renal failure, (4) not cured, (5) dead) were used. DOOR is a recently developed statistical approach designed to unify important patient and clinician outcomes. Inverse probability of treatment weighted (IPTW) ordered logistic regression was used to model the odds of moving down ranked DOOR categories (i.e., having a worse outcome). The probability of a patient treated with CZA or a PBR having a worse DOOR category was also calculated. IPTW logistic regression was used to model the odds of 14-day mortality.

Results. 43 patients (CZA, n = 24; PBR, *n* = 19) with similar demographics and relative illness were included. *Klebsiella pneumoniae* (*n* = 21) and *Escherichia coli* (*n* = 16) were most common. 16/43 (37%) were CP CRE, 19/43 (44%) were non-CP CRE, and the remainder were unknown. The probability of a better DOOR for patients treated with CZA was 58% (95% CI 53% - 62%). Patients treated with CZA had an 81% reduction in IPTW-adjusted odds of a worse DOOR (OR 0.19, 95% CI 0.05 – 0.76; *P* = 0.02). 14-day mortality was 2/24 (8%) for patients receiving CZA vs. 5/19 (26%) for patients treated with PBR (IPTW-adjusted OR 0.12, 95% CI 0.02 – 0.82, *P* = 0.03).

Conclusion. These data suggest that CZA-based treatment, compared with PBR, has a superior integrated benefit-risk profile for the treatment of CRE bacteremia in cancer patients with a high burden of non-CP CRE. These findings build upon available data and suggest that CZA is preferred to PBR for CRE with heterogenous resistance mechanisms.

Disclosures: Samuel L. Aitken, PharmD, Melinta Therapeutoics: Grant/Research Support, Research Grant; Merck, Sharpe, and Dohme: Advisory Board; Shionogi: Advisory Board.

2247. Real-world Experience with Meropenem–Vaborbactam (M/V) for Treatment of Carbapenem-Resistant Enterobacteriaceae (CRE) Infections

Ryan K. Shields, PharmD, MS[1]; Erin K. McCreary, PharmD, BCPS, BCIDP[2];
Rachel V. Marini, PharmD[3]; Ellen G. Kline, MS[4]; Chelsea E. Jones, BA[1];
Binghua Hao, MD, PhD[1]; Cornelius J. Clancy, MD[1]; Minh-Hong Nguyen, MD[1];
[1]University of Pittsburgh, Pittsburgh, Pennsylvania; [2]University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; [3]UPMC Presbyterian, Pittsburgh, Pennsylvania; [4]University of Pittsburgh, School of Medicine, Pittsburgh, Pennsylvania

Session: 246. Clincal Outcomes of Infections with Resistant Organisms
Saturday, October 5, 2019: 12:15 PM

Background. M/V demonstrates *in vitro* activity against KPC-producing CRE, but real-world clinical experience is limited.

Methods. Patients treated for > 48 hours with M/V for CRE infections were included. Success was defined as improved symptoms, absence of recurrent infection, and survival at 30 days. Microbiologic failures (MF) were defined as isolation of the same species post-treatment (tx). KPC and *ompK36* mutations were detected by sequencing of PCR products.

Results. 19 patients were included; 58% were men; median age was 53. 11% were transplant recipients and median Charlson score was 3 (range: 0–10). Infection types included bacteremia (*n* = 7), pneumonia (6; 5 ventilator-associated), soft tissue (2), tracheobronchitis (2), intra-abdominal (1), and pyelonephritis (1). 68% of patients were in the ICU; median APACHE II and SOFA scores were 18 (7–40) and 4 (1–13), respectively. CR pathogens included *K. pneumoniae* (14), *K. oxytoca* (2), *E. coli* (2), and *C. freundii* (1); 89% harbored KPC, including KPC-2 (6), KPC-3 (10), and KPC-3 with a D179Y mutation (1). All were susceptible to M/V (median MIC = 0.03 µg/mL [0.015–0.12]). Median duration of tx was 8 days (3 – 28); 89% received monotherapy. Success and survival rates at 30d were 63% and 89%, respectively. Failures were due to death (2), recurrent infection (2), worse symptoms (2), and persistent bacteremia (1). Success rates for bacteremia and pneumonia were 57% and 67%, respectively. MF within 90 days occurred in 32% due to *K. pneumoniae* (5) or *E. coli* (1). MF were classified as intra-abdominal abscess (3), pneumonia (1), and respiratory (1) or urinary (1) colonization. The median time to MF was 32 days (15 – 67). M/V MICs were increased ≥8-fold against 67% (4/6) of recurrent isolates. 1 pt developed intra-abdominal infection due to M/V non-susceptible KPC-3 *K. pneumoniae* isolate (MIC = 8) following a 12-day of M/V; the recurrent isolate differed from the parent by an IS*5* insertion in the *ompK36* gene promoter. M/V was well-tolerated, 1 patient developed eosinophilia.

Conclusion. In this cohort of critically-ill patients with CRE infection, tx with M/V yielded outcomes comparable to prior cohorts treated with ceftazidime–avibactam. M/V non-susceptibility emerged in 1 isolate. Our findings require validation in future studies.

Disclosures. **All authors:** No reported disclosures.

2248. Clinical and Microbiological Outcomes Associated with Real-World Use of Ceftolozane/Tazobactam

Nicolo Cabrera, MD[1]; Truc T. Tran, PharmD[2]; William R. Miller, MD [2];
An Q. Dinh, BS[2]; Blake Hanson, PhD[3]; Jose M. Munita, MD[4];
Samuel A. Shelburne, MD, PhD[5]; Samuel A. Shelburne, MD, PhD[5];
Samuel L. Aitken, PharmD[5]; Samuel L. Aitken, PharmD[5];
Kevin W. Garey, PharmD, MS, FASHP[6]; Laura A. Puzniak, PhD[7];
Cesar A. Arias, MD, MSc, PhD, FIDSA[8]; [1]University of Texas Health Science Center at Houston, Houston, Texas; [2]Center for Antimicrobial Resistance and Microbial Genomics, UTHealth, Houston, Texas, Houston, Texas; [3]University of Texas Health Science Center School of Public Health, Houston, Texas; [4]Genomics and Resistant Microbes (GeRM) Group. Millennium Initiative for Collaborative Research On Bacterial Resistance (MICROB-R), Santiago, Region Metropolitana, Chile; [5]The University of Texas MD Anderson Cancer Center, Houston, Texas; [6]University of Houston College of Pharmacy, Houston, Texas; [7]Merck & Co., Inc., Kenilworth, New Jersey; [8]CARMiG, UTHealth and Center for Infectious Diseases, UTHealth School of Public Health, HOU, Texas; Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, BOG, COL, Houston, Texas

Session: 246. Clincal Outcomes of Infections with Resistant Organisms
Saturday, October 5, 2019: 12:15 PM

Background. Ceftolozane/tazobactam (C/T) is a novel cephalosporin/β-lactamase inhibitor combination for treating Gram-negative infections, particularly Pseudomonas aeruginosa (PA). C/T has been FDA-approved for complicated intra-abdominal and urinary tract infections and has just completed a trial in ventilator nosocomial pneumonia, but real-world outcome data are still emerging.

Methods. Demographic, microbiologic, treatment and outcome data of patients who received C/T for ≥48 hours from January 2016 to August 2018 at multiple centers within a single hospital system were retrospectively collected. Available isolates were analyzed for C/T susceptibility (by Etest) and whole-genome sequencing (WGS). Spades v.3.11.1 was used for assembly, multi-locus sequence typing v2.10 performed for in silico MLST with the PubMLST database and Abricate v0.7 was used for resistance gene screening with the CARD database.

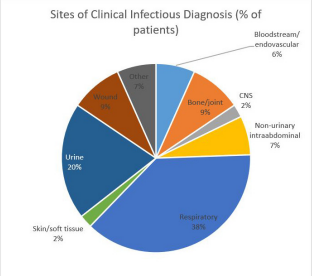
Results. Among 45 patients, 58% were non-white, 53% were female and 13% were immunocompromised. The median age was 64 years (IQR, 50 to 69). At the time of the index event, a high proportion of patients required ICU care (42%) and pressor support (13%) as well as had invasive devices in place (64%). A minority (2.4%) had prior exposure to C/T. Respiratory infections were most common (38%) followed by urinary tract (20%). Concomitant Gram-negative agents were used in 18%. 69% achieved clinical success (i.e., recovery from infection-related signs and symptoms). The in-hospital mortality rate was 16% of which 5 out of 7 were attributed to infection. Microbiology was available for 91% of patients; 84% had PA isolates resistant to at least 3 antipseudomonal classes (Figures 1 and 2). Ten PA isolates were analyzed with WGS (Table 1). C/T resistance arose during therapy in one patient (MIC increase from 1 to 128 µg/mL). WGS showed a substitution in AmpC β-lactamase (A46D) and presence of *blaCARB-2*.

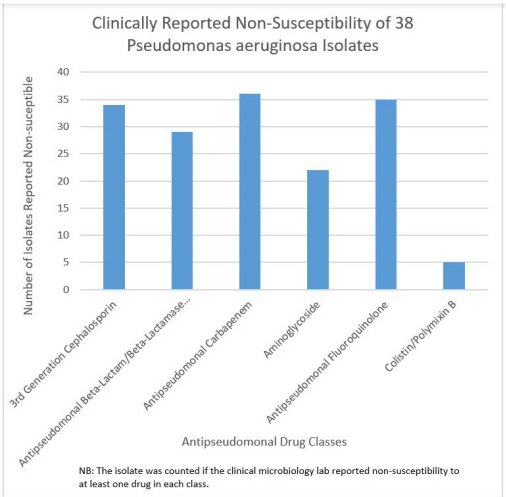
Conclusion. Although C/T was used in a critically ill population with highly resistant organisms, cure rates were high and mortality was low. Acquired β-lactamases were not frequently seen among the PA isolates. C/T is a vital therapeutic option, particularly on MDR isolates for which options are limited.

Table 1 Whole genome sequence analysis of 10 *P. aeruginosa* isolates collected from patients receiving C/T

Isolate No.	Date of collection*	Source	C/T MIC (µg/ml)	ST	aminoglycoside resistance	β-lactamase	Other
1	-2	respiratory	0.75	novel	*aph(3')-IIb*		*catB7*, *fosA*
2	-3	blood	0.5	308	*aph(3')-IIb*		*catB7*, *fosA*
3	-8	wound	1	novel	*aph(3')-IIb*		*catB7*, *fosA*
4	0	respiratory	1.5	235	*aph(3')-IIb*	bla_{OXA-2}	*catB7*, *fosA*
5	-5	respiratory	1.5	235	*aph(3')-IIb*		*catB7*, *fosA*
6	21	drainage	128	111	*aph(3')-IIb*	bla_{CARB-2}, $AmpC_{A46D}$	*catB7*, *fosA*
7	-2	biopsy	3	532	*aph(3')-IIb*		*catB7*, *fosA*
8	-9	respiratory	1.5	novel	*aph(3')-IIb*	bla_{OXA-2}	*catB7*, *fosA*
9	-3	tissue	0.75	novel	*aph(3')-IIb*		*catB7*, *fosA*
10	-22	respiratory	4	novel	*aph(3')-IIb*		*catB7*, *fosA*

C/T - ceftolozane/tazobactam, MIC - minimum inhibitory concentration, ST - sequence type as determined by MLST
* day 0 is start date of C/T therapy





Disclosures: Samuel L. Aitken, PharmD, Melinta Therapeutoics: Grant/Research Support, Research Grant; Merck, Sharpe, and Dohme: Advisory Board; Shionogi: Advisory Board.

2249. Impact of Minimum Inhibitory Concentration on Clinical Outcomes of Daptomycin for VRE Bloodstream Infection Among Neutropenic Oncology Patients

Elisabeth Caulder, PharmD; Elizabeth Palavecino, MD;
James Beardsley, PharmD; James Johnson, PharmD; Vera Luther, MD;
Christopher Ohl, MD; John Williamson, PharmD; Wake Forest Baptist Health System, Winston Salem, North Carolina

Session: 246. Clincal Outcomes of Infections with Resistant Organisms
Saturday, October 5, 2019: 12:15 PM

Background. Vancomycin-resistant Enterococcus (VRE) bloodstream infection (BSI) is a significant cause of morbidity and mortality in immunocompromised patients. This study aimed to assess the impact of daptomycin (DAP) MIC on outcomes of treatment for VRE BSI in neutropenic oncology patients.

Methods. This was a retrospective, observational, single-center, cohort study at an academic medical center. Included: age ≥ 18, neutropenia, admitted to oncology unit, and DAP for VRE BSI. Excluded: death within 24 hours after initiation of DAP, polymicrobial BSI, and linezolid use for > 48 hours before DAP initiation. Patients with VRE BSI 2008–2018 were identified using a report from the micro lab. Data were collected by electronic medical record review. The primary outcome of the study was clinical success, defined as culture sterilization, hypotension resolution, defervescence, and no need to change DAP due to persistent signs/symptoms of infection. Patients were analyzed according to DAP MIC ≤ 2 vs. ≥ 4 mg/L. Multivariable logistic regression analysis was performed to identify factors associated with clinical success.

Results. 44 patients met study criteria (MIC ≤ 2, n = 26; MIC ≥ 4, n = 18). Mean age was 58 years, 59% were male, and median ANC was 0. Median Charlson Comorbidity Index Score and Pitt Bacteremia Score (Pitt) were 5 and 1, respectively. 34% required ICU admission. More patients achieved clinical success with MIC ≤ 2 (88% vs. 56%; P = 0.03). Time to success (2.4 vs. 4 days, P = 0.02) and time to culture sterilization (2.2 vs. 2.9 days, P = 0.24) were shorter with MIC ≤ 2. Mortality was similar between groups (31% vs. 33%). Time to culture sterilization (P = 0.008), neutropenia resolution (P = 0.02), MIC group (P = 0.096), and Pitt (P = 0.52) were included in the multivariable model.

Conclusion. DAP MIC should be considered when choosing therapy for VRE BSI among neutropenic oncology patients, particularly those expected to have prolonged neutropenia and those with persistently positive cultures.

	Success (n=33)	Failure (n=11)	p
Age	58	58	0.55
ICU, %	30	45	0.47
Serum creatinine, mg/dL	0.75	1.2	0.32
Pitt	1	2	0.02
MIC ≤ 2, %	70	27	0.03
Time to sterilization, days	2.3	4.7	<0.001
Time to defervescence, days	1.55	2.13	0.87
Neutropenia resolution, %	45	0	0.01
DAP dose, mg/kg	7.3	7.6	0.74

Disclosures. **All authors:** No reported disclosures.

2250. Combination Vancomycin Plus Cefazolin for Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections

Sarah CJ. Jorgensen, PharmD, BCPS[1]; Trang D. Trinh, PharmD, MPH[2];
Evan J. Zasowski, PharmD, MPH[3]; Sara Alosaimy, PharmD, BCPS[1];
Sarah Melvin, RN[1]; Sahil Bhatia, MPH [1]; Sorabh Dhar, MD[4];
Ryan P. Mynatt, PharmD, BCPS-AQ ID[5];
Jason M. Pogue, PharmD, BCPS, BCIDP[6]; Michael J. Rybak, PharmD, MPH, PhD[7];
[1]Wayne State University, Detroit, Michigan; [2]University of California San Francisco, San Francisco, California; [3]Tuoro University California, Vallejo, California; [4]Detroit Medical Center, Wayne State University, John D Dingell VA medical center, Detroit, Michigan; [5]Detroit Medical Center, Detroit, Michigan; [6]University of Michigan College fo Pharmacy, Ann Arbor, Michigan; [7]Anti-Infective Research Laboratory, College of Pharmacy and Health Sciences, Wayne State University, Detroit, Michigan

Session: 246. Clincal Outcomes of Infections with Resistant Organisms
Saturday, October 5, 2019: 12:15 PM

Background. Combination β-lactam and vancomycin (VAN) prevent the emergence of resistance and result in synergistic antimicrobial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) *in vitro*. We sought to provide clinical translation to these data and determine if patients with MRSA bloodstream infection (BSI) treated with VAN + cefazolin (VAN/CFZ) via our MRSA BSI clinical pathway had improved clinical outcomes compared VAN alone.

Methods. Multicenter, retrospective, comparative cohort study from 2006 to 2019 in adults with MRSA BSI treated with VAN for ≥ 72 hours. VAN/CFZ was defined as VAN + CFZ within ≤ 72 hours of index culture for ≥ 24 hours. Other β-lactams were allowed for < 48 h in the VAN/CFZ group. The VAN alone group could not have other β-lactams within 7 days of treatment initiation. The primary outcome was clinical failure defined as a composite of 30-d all-cause mortality, 60-day recurrence, and persistent BSI (≥ 7 days). The independent effect of VAN/CFZ on clinical failure was evaluated with multivariable logistic regression. The primary safety endpoint was nephrotoxicity within 7 days of treatment initiation.

Results. A total of 237 patients were included (104 VAN/CFZ, 133 VAN). The most common BSI sources were skin/soft tissue (29.1%), IV catheter (21.9%), osteoarticular (20.3%) and infective endocarditis (16.0%). Demographic and clinical characteristics were similar between groups except VAN/CFZ had a higher median APACHE II score (18 vs. 13, P = 0.011). VAN/CFZ patients were also more likely to have received an infectious disease consult (100% vs. 81.2%, P < 0.001). Median (IQR) duration of CFZ was 115 (87–164) hours. After controlling for age, APACHE II score, ID consult and infection source, VAN/CFZ was associated with reduced odds of clinical failure (aOR 0.425, 95% CI 0.228, 0.792). Bivariate outcomes are shown in the table:

Conclusion. Patients with MRSA BSI treated with VAN/CFZ vs. VAN experienced fewer clinical failures, supporting additional studies evaluating the role of adjuvant CFZ for MRSA BSI.

	VAN/CFZ n=104 n (%)	VAN n=133 n (%)	P value
Clinical failure	26 (25.0)	49 (36.3)	0.052
30-d mortality	8 (7.7)	11 (8.3)	0.871
60-d recurrence	7 (6.7)	16 (12.0)	0.171
BSI ≥ 7 d	17 (16.3)	32 (24.1)	0.146
Nephrotoxicity	4 (3.8)	10 (7.5)	0.234

Disclosures. **All authors:** No reported disclosures.

2251. Estimating the Need for Novel Gram-Negative Active Antibiotics in US Hospitals

Jeffrey R. Strich, MD[1]; Sarah Warner, MPH[1]; Yi Ling Lai, MPH[2];
Cumhur Y. Demirkale, PhD[1]; John H. Powers, MD[3];
Robert L. Danner, MD[1]; Sameer S. Kadri, MD, MS[4]; [1]National Institutes of Health, Bethesda, Maryland; [2]National Institutes of Allergy and Infectious Disease, National Institutes of Health, Bethesda, Maryland; [3]Support to National Institute of Allergy and Infectious Disease, Bethesda, Maryland; [4]NIH Clinical Center, Bethesda, Maryland

Session: 246. Clincal Outcomes of Infections with Resistant Organisms
Saturday, October 5, 2019: 12:15 PM

Background. Assessing the unmet need for novel antibiotics could inform appropriate utilization, enrollment in trials and ensure balance in aligning incentives and investments in therapeutic development.

Methods. The *Cerner Healthfacts* electronic health record repository was queried to identify inpatient treatment opportunities for Gram-negative active agents (GNAA) displaying either difficult-to-treat resistance (DTR; resistance to all β-lactams including carbapenems and fluoroquinolones) or extended-spectrum cephalosporin resistance (ECR). The former was quantified by aggregating episodes of confirmed DTR infection (i.e., DTR strain isolated and concomitant antibiotic(s) received) or suspected (i.e., 1–2 days of empiric colistin/polymyxin-B or aminoglycosides and no DTR pathogen isolated). Aggregate days of therapy (DOT) were reported as a range, multiplying episodes by site-specific or uniform 14-day treatment durations, respectively. Recursive partition and cluster analyses were performed for hospital characteristics and contributions of outbreaks to DTR treatment opportunities, respectively.

Results. Between 2009 and 2015, across 2,996,271 encounters, 1,352 episodes of potential targeted treatment were identified, which combined with empiric treatment episodes, represent 39–138 DOT/10,000 encounters for a DTR-GNAA. Similarly, 9,535 episodes of potential targeted therapy for an ECR-GNAA were identified (representing 211-466 DOT/10,000 encounters). The most common candidate site and pathogens for DTR-GNAA were lower respiratory and *A. baumannii* and *P. aeruginosa*