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

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

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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.

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

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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.

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

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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