culture only. For Sp cultured from NP, a concomitant *lytA* PCR value of ≥ 1000 gene copies/mL was required. All isolates underwent susceptibility testing, and a subset of isolates underwent molecular or phenotypic characterization including whole-genome sequencing for FQ resistance mechanisms, PCR for PVL/*mecA* genes (*S. aureus*), β-lactamases (*Haemophilus/Moraxella* spp), and serotyping (Sp).

Results. Included in submitted image.

Conclusion. DLX demonstrated potent in vitro and clinical activity against CABP pathogens, including Sp [MRSP, MDRSP, PRSP], MRSA, *Haemophilus* species, Enterobacteriaceae, *P. aeruginosa,* and the atypical pathogens Cp, Mp, and Lp.
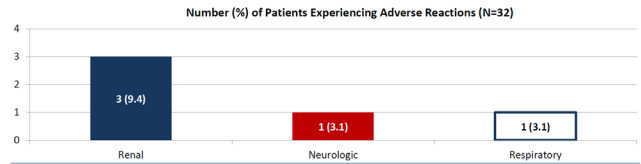
Pathogens	Baseline·Frequency (All·diagnostic·methods) DLX·MITT (N=257) n·(%)	Micro·Success·in·DLX·Pts Micro·Evaluable·@·TOC n/N·(%)	DLX·MIC₉₀ µg/mL MITT
S. pneumoniae	120·(46.7)	102/110·(92.7)	0.015·
PRSP	8·(3.1)	7/8·(87.5)	0.015
MDRSP	4·(1.6)	4/4·(100.0)	0.015
MRSP	17·(6.6)	15/17·(88.2)	0.015
H. parainfluenzae	35·(13.6)	31/35·(88.6)	0.5
M. pneumoniae	35·(13.6)	29/30·(96.7)	0.5
L. pneumophila	29·(11.3)	27/29·(93.1)	0.00025-0.001
S. aureus	27·(10.5)	25/27·(92.6)	0.004
MSSA	25·(9.7)	23/25·(92.0)	0.004
MRSA	2·(0.8)	2/2·(100.0)	0.002-0.004
H. influenzae	27·(10.5)	22/24·(91.7)	0.002
C. pneumoniae	25·(9.7)	24/24·(100.0)	-
K. pneumoniae	17·(6.6)	14/17·(82.4)	0.25
E. coli	16·(6.2)	13/13·(100.0)	4
P. aeruginosa	13·(5.1)	11/12·(91.7)	4
K. oxytoca	6·(2.3)	6/6·(100.0)	2
M. catarrhalis	6·(2.3)	6/6·(100.0)	0.004

2231. Safety of Nebulized Colistin as Adjunctive Treatment of Lower Respiratory Tract Infections

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Background. Systemic antibiotics used in treatment of drug-resistant lower-respiratory tract infections (LRTI) may have poor lung penetration or narrow therapeutic indices. Nebulized administration of colistin allows direct instillation of active agent to maximize concentrations at the site of infection. Theoretically, local administration also avoids treatment-limiting toxicities and adverse drug reactions (ADR). Current literature supports efficacy of nebulized colistin as adjunctive treatment for LRTI. However, there is a paucity of data surrounding safety and tolerability of this administration technique.

Methods. The electronic medical record (EMR) was queried to identify patients treated with nebulized colistin between January 1, 2016 and December 31, 2018. The following data were collected from the EMR and hospital ADR reporting systems: demographics, treatment regimen, serum creatinine (SCr), concomitant nephrotoxins, infecting pathogen, treatment-emergent ADRs, and drug toxicities. The primary outcome was prevalence of renal (acute kidney injury [AKI]), neurologic (seizure, visual disturbance), or respiratory (bronchospasm) ADRs secondary to colistin nebulization therapy. AKI was defined according to the RIFLE criteria.

Results. Thirty-two patients were administered nebulized colistin during the study period. Approximately 19% of patients had a baseline renal impairment. Cultures were positive in 29 patients of which 11 organisms were resistant to all tested antimicrobials. The most common infecting pathogen was *A. baumanii* (*n* = 15) followed by *K. pneumoniae* (*n* = 9). The median duration of therapy was 4.6 days. Seventeen patients (53.1%) were exposed to concomitant nephrotoxins. Three patients experienced AKI of which two received simultaneous furosemide and one had underlying renal dysfunction and received concomitant vancomycin. The one observed neurologic reaction, seizure, occurred in a patient with underlying epilepsy. No patients had documented visual disturbances or bronchospasm.

Conclusion. The results of our study are consistent with the principle that localized administration of colistin results in a lower incidence of systemic adverse events. Nebulized colistin is a safe adjunct for managing LRTI. Renal, pulmonary, and neurologic reactions in this study were likely not treatment-related.

Number (%) of Patients Experiencing Adverse Reactions (N=32)

2232. A Global Phase 3 Study of Delafloxacin (DLX) Compared with Moxifloxacin (MOX) in Patients with Community-acquired Bacterial Pneumonia (CABP)

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Background. DLX is an IV/oral fluoroquinolone with no QT restrictions, and activity against Gram-positive, Gram-negative and atypical pathogens. DLX is approved for treatment of ABSSSI including those due to MRSA and Gram-negative pathogens. A Phase 3 trial of patients with CABP was recently completed.

Methods. Global active-comparator double-blind trial; adults with CABP with at least 2 clinical symptoms, physical signs, and radiographic evidence of pneumonia. Randomized 1:1 to DLX or MOX treatment for 5–10 days. Randomization stratified by PORT Class, history of COPD/asthma, and prior single-dose antibiotic use (limit 25%). Patients received a minimum of 3 days IV treatment, then were switched to oral at MD discretion. The primary endpoint for FDA was the Early Clinical Response (ECR): improvement at 96 hours after first dose of study drug in at least 2 of the baseline symptoms in the Intent to Treat (ITT) population.

Results. 859 patients were randomized; both groups were comparable. Patient characteristics: mean age 60 (range 18–93, 21% ≥ age 75); 58.7% male; 28.6% multi-lobar pneumonia; 26.8% PORT class IV/V. Bacterial pathogens were identified in 60.5% at baseline; most commonly *S. pneumoniae,* as well as *S. aureus,* atypicals and Gram-negatives. Patients received treatment ~ 8.5 days (6.3 days of IV, 2.2 days oral). DLX was non-inferior to MOX in ECR 88.9% DLX vs. 89.0% MOX [Δ−0.2 (CI -4.4, 4.1)] in the ITT population; ECR in the evaluable population was 91.1% DLX vs. 91.8% MOX [Δ−0.6 (CI -4.5, 3.2)]. Day 28 Mortality was 1.9% DLX vs. 1.4% MOX. In the micro evaluable population, DLX was comparable to MOX in eradication, 92.5% DLX vs. 93.5% MOX at Test of Cure 5–10 days after treatment, [Δ −1.0 (CI -5.8, 3.6)]. 30.5% DLX and 26.2% MOX patients had ≥1 treatment-emergent adverse events (AEs). The most common DLX AEs were diarrhea and transaminase elevations, which were mild-to-moderate and did not routinely lead to discontinuation (DC). Treatment DC due to treatment-related AEs was seen in 9 DLX and 4 MOX patients. There were no potential QT AEs with DLX.

Conclusion. IV/oral DLX was comparable to IV/oral MOX for treatment of CABP in patients. DLX has no preclinical signals for QT prolongation and has no QT prolongation in a validated challenge study. DLX appears effective and well tolerated in patients with CABP.

2233. Efficacy and Symptom Resolution by Visit in Adults With Community-Acquired Bacterial Pneumonia (CABP) Treated With Lefamulin (LEF) or Moxifloxacin (MOX): Pooled Analysis of Lefamulin Evaluation Against Pneumonia (LEAP) 1 and LEAP 2 Study Results

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Background. Efficacy and safety of LEF were shown in 2 noninferiority trials (LEAP 1/2) vs. MOX in adults with CABP. We assessed the efficacy of LEF by visit based on a pooled analyses of LEAP 1/2 data.

Methods. In LEAP 1, PORT III–V patients (patients) received LEF 150 mg IV q12h for 5–7 days or MOX 400 mg IV q24h for 7 days, with optional IV-to-oral switch (600 mg LEF q12h or 400 mg MOX q24h). In LEAP 2, PORT II–IV patients received oral LEF 600 mg q12h for 5 days or oral MOX 400 mg q24h for 7 days. Criteria for defining the FDA primary endpoint of early clinical response (ECR) at 96 ± 24 hours after first dose were applied to each visit through late follow-up (LFU; days 27–34) in the intent-to-treat (ITT; all randomized patients) population. Investigator assessment of clinical response (IACR) was examined at end of treatment (EOT; within 2 days after last dose), test-of-cure (TOC; 5–10 days after last dose; EMA primary endpoint), and LFU in the modified ITT (mITT; received ≥1 dose of study drug) and clinically evaluable (CE; met predefined evaluability criteria) populations. Results are presented by visit for pooled LEAP 1/2 data.

Results. 1289 ITT patients were randomized (LEF, *n* = 646; MOX, *n* = 643). Most patients in both groups achieved ECR at Day 3, with further increases through Day 7 and sustained efficacy through LFU (Fig 1). In mITT patients, IACR success rates at EOT/TOC/LFU were 87.1/85.0/83.2% with LEF and 88.1/87.1/86.1% with MOX; results were consistent in CE patients. The proportions of ITT patients with resolution of all baseline signs/symptoms of CABP increased similarly by visit in both treatment groups (Fig 2). Most patients did not achieve complete sign/symptom resolution until TOC, with fever generally being the first and cough the last to resolve. There was no apparent relationship between ECR and age, gender, renal status, SIRS, PORT, prior antibiotic use, baseline pathogens, typical/atypical pathogens, or mono/polymicrobial pathogens. The high percentage of patients at LFU with baseline symptom resolution suggests that symptom resolution was sustained.

Conclusion. In this pooled analysis, efficacy results were similar by visit in the LEF and MOX groups, with high ECR rates maintained through LFU. LEF will provide a potential new effective systemic monotherapy alternative to fluoroquinolones for the empiric treatment of CABP.

Figure 1. ECR Rates by Visit (ITT Population)
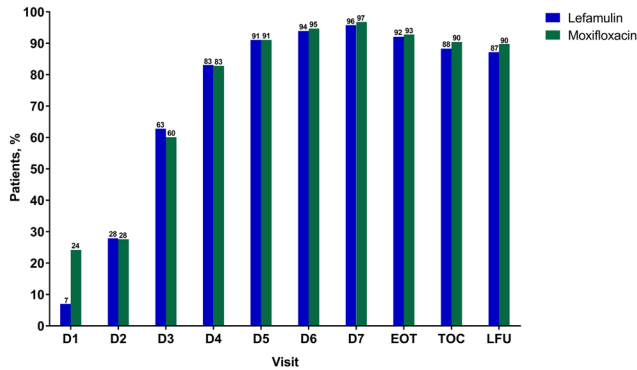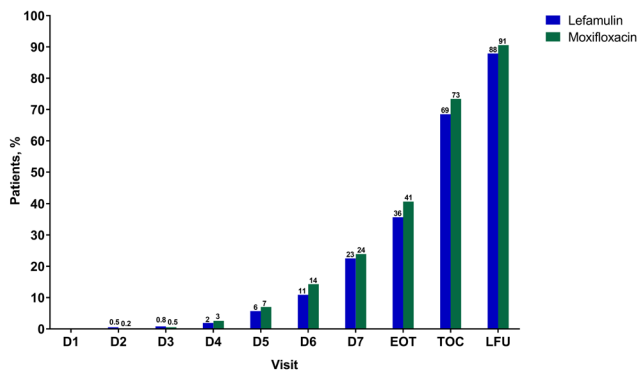

Figure 2. Patients With Resolution of All Baseline Signs/Symptoms of CABP by Visit (ITT Population)

*Includes cough, dyspnea, purulent sputum production, and chest pain.

Disclosures. All authors: No reported disclosures.

2234. Outcomes by Age and Gender from a Global Phase 3 Study of Delafloxacin (DLX) in Community-Acquired Bacterial Pneumonia (CABP)

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Background. Delafloxacin (DLX) is a fluoroquinolone, approved in the United States for treatment of ABSSSI. DLX has no preclinical signals for QT prolongation and has no QT prolongation in a validated challenge study. Risk of QT prolongation is a consideration in antibiotic selection for elderly hospitalized CABP patients. A Phase 3 CABP trial with DLX was analyzed with a focus on age and gender.

Methods. Data on age and gender were reviewed from a multicenter, randomized, double-blind trial of adults with CABP. Patients were randomized 1:1 to DLX or moxifloxacin (MOX) treatment for 5–10 days. Patients received a minimum of 3 days of IV treatment, then were switched to oral at MD discretion. A key clinical endpoint was the investigator-assessment at Test of Cure (TOC) 5–10 days after the end of treatment. Clinical success was defined as complete or near resolution of signs and symptoms and no further antibiotics needed

Results. In the overall study, 859 patients were randomized with a mean age of 60 years (55.5% <65, 44.5% ≥65, 21.2% ≥75; range 18–93); 58.7% were male; 25.4% and

1.4% were PORT class IV and V; 28.6% multi-lobar pneumonia. Table shows the comparison of DLX and MOX clinical response at TOC in the Intent to Treat (ITT) population. Overall, DLX was well tolerated, with similar related adverse events (AE) between treatment groups regardless of age (< 65: 16.7% DLX, 13.3% MOX; ≥ 65: 13.4% DLX, 11.7% MOX) or gender (male: 16.0% DLX, 11.1% MOX; female 14.0% DLX, 14.9% MOX). The most common treatment-related AEs for DLX were diarrhea and transaminase elevations which were mild-to-moderate and did not routinely lead to discontinuation. There were no reports of potential QT prolongation on DLX.

Conclusion. Based on age and gender, DLX had comparable outcomes to MOX in clinical success at TOC. DLX was also well tolerated regardless of age or gender. DLX may offer a promising alternative in the treatment of CABP including elderly patients.

		Clinical Success @ TOC (ITT)		
	Subgroup	DLX IV/ PO % (n/N)	MOX IV/PO % (n/N)	Delta D-M (95% CI)
Age % (n/N)	<65	91.7 (209/228)	88.8 (221/249)	2.9 (-2.5, 8.4)
	≥65	89.2 (181/203)	91.1 (163/179)	-1.9 (-8.0, 4.3)
	≥75	90.6 (77/85)	89.7 (87/97)	0.9 (-8.5, 9.9)
Gender % (n/N)	Male	88.8 (223/251)	88.8 (225/253)	-0.1 (-5.7, 5.5)
	Female	92.8 (167/180)	90.9 (159/175)	1.9 (-3.9, 8.0)

Disclosures. All authors: No reported disclosures.

2235. Fecal Biomarkers for *Clostridioides difficile* Infection in Cancer Patients

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Background. The diagnosis of *C. difficile* infection (CDI) relies on using a nucleic acid amplification test (NAAT) followed by confirmatory toxin enzyme immunoassay (EIA). This study examined the utility of fecal biomarkers and *C. difficile* bacterial quantity (BQ) in differentiating patients with true infection (NAAT+/EIA+) from patients with colonization (NAAT+/EIA-) in the context of *C. difficile* ribotypes.

Methods. We studied 136 patients with diarrhea and CDI identified by NAAT in stools for which a confirmatory toxin A, B, EIA was performed. Fecal IL-8, IL-1β, calprotectin, and lactoferrin were studied by ELISA. *C. difficile* BQ was determined by 16S rRNA qPCR. Data were stratified according to cancer diagnosis into three groups [hematologic (H) *n* = 43, solid tumor (ST) *n* = 62, or stem cell transplant (SCT) *n* = 31].

Results. Stools were EIA+ in 36/136 (26%) of the cohort. Although ST patients had a higher Charlson co-morbidity index when compared with the other two groups (*P* < 0.002), demographic characteristics and symptoms at the time of presentation were similar between groups regardless of EIA status. Most common ribotypes identified included F106 and F014-020. Ribotype distribution differed according to oncologic diagnosis as determined by the Shannon diversity index. There were fewer distinct *C. difficile* ribotypes in the SCT (*n* = 8) vs. ST (*n* = 15) and H (*n* = 15) groups (*P* < 0.001 and *P* < 0.002, respectively). BQ were higher in EIA+ than EIA- across all strata (log of BQ/mg 2.38 ± 1.49 vs. 0.92 ± 1.28, *P* > 0.001). Similarly, higher levels of fecal IL-8 (1.72 ± 1.9 vs. 0.83 ± 1.6 ng/mL), IL-1β (3.74 ± 13.7 vs.. 1.21 ± 4.6) and calprotectin (14.9 ± 27 vs. 6 ±1.8 ug/mL) levels were seen in EIA+ patients. While IL-8, IL-1β, and calprotectin were increased in EIA+ ST and H, no differences were seen in the SCT group. A sensitivity analysis using ROC curves, revealed that BQ resulted in a greater area under the curve than fecal markers of inflammation (A = 0.77, *P* < 0.001, 95% CI [0.67–0.86]).

Conclusion. In this study in cancer and immunocompromised patients, *C. difficile* bacterial burden regardless of infecting ribotype and fecal cytokines showed to be a helpful assay in distinguishing true CDI from colonization.

Table 1: Clinical presentation by Oncological Diagnosis Group

	Hematological	Solid Tumor	SCT	P value
Total N= 136	43	62	31	
Risk Factors for Diarrhea				
Inpatient	42(98)	61(98)	31(100)	1.000
Community Associated	2(5)	11(18)	2(7)	**0.011**
Healthcare Facility Associated (within 12 wks post discharge)	6(14)	7(11)	7(23)	
Healthcare Facility Associated (within 4 wks post discharge)	18(42)	21(34)	3(10)	
Healthcare Facility Onset (>48hr post admission)	17(40)	23(37)	19(61)	
International travel	1(2)	0	1(3)	0.696
Antibiotic use	41(95)	51(82)	30(97)	**0.042**
Immunosuppression	32(74)	29(47)	28(90)	>0.001
Chemotherapy	36(84)	30(48)	27(87)	>0.001
Clinical Presentation				
Charlsons's Comorbidity Index Median (Range)	5(1-14)	6(2-16)	5(1-16)	KW= **0.002** (H vs S)=0.012 (H vs SCT)=0.327 (S vs SCT)=0.001
Zar's score Median (Range)	1(0-4)	1(0-3)	1(0-4)	KW= 0.636
Duration of symptoms prior to CDI (days) Median (Range)	1.5(1-14)	2(1-21)	1.5(1-21)	KW= 0.170