Table 1. Baseline Patient Demographics and Characteristics

	LEF		MOX	
Analysis population	PORT III patients (*n*=341)	PORT IV/V patients (*n*=121)	PORT III patients (*n*=334)	PORT IV/V patients (*n*=117)
Age, years, mean (SD)	60.7 (15.3)	69.1 (14.2)	58.8 (14.3)	70.7 (12.6)
Male, *n* (%)	202 (59.2)	86 (71.1)	183 (54.8)	71 (60.7)
White, *n* (%)	277 (81.2)	92 (76.0)	277 (82.9)	96 (82.1)
Renal Status,* *n* (%)				
Normal function	148 (43.4)	34 (28.1)	166 (49.7)	25 (21.4)
Mild impairment	129 (37.8)	30 (24.8)	104 (31.1)	36 (30.8)
Moderate impairment	61 (17.9)	51 (42.1)	63 (18.9)	51 (43.6)
Severe impairment	3 (0.9)	4 (3.3)	1 (0.3)	4 (3.4)
SIRS, *n* (%)	330 (96.8)	116 (95.9)	318 (95.2)	108 (92.3)

Data for PORT I/II pts not shown.
*Normal: CrCl ≥90 mL/min; mild impairment: CrCl 60–<90 mL/min; moderate impairment: CrCl 30–<60 mL/min; severe impairment: CrCL<30 mL/min.

Table 2. TEAEs in PORT Risk Class III and IV/V Patients

	LEF		MOX	
Patients with ≥1, *n* (%)	PORT III pts (*n*=337)	PORT IV/V pts (*n*=120)	PORT III pts (*n*=333)	PORT IV/V pts (*n*=116)
Any TEAE	97 (28.8)	55 (45.8)	98 (29.4)	51 (44.0)
TEAE severity				
Mild	56 (16.6)	24 (20.0)	62 (18.6)	26 (22.4)
Moderate	32 (9.5)	18 (15.0)	26 (7.8)	14 (12.1)
Severe	9 (2.7)	13 (10.8)	10 (3.0)	11 (9.5)
Serious TEAE	12 (3.6)	15 (12.5)	14 (4.2)	13 (11.2)
TEAE leading to study drug discontinuation	8 (2.4)	9 (7.5)	8 (2.4)	8 (6.9)
TEAE leading to death by study Day 28	3 (0.9)	5 (4.2)	2 (0.6)	5 (4.3)
TEAE leading to death (over entire study duration)	5 (1.5)*	5 (4.2)	2 (0.6)	6 (5.2)†

TEAE=treatment-emergent adverse event.
*Two patients in the lefamulin group had a TEAE leading to death after study Day 28: one on study Day 32 and one on study Day 57.
†One patient in the moxifloxacin group had a TEAE leading to death on study Day 48.

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665. *In vitro* Activity of Omadacycline Against Recent (2018) Bacterial Pathogens from the United States and Europe Obtained from Skin and Skin Structure, Respiratory, and Urinary Tract Infections

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Background. Omadacycline (OMC) was FDA approved to treat acute bacterial skin and skin structure infection (ABSSSI) and community-acquired bacterial pneumonia (CABP) for indicated organisms in 2018. Phase 2 OMC clinical trials for uncomplicated urinary tract infection (uUTI; NCT03425396) and acute pyelonephritis (NCT03757234) are ongoing. OMC is active against bacterial isolates expressing common tetracycline, penicillin, fluoroquinolone, and macrolide resistance mechanisms.

Methods. Isolates (14,000) were collected in 2018 from 31 medical centers located in the United States and 38 medical centers in Europe, including 3,458 staphylococci, 1,551 streptococci, 746 enterococci, 574 *Haemophilus* spp., and 5,690 *Enterobacterales* isolates. One isolate per patient infection episode was tested. Identifications were confirmed by MALDI-TOF MS and susceptibility testing was performed using CLSI broth microdilution methods.

Results. OMC ($MIC_{50/90}$, 0.12/0.25 mg/L) was highly active against *S. aureus* isolates from skin and skin structure infection (SSSI; 99.3% susceptible [S]) including MRSA (97.7%S) and MSSA (99.9%S) (table). Similarly, OMC demonstrated potent activity against *S. aureus* isolates from respiratory tract infection (RTI; $MIC_{50/90}$, 0.12/0.25 mg/L) including MSSA (98.2%S). All *S. lugdunensis* isolates from SSSI were S (100.0%) to OMC. All *Streptococcus* anginosus group (100.0%) and 97.6% of *S. pyogenes* isolates from SSSI were S to OMC as were 98.0% of *S. pneumoniae* from RTI. No streptococci were resistant (R) to OMC. OMC ($MIC_{50/90}$ 0.12/0.25 mg/L) had potent activity against *E. faecalis* isolates from SSSI (99.0%S). OMC S against *E. cloacae* and *K. pneumoniae* isolates from SSSI was 92.1% S and 89.4% S, respectively. Similarly, 86.2% of *K. pneumoniae* isolates from RTI were S to OMC. Susceptibility of *H. influenzae* isolates from RTI to OMC was 99.8%S (no isolates were R). ≥90.0% of *E. coli* ($MIC_{50/90}$, 1/2 mg/L) and *K. pneumoniae* ($MIC_{50/90}$, 2/4 mg/L) UTI isolates were inhibited by ≤4 mg/L of OMC.

Conclusion. OMC was highly active against bacterial pathogens associated with ABSSSI, CABP, and UTI including staphylococci (97.7%-100.0%S), streptococci (97.6%-100.0%S), *E. faecalis* (99.0%S). *E. cloacae* (92.1%S), *K. pneumoniae* (86.2%-89.4%S), and *E. coli.*

Organism (no. of isolates)	Infection type	MIC_{50}	MIC_{90}	%S	%R	FDA Breakpoint Applied
S. aureus (1,475)	SSSI	0.12	0.25	99.3	0.2	ABSSSI
MRSA (432)	SSSI	0.12	0.25	97.7	0.7	ABSSSI
MSSA (1,043)	SSSI	0.12	0.25	99.9	0.0	ABSSSI
S. aureus (699)	RTI	0.12	0.25	95.3	2.9	CABP[a]
MRSA (248)	RTI	0.12	0.5	89.9	7.3	CABP[a]
MSSA (451)	RTI	0.12	0.25	98.2	0.4	CABP
S. lugdunensis (29)	SSSI	0.06	0.06	100.0	0.0	ABSSSI
S. anginosus gr (13)	SSSI	0.06	0.12	100.0	0.0	ABSSSI
S. pyogenes (125)	SSSI	0.06	0.12	97.6	0.0	ABSSSI
S. pneumoniae (794)	RTI	0.06	0.12	98.0	0.0	CABP
E. faecalis (101)	SSSI	0.12	0.25	99.0	0.0	ABSSSI
H. influenzae (512)	RTI	0.5	1	99.8	0.0	CABP
E. cloacae (89)	SSSI	2	4	92.1	3.4	ABSSSI
K. pneumoniae (141)	SSSI	2	8	89.4	5.7	ABSSSI
K. pneumoniae (290)	RTI	2	8	86.2	7.9	CABP
K. pneumoniae (275)	UTI	2	4	--	--	
E. coli (865)	UTI	1	2	--	--	

[a] Omadacycline CABP breakpoint for MSSA applied for comparison purposes.

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666. Efficacy and Safety of Cefiderocol According to Renal Impairment in Patients With Complicated Urinary Tract Infection (cUTI) in a Phase 2 Study

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Background. Cefiderocol, a novel siderophore cephalosporin with broad activity against Gram-negative bacteria, requires dose adjustment in patients with renal impairment or augmented renal clearance, similarly to other β-lactams. The efficacy and safety of cefiderocol were assessed according to degree of renal impairment as part of a pivotal study vs. imipenem–cilastatin (IPM/CS) in patients with cUTI (NCT02321800).

Methods. A total of 448 randomized adults with cUTI received cefiderocol (2 g) or IPM/CS (1 g / 1 g), IV, q8h, for 7–14 days (safety population), with 371 patients in the microbiological intent-to-treat (Micro-ITT) population. Dose adjustments were made based on body weight (to enable IPM/CS blinding) and creatinine clearance (CrCL). The composite (clinical and microbiological) outcome at a test of cure (TOC; 7 days after treatment cessation) was analyzed by CrCL subgroup. Adverse events (AEs) according to renal subgroup were monitored throughout the study.

Results. A treatment difference in the composite outcome at TOC in favor of cefiderocol vs. IPM/CS was observed across renal subgroups (table), with greater differences in moderate and severe groups, consistent with that observed in the overall population (n = 371; 18.0%, 95% confidence interval: 7.5; 28.5). The incidence of AEs in the cefiderocol group was comparable across all renal subgroups. Conversely, AE incidence increased with the degree of impairment in the IPM/CS group (table).

Conclusion. In contrast to IPM/CS, the efficacy of cefiderocol was maintained across all renal function subgroups with no increase in the rate of AEs. These findings underscore the efficacy and safety of cefiderocol in patients with renal impairment and support the adequacy of the dose adjustment.

Table.

	Renal subgroup, CrCL mL/min			
	>80 (Normal)	>50–80 (Mild)	30–50 (Moderate)	<30 (Severe)
Composite outcome at TOC, Micro-ITT population, n/N (%)				
Cefiderocol (n=250)	97/124 (78.2)	49/78 (62.8)	30/41 (73.2)	5/7 (71.4)
IPM/CS (n=119)	31/51 (60.8)	22/41 (53.7)	11/23 (47.8)	1/4 (25.0)
Difference (95% CI)	17.4 (2.2; 32.7)	9.2 (–9.5; 27.8)	25.3 (0.8; 49.9)	46.4 (na)
AEs, safety population, n/N (%)				
Cefiderocol (n=298)	62/152 (40.8)	35/89 (39.3)	22/49 (44.9)	3/8 (37.5)
IPM/CS (n=148)	26/63 (41.3)	27/50 (54.0)	18/28 (64.3)	5/7 (71.4)
na: not available				

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

667. Preclinical Pharmacokinetic and Pharmacodynamic Characterization of EDP-938, a Novel and Potent NonFusion Replication Inhibitor of Respiratory Syncytial Virus

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