and CC 25.5 kg/m^2 (22.1 – 28.2); p=.029. A BMI cutpoint was not identified in CART analysis.

Conclusion. There is a relationship between increased BMI and 90-day CF in patients treated with dalbavancin. A higher BMI was found among those with with CF. Future studies are necessary to determine if a BMI based weight adjustment is necessary.

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1075. *In vitro* Activity of Gepotidacin against *Escherichia coli* Causing Urinary Tract Infections in the United States, Including Molecularly Characterized Fluoroquinolone Resistant Subsets

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Background. Gepotidacin (GEP) is a novel bacterial type II topoisomerase inhibitor in Phase 3 clinical trials for the treatment of gonorrhea and uncomplicated urinary tract infections (UTI). This study characterized fluoroquinolone (FQ)-not susceptible (not S) *E. coli* causing UTI in U.S. patients and evaluated the *in vitro* activity of GEP and comparators against various drug resistance (R) subsets.

Methods. 1,035 *E. coli* collected from 38 U.S. sites were included as part of the GEP Global UTI Surveillance Program (2019). Isolates were tested for susceptibility by broth microdilution. *E. coli* with MICs ≥0.5 mg/L for ciprofloxacin (not S) and/or ≥1 mg/L for levofloxacin (not S) were selected for screening of FQ-R mechanisms, and subjected to genome sequencing, followed by screening of FQ-R genes and QRDR mutations in GyrA, GyrB, ParC and ParE.

Results. A total of 26.8% (277/1,035) *E. coli* met the screening criteria for FQ-not S (Table). Overall, GEP had MIC_{90} values of 2 mg/L and 4 mg/L against FQ-S and FQ-not S isolates, respectively. Nitrofurantoin had activity against the FQ-S and FQ-not S subsets (98.8% and 94.2%S, respectively), whereas amoxicillin-clavulanate (86.5% and 59.6%S) and trimethoprim-sulfamethoxazole (75.8% and 37.0%S) had limited activity. Most FQ-not S isolates (52.7%; 146/277) had double mutations in GyrA and ParC, followed by those isolates (20.6%; 57/277) with double mutations in GyrA and single mutations in ParC and ParE. The third most common genotype was represented by isolates (14.8%;41/277) with double mutations in GyrA and a single mutation in ParC. GEP had MIC_{50} values of 1 mg/L or 2 mg/L and MIC_{90} values of 2 mg/L or 4 mg/L when tested against isolates with various combinations of QRDR mutations. 4.3% (12/277) of FQ-not S *E. coli* carried *qnrB* (6) or *qnrS* (6), and GEP ($MIC_{50/90}$, 8/16 mg/L) had MICs of 0.5–32 mg/L against this subset.

Conclusion. GEP demonstrated potent activity against FQ-S and FQ-not S *E. coli* causing UTI in the U.S. In addition, GEP MIC did not seem to be affected by any combinations of FQ-R genes and QRDR mutations tested, except against the rare presence of *qnrB/S* genes. These data support the clinical development of GEP as a treatment option for UTI caused by FQ-S and FQ-not S *E. coli* isolates.

Table

Phenotype/genotype			No	MIC_{50}/MIC_{90} in mg/L (% susceptible by CLSI M100 criteria)				
				Gepotidacin	A/C	CIP	NIT	TMP/SMX
FQ-S			758	2/2 (-)	4/16 (86.5)	0.008/0.12 (100.0)	16/32 (98.8)	≤0.12/>16 (75.8)
FQ-not susceptible			277	2/4 (-)	8/16 (59.6)	>4/>4 (0.4)	16/32 (94.2)	>16/>16 (37.0)
GyrA	ParC	ParE						
Single[a]	WT	WT	8	2/- (-)	8/- (62.5)	0.5/- (12.5)	16/- (87.5)	>16/- (25.0)
Single[a]	Single[b]	WT	18	1/2 (-)	8/16 (72.2)	0.5/>4 (0.0)	16/32 (100.0)	>16/>16 (22.2)
Double[c]	Single[c]	WT	41	1/4 (-)	8/32 (63.4)	>4/>4 (0.0)	16/32 (90.2)	>16/>16 (19.5)
Double[d]	Single[d]	Single[d]	57	1/2 (-)	8/16 (75.4)	>4/>4 (0.0)	16/32 (100.0)	>16/>16 (35.7)
Double[e]	Double[e]	WT	146	2/4 (-)	8/16 (51.4)	>4/>4 (0.0)	16/32 (93.8)	>16/>16 (45.2)
Qnr[f]			12	8/16 (-)	8/32 (58.3)	>4/>4 (0.0)	16/16 (91.7)	>16/>16 (25.0)

WT, wildtype; A/C, amoxicillin-clavulanate (2:1 ratio); CIP, ciprofloxacin; NIT, nitrofurantoin; TMP/SMX, trimethoprim-sulfamethoxazole; "-" CLSI breakpoint not available; GyrA, DNA gyrase subunit A; GyrB, DNA gyrase subunit B; ParC, DNA topoisomerase IV subunit A; ParE, DNA topoisomerase IV subunit B. Mutations in GyrB were not detected. Most prevalent combinations of QRDR mutations are shown; other genotypes were as follows: 4 isolates with wildtype sequences for all four genes, 1 isolate with double mutations in GyrA, and 2 isolates with double mutations in GyrA and ParC, plus a single alteration in ParE.

[a] S83L in GyrA.

[b] S80I, S80R or E84G.

[c] S83L/D87N or S83L/D87Y in GyrA and S80I in ParC.

[d] S83L in GyrA, S80I in ParC and L416F in ParE.

[e] S83L/D87N in GyrA and S80I/E84A, S80I/E84G, S80I/E84K or S80I/E84V in ParC.

[f] Represents the following genes *qnrB4* (1), *qnrB6* (2), *qnrB19* (3) and *qnrS1* (6) with or without mutations in QRDR.

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