1695. Tebipenem: An Oral Carbapenem with activity against Multi-drug Resistant Urinary Tract Infection isolates of *Escherichia coli* collected from US Medical Centers during 2019

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Session: P-73. UTIs

Background. *Escherichi coli* (EC) is a predominant urinary tract infection (UTI) pathogen where increasing prevalence of extended spectrum-β-lactamase (ESBL) continues to compromise the use of currently available oral antibiotics. ESBL-producing EC exhibit coresistance to the fluoroquinolones (FQs) and trimethoprim-sulfamethoxazole (TMP-SMX) making treatment of UTIs outside the hospital difficult and intravenous (IV) agents are often needed. Tebipenem (TBP) is an oral carbapenem with similar activity to IV carbapenems in clinical development for treating complicated UTIs (cUTI). This study assessed the activity of TBP against EC collected from UTIs in the US including isolates R to oral agents.

Methods. 1133 EC from UTIs in the 2019 STEWARD Surveillance Program were tested for susceptibility to TBP and comparators. Isolates were collected from medical centers geographically distributed across the US Census regions, centrally tested, and susceptibility (S) interpreted according to CLSI criteria.

Results. Overall prevalence of ESBL EC from UTI was 15.4% and R to oral cefuroxime, levofloxacin and TMP-SMX were: 15.6%, 23.9% and 33.5%, respectively. In contrast, low R was observed for the IV carbapenems. All EC were inhibited by TBP at ≤0.5 µg/mL and the MIC_{90} was 0.015 µg/mL compared with MIC_{90}s of 0.03 µg/mL for meropenem (MER) and ertapenem (ETP). Using a tentative PK/PD cut off of 0.12 µg/mL 99.7% of EC were inhibited by TBP. The MIC_{90}s for LEV and TMP-SMX were 32 and >16 µg/mL, respectively, against ESBL EC with R rates at ≥66.3%. MIC_{90}s of 0.03, 0.03 and 0.12 µg/mL, respectively, were noted for TBP, MER (100% S) and ETP (99.6% S). TBP was active against LEV-R, TMP-SMX-R and MDR (≥3 classes) EC with MIC_{90}s of 0.03 µg/mL.

Conclusion. R to oral agents remains high, raising concerns on empiric use. Carbapenems remain active against EC due to their stability to ESBLs and are not compromised by co-resistance. TBP is an oral carbapenem with similar activity to IV carbapenems based on comparison of MIC_{90} values. Although no breakpoints are available, ≥99.7% of EC were inhibited by TBP at ≤0.12 µg/mL highlighting potential as a new oral option for cUTIs in an era of ESBL mediated co-resistance to the FQs and TMP-SMX.

Disclosures. Ian A. Critchley, PhD, Spero Therapeutics (Employee, Shareholder) Nicole S. Cotroneo, BS, Spero Therapeutics (Employee, Shareholder) Michael J. Pucci, PhD, Spero Therapeutics (Employee)Spero Therapeutics (Employee) Akash Jain, PhD, Spero Therapeutics (Employee) Rodrigo E. Mendes, PhD, A. Menarini Industrie Farmaceutiche Riunite S.R.L. (Research Grant or Support)Allergan (Research Grant or Support)Allergan (Research Grant or Support)Basilea Pharmaceutica International, Ltd (Research Grant or Support)Cipla Ltd. (Research Grant or Support)Department of Health and Human Services (Research Grant or Support)GlaxoSmithKline (Research Grant or Support)Melinta Therapeutics, Inc. (Research Grant or Support)Merck (Research Grant or Support)Merck (Research Grant or Support)Pfizer (Research Grant or Support)

1696. The Black Box of Using Health Claims-Based Analyses to Estimate UTI Prevalence in Community-Dwelling Women

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Session: P-73. UTIs

Background. Urinary tract infections (UTIs) are common in women but most epidemiology studies occurred in specialized settings (university health clinics) or used outdated methods (random digit dialing). Currently, women receive UTI care in systems with electronic health records (EHR), thus documenting care of a wider female demographic in real-world settings. We estimated the prevalence of acute, uncomplicated UTIs in community-dwelling women in a health claims database using various operational definitions of UTI.

Methods. We conducted a retrospective analysis of claims data from the OptumLabs® Data Warehouse (OLDW), a de-identified claims and clinical information repository for privately insured and Medicare Advantage enrollees in a large, private US health plan. Non-pregnant female patients ≥ 15 years of age with two years of continuous enrollment between 2007-2015 and a visit encounter in an outpatient office, urgent care, or emergency department were included. Women with lower urinary tract disease/abnormalities, neurological disease, urological treatment, procedures or urinary catheter use, cancer or HIV treatment were excluded. Decision rules for identifying UTIs were derived using one or more combinations of: relevant ICD-9 codes, UTI symptom diagnosis codes, positive urine test results, and/or antibiotic prescription recorded in the EHR and claims. Prevalence rates were calculated for each decision rule.

Results. Of the 7,337,700 females in the claims database, 947,041 (12.97%) had an index UTI diagnosis or symptoms and met eligibility criteria. The table below illustrates prevalence rates according to each decision rule. As shown, applying decision rules based on common UTI definitions resulted in large differences in prevalence rates.

Table

Decision Rule	Rate Estimate Per 100,000
ICD-9 Code for UTI	5,279
EHR symptoms for UTI	9,775
ICD-9 Code for UTI or EHR symptoms	12,907
... and antibiotic prescription	4,928
... and positive urine dipstick/urinalysis	319
... and positive urine culture (> 100,000 CFU/ml)	17
... and EITHER positive urine dipstick/urinalysis or positive urine culture	323
... and antibiotic prescription	146
... and EITHER negative urine dipstick/urinalysis or negative urine culture	737
... and antibiotic prescription	236
... and NO urine dipstick/urinalysis or urine culture result available	11,687
... and antibiotic prescription	4,446

Conclusion. Using common definitions for UTI to analyze claims data from an insurer of large proportions of the US, we obtained significantly different prevalence rates. This study highlights major limitations in using EHR and claims data for UTI quality initiatives such as tracking of practices associated with antimicrobial stewardship and lends credibility to proposals to track these infections as a reportable disease.

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

1697. The Burden Of Multidrug-Resistant Urinary Tract Infections

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Session: P-73. UTIs

Background. Urinary tract infections (UTIs) are the most common reason for consultation and for antibiotic use. Many factors interfere and increase the risk for antimicrobial resistance. We aimed to study the clinical, laboratory and evolutionary particularities associated with multidrug-resistant (MDR) UTIs.

Methods. We conducted a retrospective study including all patients hospitalized for UTIs in the infectious diseases department between 2011 and 2018.

Results. A total of 867 cases of UTIs were included in the study, among which 407 cases (46.9%) were MDR. There were 306 males (35.3%). The mean age was 53±21 years. Overall, MRD UTIs were significantly associated to male gender (39.1% vs 32%; p=0.02). Patients aged ≥65 years were significantly more affected with MRD UTIs (54.5% vs 36.5%; p< 0.001). Previous medical history of diabetes (38.1% vs 24.6%; p< 0.001), antibiotic consumption (30.7% vs 13%; p< 0.001) and surgical intervention of the urinary tract (13% vs 5.4%; p< 0.001) were significantly associated with MDR UTIs. The mean delay to hospitalization was significantly longer among MDR UTIs cases (5[3-10 days] vs 3[2-7 days]; p< 0.001). In total, MDR UTIs were more frequently documented to *Klebsiella pneumoniae* (19.4% vs 12%; p=0.002). Comparison of the disease evolution showed that MRD UTIs were significantly associated with complications (9.1% vs 5.2%; p=0.02), recurrence (4.4% vs 1.5%; p=0.01) and death (2.2% vs 0.4%; p=0.02). As to laboratory investigations and antibiotic duration, no significant difference was noted.

Conclusion. Our study showed that MDR UTIs were associated with not only complications, but also with a poor prognosis. The continuous surveillance for antimicrobial resistance and the rational use of antibiotics are crucial in order to improve the prognosis.

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

1698. Trends in antimicrobial resistance among outpatient urine *E. coli* isolates in US females ≥12 years of age: A multicenter evaluation from 2011 to 2019

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Session: P-73. UTIs

Background. *E. coli* is the predominant uropathogen isolated in uncomplicated urinary tract infections (UTI). Surveillance data suggest increasing antimicrobial resistance (AMR), although recent data from the outpatient setting are limited. Treatment is typically empiric and should be guided by local resistance rates; however, this is challenging in the absence of routine culture and assessment of regional AMR. We characterized AMR trends for *E. coli* isolated from females with outpatient UTI in the US, from 2011 to 2019.

Methods. A retrospective multicenter cohort study of antimicrobial susceptibility using data from the BD Insights Research Database (Franklin Lakes, NJ) was conducted. The first *E. coli* urine culture isolates representing each distinct susceptibility pattern within 30 days of index urine from 2011–2019 were included from females ≥ 12 years old. *E. coli* isolates were identified as not-susceptible (NS) if intermediate or resistant to trimethoprim-sulfamethoxazole (TMP-SMX NS), fluoroquinolone (FQ NS), nitrofurantoin (NFT NS), ESBL+ (by commercial panels or intermediate/resistant to ceftriaxone, cefotaxime, ceftazidime or cefepime), and multi-drug resistant (MDR), defined as NS to ≥ 2 or ≥ 3 of FQ, TMP-SMX, NFT or ESBL+. Descriptive analyses characterized AMR (%) over time and generalized estimating equations were used to statistically assess AMR trends over time.

Results. A total of 1,513,882 *E. coli* isolates were tested at 106 to 295 US centers between 2011 and 2019. Over the study period, AMR remained persistently high (> 20%) for FQ and TMP-SMX and increased for the MDR (≥ 3 drugs) phenotype (from 3.1% to 4.0%) (Table). Prevalence of the ESBL+ phenotype increased year-on-year (from 4.1% to 7.3%). Modeling confirmed a significant increasing trend for the ESBL+ (7.7%/year) and MDR (≥ 3 drugs) phenotypes (2.7%/year) (P< 0.001), with decreasing or no trend change for NFT NS and other AMR phenotypes (Table).

Table. Descriptive Statistics and Model-estimated Annual Change of AMR (count and % not-susceptible out of isolates tested) in E. coli among US Females (≥12 years of age) with Outpatient UTI

Year	Total *E. coli* Tested, N	Phenotype category, % (n)					
		ESBL+	NFT NS	FQ NS	TMP-SMX NS	≥2 Drug classes	≥3 Drug classes
Overall	1,513,882	6.4 (96,306)	3.8 (56,954)	21.1 (319,354)	25.4 (384,304)	14.4 (217,329)	3.8 (57,673)
2011	67,415	4.1 (2,796)	4.0 (2,688)	21.2 (14,228)	25.2 (16,981)	14.3 (9,649)	3.1 (2,108)
2012	78,257	4.3 (3,336)	5.1 (3,993)	21.9 (17,150)	25.9 (20,249)	15.0 (11,771)	3.4 (2,634)
2013	96,431	4.6 (4,428)	5.2 (5,047)	21.8 (21,004)	26.1 (25,159)	15.1 (14,602)	3.5 (3,374)
2014	124,424	5.9 (7,304)	5.3 (6,541)	21.9 (27,297)	26.2 (32,604)	15.3 (19,073)	3.9 (4,796)
2015	167,424	6.3 (10,583)	4.0 (6,636)	21.8 (36,527)	25.8 (43,212)	14.9 (25,011)	3.9 (6,606)
2016	211,065	6.6 (13,984)	3.1 (6,601)	21.9 (46,278)	25.3 (53,481)	14.6 (30,718)	3.9 (8,209)
2017	241,545	6.9 (16,668)	3.0 (7,170)	20.7 (49,998)	25.0 (60,334)	13.9 (33,529)	3.8 (9,139)
2018	259,797	6.8 (17,611)	3.4 (8,825)	20.2 (52,408)	25.1 (65,095)	13.7 (35,648)	3.8 (9,993)
2019	267,524	7.3 (19,576)	3.5 (9,453)	20.3 (54,359)	25.1 (67,189)	14.0 (37,328)	4.0 (10,184)
Overall Model Estimate		6.8 (6.7–6.8)	4.0 (4.0–4.1)	23.0 (22.9–23.2)	26.0 (25.9–26.1)	15.7 (15.5–15.8)	4.2 (4.1–4.3)
***Trend*: average yearly change in NS, % (95% CI)**		7.7% (7.2% to 8.2%; p<.0001)	-6.1% (-6.5% to 5.6%; p<.0001)	-0.6% (-0.8% to 0.4%; p<.0001)	0.0% (-0.2% to 0.1%; p=.6737)	-0.8% (-1.1% to 0.6%; p<.0001)	2.7% (2.2% to 3.2%; p<.0001)

Models were adjusted by hospital characteristics (bed size, urban/rural status, and teaching status)

≥ 2 Drug NS, not-susceptible to ≥2 drug classes; ≥3 Drug NS, not-susceptible to ≥ 3 drug classes; AMR, antimicrobial resistance; CI, confidence interval; ESBL+, extended spectrum β-lactamase positive; FQ, fluoroquinolone; NFT, nitrofurantoin; NS, not-susceptible; TMP-SMX, trimethoprim-sulfamethoxazole; US, United States; UTI, urinary tract infection

Conclusion. Characterization of AMR trends for *E. coli* over the last decade, in outpatient *E. coli* isolates in US females, shows persistently high AMR to FQ and TMP-SMX, and increasing AMR trends for the ESBL+ and MDR (≥ 3 drugs) phenotypes.

Disclosures. Vikas Gupta, PharmD, BCPS, Becton, Dickinson and Company (Employee, Shareholder)GlaxoSmithKline plc. (Other Financial or Material Support, Funding) Aruni Mulgirigama, MBBS, GlaxoSmithKline plc. (Employee, Shareholder) Ashish V. Joshi, PhD, GlaxoSmithKline plc. (Employee, Shareholder) Nicole Scangarella-Oman, MS, GlaxoSmithKline plc. (Employee, Shareholder) Kalvin Yu, MD, Becton, Dickinson and Company (Employee)GlaxoSmithKline plc. (Other Financial or Material Support, Funding) Gang Ye, PhD, Becton, Dickinson and Company (Employee)GlaxoSmithKline plc. (Other Financial or Material Support, Funding) Fanny S. Mitrani-Gold, MPH, GlaxoSmithKline plc. (Employee, Shareholder)

1699. Variation of antimicrobial resistance by age groups for outpatient UTI isolates in US females: A multicenter evaluation from 2011 to 2019

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Session: P-73. UTIs

Background. An estimated 12% of women experience ≥ 1 episode of urinary tract infection (UTI) annually. Incidence is bimodal, with peaks occurring in young, sexually active women (18–24 years) and in post-menopausal women. Previous studies suggest the prevalence of antimicrobial resistance (AMR) in UTI is rising; however recent AMR data for community-acquired UTI are lacking. We estimated the prevalence of AMR among US females with outpatient UTI in 2011–2019, stratified by age.

Methods. A retrospective, multicenter, cohort study of AMR among non-duplicate urine isolates in US females (≥ 12 years of age) from 296 institutions from 2011–2019 (BD Insights Research Database, Franklin Lakes, NJ). Phenotypes examined for *Enterobacterales* (ENT) were: extended spectrum β-lactamase positive (ESBL+; determined by commercial panels or intermediate/resistant to ceftriaxone, cefotaxime, ceftazidime or cefepime); nitrofurantoin (NFT) not-susceptible (NS); fluoroquinolone (FQ) NS; trimethoprim-sulfamethoxazole (TMP-SMX) NS; and NS to ≥ 2 or ≥ 3 drug classes (including ESBL+). Gram-positive phenotypes were, methicillin resistant *S. aureus and S. saprophyticus* and vancomycin-resistant *Enterococcus*. Isolates were stratified by patient age (≥ 12 to < 18, ≥ 18 to < 55, ≥ 55 to < 65, ≥ 65 to < 75, ≥ 75 years). Chi-square tests were used to evaluate AMR difference between groups.

Results. In total, urine isolates were collected from 106 to 296 (2011–2019) US sites. Overall, the prevalence of antimicrobial NS increased with age for all *E. coli* phenotypes (all P< 0.001; Table 1), and for non-*E. coli* ENT (all P< 0.001), except NFT NS, which decreased from 70.6% to 59.7% (P=0.002; Table 2). The greatest difference between age groups in prevalence of resistance was observed for FQ NS *E.coli*: 5.8% (≥ 12 to < 18 years) vs 34.5% (≥ 75 years). For the multi-drug resistant *E. coli* phenotypes, resistance increased with age, ranging from 4.8–22.4% and 0.9–6.5% for ≥ 2 and ≥ 3 drug NS, respectively. Overall, the prevalence of resistance for Gram-positive phenotypes increased with age (all P< 0.001; Table 3).

Table 1. Prevalence of antimicrobial resistance among E. coli isolates in US females with outpatient UTI by age group.

E. coli	Phenotype Category																	
	ESBL+			NFT NS			FQ NS			TMP/SMX NS			≥2 Drug NS			≥3 Drug NS		
Age group, years	*tested*	*NS*	*%NS*	*tested*	*NS*	*%NS*	*tested*	*NS*	*%NS*	*tested*	*NS*	*%NS*	*tested*	*NS*	*%NS*	*tested*	*NS*	*%NS*
≥12 to <18	48,976	1,142	2.3	48,976	1,071	2.2	48,976	2,859	5.8	48,976	9,519	19.4	48,976	2,336	4.8	48,976	425	0.9
≥18 to <55	700,604	30,256	4.3	700,604	20,776	3.0	700,604	91,891	13.1	700,604	174,411	24.9	700,604	66,580	9.5	700,604	14,622	2.1
≥55 to <65	186,708	13,047	7.0	186,708	6,722	3.6	186,708	42,076	22.5	186,708	47,318	25.3	186,708	28,758	15.4	186,708	7,862	4.2
≥65 to <75	222,516	17,866	8.0	222,516	9,394	4.2	222,516	60,189	27.0	222,516	57,271	25.7	222,516	40,207	18.1	222,516	11,522	5.2
≥75	355,078	33,995	9.6	355,078	18,991	5.3	355,078	122,339	34.5	355,078	95,785	27.0	355,078	79,448	22.4	355,078	23,242	6.5

≥2 Drug NS, not-susceptible to ≥2 drug classes; ≥3 Drug NS, not-susceptible to ≥3 drug classes; ESBL+, extended spectrum β-lactamase positive; FQ, fluoroquinolone; NFT, nitrofurantoin; NS, not-susceptible; TMP/SMX, trimethoprim-sulfamethoxazole; US, United States; UTI, urinary tract infection.

Table 2. Prevalence of antimicrobial resistance among non-E. coli ENT isolates in US females with outpatient UTI by age group.

Non-*E. coli* ENT*	Phenotype Category											
	ESBL+: KP/KPO and PM			NFT NS			FQ NS			TMP/SMX NS		
Age group, years	*tested*	*NS*	*%NS*	*tested*	*NS*	*%NS*	*tested*	*NS*	*%NS*	*tested*	*NS*	*%NS*
≥12 to <18	5,511	127	2.3	7,101	5,013	70.6	7,101	114	1.6	7,101	504	7.1
≥18 to <55	105,100	3,523	3.4	130,562	88,383	67.7	130,562	5,699	4.4	130,562	11,077	8.5
≥55 to <65	48,774	2,628	5.4	59,979	38,051	63.4	59,979	5,880	9.8	59,979	8,070	13.5
≥65 to <75	71,625	3,726	5.2	88,161	53,637	60.8	88,161	9,319	10.6	88,161	12,104	13.7
≥75	142,706	7,817	5.5	178,185	106,324	59.7	178,185	28,181	15.8	178,185	28,466	16.0

*Non-*E. coli Enterobacterales* isolates included: *K. pneumoniae*, *K. oxytoca*, *E. cloacae*, *E. aerogenes*, *P. mirabilis*, *M. morganii*, *C. freundii*, *and S. marcescens*

ENT, *Enterobacterales*; ESBL+, extended spectrum β-lactamase positive; FQ, fluoroquinolone; KP/KPO, *K. pneumoniae/oxytoca*; NFT, nitrofurantoin; NS, not-susceptible; PM, *P. mirabilis*; TMP/SMX, trimethoprim-sulfamethoxazole; US, United States; UTI, urinary tract infection.

Table 3. Prevalence of antimicrobial resistance among Gram-positive isolates in US females with outpatient UTI by age group.

Age group, years	Phenotype Category								
	S. aureus			*S. saprophyticus*			*Enterococcus*		
	tested	*Ox/Meth resistant*	*MRSA, %*	*tested*	*Ox/Meth-resistant*	*Ox/Meth-resistant, %*	*tested*	*Vanco resistant*	*VRE, %*
≥12 to <18	1,221	200	16.4	2,654	1,457	54.9	2,082	11	0.5
≥18 to <55	14,763	4,048	27.4	15,688	8,684	55.4	37,446	1,260	3.4
≥55 to <65	2,919	1,231	42.2	553	301	54.4	15,675	1,092	7.0
≥65 to <75	3,508	1,694	48.3	178	102	57.3	24,383	2,032	8.3
≥75	7,818	4,616	59.0	81	51	63.0	53,179	4,836	9.1

MRSA, methicillin-resistant *S. aureus*; OX/Meth-R, oxacillin/methicillin-resistant; UTI, urinary tract infection; Vanco, vancomycin; VRE, vancomycin-resistant *Enterococcus*.

Conclusion. The prevalence of AMR in *E. coli* and non-*E. coli* ENT increased with age among US females presenting for care in the outpatient setting overall. A similar trend increase by age is also seen in Gram-positive isolates.

Disclosures. Vikas Gupta, PharmD, BCPS, Becton, Dickinson and Company (Employee, Shareholder)GlaxoSmithKline plc. (Other Financial or Material Support, Funding) Aruni Mulgirigama, MBBS, GlaxoSmithKline plc. (Employee, Shareholder) Ashish V. Joshi, PhD, GlaxoSmithKline plc. (Employee, Shareholder) Nicole Scangarella-Oman, MS, GlaxoSmithKline plc. (Employee, Shareholder) Kalvin Yu, MD, Becton, Dickinson and Company (Employee)GlaxoSmithKline plc. (Other Financial or Material Support, Funding) Gang Ye, PhD, Becton, Dickinson and Company (Employee)GlaxoSmithKline plc. (Other Financial or Material Support, Funding) Fanny S. Mitrani-Gold, MPH, GlaxoSmithKline plc. (Employee, Shareholder)

1700. What Is Specific With Bacterial Escherichia Coli Urinary Tract Infection

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Session: P-73. UTIs

Background. Bacterial urinary tract infections continue to be a major health problem, responsible for a significant morbidity and mortality. Its prognosis is more severe than non-bacterial forms. The aim of this work was to study the clinical and evolutionary features of bacterial urinary tract infections caused by *Escherichia coli* (*E.coli*).

Methods. We conducted a retrospective study including all patients hospitalized in infectious diseases department for urinary tract infection (UTI) caused by *E.coli* between 2010 and 2017.

Results. During the study period, we enrolled 613 cases of UTI caused by *E.coli*, among whom 75 cases (12.2%) were bacterial. There were 47 females (62.7%). The mean age was 59 ±17 years. Thirty-three patients were aged ≥ 65 years (44%). Diabetes was noted in 38 cases (50.7%) and renal lithiasis in 14 cases (18.7%). A history of UTI was reported in 13 cases (17.3%). The most common clinical presentation was acute pyelonephritis (59 cases; 78.7%) and followed by prostatitis (8 cases; 10.6%). Renal