1197. Frequency of Antimicrobial Resistance in Shiga Toxin-Producing *Escherichia coli* (STEC) and Non-Typhoidal *Salmonella* (NTS) Clinical Infections and Association with Epidemiological Factors

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Session: 146. Enteric Infections and Diagnostics
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Background. STEC and NTS are leading causes of foodborne infections in the US. Monitoring resistance in these pathogens is essential to understand the distribution of resistance profiles and because of the high likelihood of horizontal transfer of resistance genes to other pathogens. Data involving resistance in clinical STEC and NTS isolates from Michigan is lacking.

Methods. Clinical STEC (n = 353) and NTS (n = 148) isolates from the MDHHS (2010–2014) were examined for resistance using disk diffusion, E-test or broth microdilution. Case information and epidemiological data for STEC isolates was extracted and associations with resistant infections were determined using chi square tests in SAS 9.3 and EpiInfo™ 7.

Results. Overall, 31 (8.8%, n = 353) STEC isolates were resistant to at least one antibiotic; high frequencies of resistance were observed for ampicillin (7.4%) and trimethoprim-sulfamethoxazole (4.0%). Resistance to ciprofloxacin (0.28%) and all three drug classes (0.28%) was less common. Preliminary results indicate that O157 resistance to ampicillin (4.8%) and trimethoprim-sulfamethoxazole (3.4%) was higher in Michigan compared with national frequencies (ampicilli$n$ = 2.7%, trimethoprim-sulfamethoxazole= 1.5%). Higher resistance frequencies were also observed in counties with high (11.3%) vs. low (7.7%) antibiotic prescription rates. For NTS, 23 (15.5%) isolates were resistant to ≥1 antibiotic. Resistance varied by serotype with high frequencies in Typhimurium (20%, n = 20), Newport (17.6%, n = 17) and Enteritidis (4.8%, n = 42); 11 (7.4%) NTS isolates were resistant to ≥3 antimicrobial classes.

Conclusion. Continuous monitoring of resistance in clinical STEC and NTS is warranted due to their importance as food pathogens. The identification of risk factors for resistance is crucial to develop alternative prevention practices to reduce the health burden of resistant infections in Michigan, which is not part of the FoodNet surveillance network.

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

1198. Antimicrobial Activity of Ceftolozane–Tazobactam Tested against Contemporary (2012–2016) *Enterobacteriaceae* and *Pseudomonas aeruginosa* from ICU vs. non-ICU Isolates Collected in US Medical Centers

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Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing
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Background. Ceftolozane-tazobactam (C-T) is a combination of a novel antipseudomonal cephalosporin and a well-described β-lactamase inhibitor. C-T was approved by the United States (US) Food and Drug Administration in 2014 for complicated urinary tract infections, including acute pyelonephritis and complicated intra-abdominal infections. C-T is currently in clinical trials for the treatment of hospital-acquired pneumonia. The Program to Assess Ceftolozane-Tazobactam Susceptibility (PACTS) monitors C-T resistance to gram-negative (GN) isolates worldwide. This study compares the activities of C-T and comparators against GN isolates from ICU patients and non-ICU patients.

Methods. A total of 3,100 GN ICU isolates and 3,271 isolates from non-ICU patients were collected from 30 US hospitals in 2012–2016. Isolates were tested for susceptibility (S) to C-T and comparators by CLSI broth microdilution methodology in a central monitoring laboratory. Other antibiotics tested included amikacin (AMK), cefepime (FEP), ceftazidime (CAZ), colistin (COL), meropenem (MER), and piperacillin-tazobactam (TZP). CLSI (2017) interpretive criteria were used for all except COL with *Enterobacteriaceae* (ENT), for which EUCAST (2017) criteria were used.

Results. The most common ENT species from ICU and non-ICU patients were similar. The 3 most common ENT for ICU and non-ICU isolates were *Klebsiella pneumoniae*, 24.1% and 25.8%; *Escherichia coli*, 19.4% and 18.2%; and *Serratia marcescens*, 14.7% and 14.3%, respectively. The most common non-enteric species was *Pseudomonas aeruginosa* (PSA) for ICU and non-ICU (72.7% and 78.2%). ICU ENT isolates generally had a lower %S than non-ICU (Table). ENT showed more variability than PSA for %S between ICU and non-ICU.

		% susceptible†						
Organism	Number	C-T	AMK	FEP	CAZ	COL	MER	TZP
ENT ICU	1,802	91.1	98.5	89.7	84.7	75.8‡	96.6	86.9
ENT non-ICU	1,578	94.0	98.7	91.8	87.8	73.7‡	98.4	89.5
PSA ICU	944	97.4	98.2	84.9	83.4	99.3	78.6	78.8
PSA non-ICU	1,324	97.3	95.2	84.6	84.0	99.5	80.9	78.5

† CLSI 2017

‡ EUCAST 2017

Conclusion. For ENT overall, MER and AMK were the most active, followed by C-T. Comparing ICU and non-ICU, MER and C-T were slightly more active vs. non-ICU ENT, while AMK %S was similar for both. For PSA, COL was the most active; C-T and AMK were similar. Activities between ICU and non-ICU isolates were similar for C-T and COL while AMK was more active vs. ICU isolates, and MER was more active vs. non-ICU. C-T showed potent activity against ICU and non-ICU isolates for ENT and PSA.

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1199. *In vitro* Activity of Cefiderocol against Globally Collected Carbapenem-Resistant Gram-Negative Bacteria Isolated from Urinary Track Source: SIDERO-CR-2014/2016

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Background. Cefiderocol (S-649266) is a novel siderophore cephalosporin active against a wide variety of Gram-negative bacteria, not only *Enterobacteriaceae* but also non-fermenting bacteria such as *Pseudomonas aeruginosa* and *Acinetobacter* spp., including carbapenem-resistant strains. This potent activity is due to its efficient penetration through the outer membrane via active iron transporter systems and its high stability to both serine- and metallo-carbapenemases.This study evaluated the *in vitro* activity of cefiderocol and comparator agents against carbapenem-resistant clinical isolates collected from urinary track source in 2014–2016 from global countries.

Methods /*Methods.* Carbapenem-resistant *Enterobacteriaceae* (CRE) and multidrug-resistant (MDR) non-fermenters (defined as resistant to imipenem, ciprofloxacin and amikacin) were collected globally from 2014 to 2016 by IHMA Inc. A total of 226 *Enterobacteriaceae*, 44 *Acinetobacter baumannii*, 45 *P. aeruginosa*, 7 *Stenotrophomonas maltophilia* and 1 *Burkholderia cepacia* isolated from a urinary track source were tested. MICs were determined for cefiderocol, cefepime (FEP), ceftazidime-avibactam (CZA), ceftolozane-tazobactam (C/T), ciprofloxacin (CIP), colistin (CST), and meropenem (MEM) by broth microdilution and interpreted according to CLSI 2016 guidelines. As recommended by CLSI, cefiderocol was tested in iron-depleted cation-adjusted Mueller Hinton broth. Quality control testing was performed on each day of testing by using *E. coli* ATCC25922 and *P. aeruginosa* ATCC27853.

Results. MIC_{90} of cefiderocol against carbapenem-resistant *Enterobacteriaceae,* MDR *P. aeruginosa*, MDR *A. baumannii*, and *S. maltophilia* were 4 μg/mL or less. However, MEM, C/T and CZA had MIC_{90}s of >64μg/mL. Cefiderocol demonstrated potent *in vitro* activity against carbapenem-resistant *Enterobacteriaceae*, *A. baumannii*, and *P. aeruginosa* isolates collected from a UTI source. At 4 μg/mL or less, cefiderocol inhibited the growth of 95.8% of the isolates.

Conclusion. These results strongly indicated that cefiderocol is a promising candidate for the treatment of the serious infections caused by cUTI isolated Gram-negative bacteria including carbapenem-resistant strains.

Disclosures. **M. Tsuji**, Shionogi & Co.: Employee, Salary; **M. Hackel**, IHMA: Employee, Salary; **R. Echols**, Shionogi & CO., LTD.: Consultant, Consulting fee; **Y. Yamano**, Shionogi & Co.: Employee, Salary

1200. Activity of the Novel Extended-spectrum β-Lactamase Inhibitor AAI101 in Combination with Cefepime Towards a Challenge Panel of *Acinetobacter baumannii*

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Background. AAI101 is a novel extended-spectrum β-lactamase inhibitor (BLI), active against ESBLs and a broad array of other BLs. AAI101 in combination with cefepime (FEP) is in Phase 2 development. Infections caused by *A. baumannii*, a pathogen endemic to the southern US and other global regions, are very challenging to treat, and often require combination therapy. This study examined the activity of FEP/AAI101 against a challenge set of *A. baumannii* clinical isolates enriched with OXA carbapenemase producers.

Methods. BLs in *A. baumannii* were identified by genotyping. Broth microdilution MICs and susceptibilities were obtained following CLSI methods and breakpoints (BPs), except for ceftazidime-avibactam (CAZ/AVI) where FDA *P. aeruginosa* BPs were used. CLSI FEP BPs were used for FEP/AAI101.

Results. All OXA-51 producers had the ISAba1 promoter. MIC_{90} data and % susceptibilities (%S) for FEP/AAI101 and comparators are shown in the Table: FEP/AAI101 was highly active against meropenem-susceptible (MPM^s) isolates. FEP/AAI101 (AAI101 fixed at 8 µg/ml) covered 67% of OXA-51 and 53% of OXA-58 strains. Lower susceptibilities were obtained for OXA-23 and OXA-24/40 producers. FEP/AAI101 was the most active β-lactam product. Colistin (COL) was the only agent with consistently high activity against all *A. baumannii* isolates.

Group		FEP	FEP/ AAI101 [4*]	FEP/ AAI101 [8*]	CAZ/ AVI [4*]	AMP/ SUL [2:1*]	PIP/ TAZ [4*]	COL
MPM^s	MIC_{90}	64	8	0.06	64	32	256	1
(*N* = 17)	%S	70.6	94.1	100	58.8	82.4	70.6	100
OXA-23	MIC_{90}	>128	>128	>128	>128	128	>256	0.5
(*N* = 30)	%S	0	0	0	3.3	0	0	96.7
OXA-24/40	MIC_{90}	>128	>128	>128	64	128	>256	4
(*N* = 30)	%S	3.3	3.3	6.7	6.7	3.3	0	86.7
OXA-51	MIC_{90}	>128	>128	>128	>128	>128	>256	0.5
(*N* = 30)	%S	0	36.7	66.7	3.3	16.7	0	100
OXA-58	MIC_{90}	>128	128	64	>128	64	>256	1
(*N* = 30)	%S	13.3	33.3	53.3	16.7	6.7	0	100
All	MIC_{90}	>128	>128	>128	>128	128	>256	1
(*N* = 137)	%S	12.4	27.7	40.1	13.9	16.1	8.8	96.4

AMP, ampicillin; SUL, sulbactam; PIP, piperacillin; TAZ, tazobactam
*BLI at fixed concentration in µg/mL or ratio as indicated

Conclusion. FEP/AAI101 was the most potent β-lactam product tested against clinical isolates of *A. baumannii* producing OXA-51 and OXA-58 β-lactamases. Infections by this difficult pathogen often require combination therapy, of which FEP-AAI101 may be a component.

Disclosures. **S. Shapiro**, Allecra: Employee, Salary

1201. Comparative *in vitro* Activities of Ceftazidime–Avibactam and Ceftolozane-tazobactam Against Characterized β-Lactamase-producing *Pseudomonas aeruginosa*

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Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing
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Background. Ceftazidime-avibactam (CAZ-AVI) and ceftolozane-tazobactam (TOL-TAZ) are cephalosporin/β-lactamase inhibitor combinations recently approved for the treatment of complicated intra-abdominal infections (cIAI) and complicated urinary tract infections (cUTI). Both agents are reported to have antibacterial activity against *P. aeruginosa* including multi-drug-resistant strains, but few studies have directly compared the activities of both agents against the same strains in a single study. This study evaluated the activities of both agents against characterized β-lactamase-producing *P. aeruginosa* using broth microdilution (BMD) and disk diffusion (DD) methods.

Methods. A total of 98 clinical isolates of *P. aeruginosa*, including characterized β-lactamase-producing strains were tested for susceptibility to CAZ-AVI and TOL-TAZ using BMD and DD and results were interpreted using FDA/CLSI breakpoints. The isolates tested included CTX-M (ESBL), AmpC, KPC, OXA and metallo-β-lactamase (MBL) producing organisms. The results from both BMD and DD were analyzed to assess the correlation between the testing methods and ability to differentiate isolates susceptible and resistant to both agents.

Results. CAZ-AVI and TOL-TAZ exhibited similar MIC values against all isolates with $MIC_{50/90}$ values of 2 and 16 µg/mL, respectively. When results were interpreted using FDA/CLSI breakpoints, the susceptibility rates for CAZ-AVI and TOL-TAZ were 82.7% and 62.2%, respectively. Isolates resistant to CAZ-AVI were predominantly MBL-producers whereas isolates resistant to TOL-TAZ included both MBL and KPC-producing *P. aeruginosa*. Both agents were active against AmpC-producing *P. aeruginosa* and both agents showed good correlation between BMD and DD methods.

Conclusion. CAZ-AVI and TOL-TAZ were active against β-lactamase-producing subsets of *P. aeruginosa* isolates in this challenge set. Both AmpC and KPC-producing *P. aeruginosa* were susceptible to CAZ-AVI whereas TOL-TAZ activity was limited to AmpC-producing organisms. Neither agent was active against MBL-producing organisms.

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1202. Activity of Ceftolozane-Tazobactam and Comparators When Tested against Bacterial Surveillance Isolates Collected from Pediatric Patients in the US during 2012–2016 as Part of a Global Surveillance Program

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Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing
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Background. Ceftolozane-tazobactam (C-T) is an antibacterial combination of a novel antipseudomonal cephalosporin and a β-lactamase inhibitor. C-T was approved by the US Food and Drug Administration in 2014 and by the European Medicine Agency in 2015 to treat complicated urinary tract infections, acute pyelonephritis, and complicated intra-abdominal infections in adults. The Program to Assess Ceftolozane-Tazobactam Susceptibility (PACTS) monitors C-T resistance to gram-negative (GN) isolates worldwide.

Methods. A total of 4121 GN isolates were collected during 2012–2016 from pediatric patients (<18 years old) in 31 US hospitals and tested for C-T susceptibility (S) by CLSI broth microdilution method in a central monitoring laboratory (JMI Laboratories). Other antibiotics tested were amikacin (AMK), cefepime (FEP), ceftazidime (CAZ), colistin (COL), levofloxacin (LVX), meropenem (MER), and piperacillin-tazobactam (TZP). Antibiotic-resistant phenotypes identified using CLSI (2017) clinical breakpoints included: carbapenem-resistant *Enterobacteriaceae* (CRE), non-CRE extended-spectrum β-lactamase screen positive (ESBL, non-CRE), ceftazidime-nonsusceptible (CAZ-NS), and meropenem-NS (MER-NS). EUCAST (2017) COL clinical breakpoints were used for *Enterobacteriaceae* (ENT).

Results. The most common infection type in hospitalized pediatric patients was pneumonia (*n* = 1,488) followed by urinary tract infection (*n* = 1,143) and bloodstream infection (*n* = 767). A total of 2,969 ENT and 1,152 non-enterics were isolated. The 5 most common species were *Escherichia coli* (EC: 1,311), *Pseudomonas aeruginosa* (PSA: 821 isolates), *Klebsiella pneumoniae* (KPN: 429), *Enterobacter cloacae* complex (ECC: 360), and *Serratia marcescens* (SM: 264). Susceptibilities of C-T and comparators for the main species and resistant phenotypes are shown in the Table. Only 7 isolates were CRE in this study.

Conclusion. C-T demonstrated good activity against pediatric ENT isolates (96.1%S), EC (99.2%S), and KPN (97.9%S). For ENT, all agents but COL had >90% S. For PSA, C-T demonstrated potent activity (99.5%S) and was the most potent antibiotic tested with activity similar to COL.

		% susceptible[a]							
Organism / organism group	N	C-T	FEP	CAZ	MER	TZP	LVX	AMK	COL[b]
ENT	2,969	96.1	95.2	91.0	99.7	94.0	92.9	99.8	81.9[c]
EC	1,311	99.2	94.0	93.8	99.8	96.9	86.2	99.7	99.8
EC ESBL, non-CRE	119	92.4	35.3	32.8	99.2	84.0	37.0	97.5	100.0
KPN	429	97.9	92.3	90.9	98.8	95.3	98.1	99.8	98.8
KPN ESBL, non-CRE	44	86.4	36.4	20.5	97.7	70.5	88.6	100.0	95.5
ECC	360	84.2	95.3	77.5	99.7	82.7	100.0	100.0	77.1
SM	264	97.3	98.1	97.0	100.0	97.0	97.7	99.6	N/A
PSA	821	99.6	94.3	92.8	92.4	90.7	90.4	97.2	99.5
CAZ-NS	59	94.9	37.3	0.0	64.4	13.6	71.2	88.1	98.3
MER-NS	62	96.8	72.6	66.1	0.0	62.9	54.8	90.3	100

[a]CLSI (2017)
[b]EUCAST (2017)
[c]Includes species that are inherently resistant to COL

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1203. In Vitro Activity of Newer Antimicrobials and Relevant Comparators Vs. 349 *Stenotrophomonas maltophilia* Clinical Isolates Obtained from Patients in Canadian Hospitals (CANWARD, 2011–2016)

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Background. *Stenotrophomonas maltophilia* is a non-fermentative gram-negative bacillus that has emerged as an important opportunistic pathogen among hospitalized, debilitated patients. Treatment options for infections caused by this organism are limited because it is intrinsically resistant to antimicrobials from multiple different classes. The purpose of this study was to evaluate the in vitro activity of several newer antimicrobial agents (ceftazidime-avibactam [CZA], ceftolozane-tazobactam [C/T], moxifloxacin [MXF], tigecycline [TGC]) and relevant comparators [e.g., trimethoprim-sulfamethoxazole [TMP-SMX]) against a large collection of *S. maltophilia* clinical isolates obtained as part of an ongoing national surveillance study (CANWARD, 2011–2016).