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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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.

Disclosures. **L. Y. Lin**, Allergan plc: Employee, Salary; **M. Vail**, Allergan plc: Employee and Intern during study conduct and analysis, Educational support; **D. Debabov**, Allergan plc: Employee, Salary; **I. Critchley**, Allergan plc: Employee, Salary

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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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).

Methods. From January 2011 to December 2016, inclusive, 12 to 15 sentinel hospitals across Canada submitted clinical isolates from patients attending ERs, medical and surgical wards, hospital clinics, and ICUs (CANWARD). Each center was asked to annually submit clinical isolates (consecutive, one per patient/infection site) from blood (100), respiratory (100), urine (25), and wound (25) infections. Susceptibility testing was performed using broth microdilution as described by CLSI. MICs were interpreted using CLSI breakpoints, where available.

Results. 349 *S. maltophilia* clinical isolates were obtained as a part of CANWARD (86% from a respiratory source). The susceptibility profile of these isolates is presented below.

Antimicrobial	MIC50 (µg/mL)	MIC90 (µg/mL)	Susceptibility Breakpoint (µg/mL)	% Susceptible
<>Ceftazidime	>32	>32	≤8	22.1
CZA	>16	>16	≤8	26.9
C/T	32	>64	Not defined	No data
Ciprofloxacin	2	16	Not defined	No data
MXF	0.5	4	Not defined	No data
Doxycycline	2	4	Not defined	No data
TGC	1	4	Not defined	No data
Colistin	4	>16	Not defined	No data
TMP-SMX	0.5	2	≤2	98.2

CZA and C/T demonstrated poor in vitro activity vs. the isolates. The in vitro activity of MXF was approximately 4 fold more potent than ciprofloxacin. TGC was marginally more active in vitro than doxycycline.

Conclusion. TMP-SMX continues to demonstrate excellent in-vitro activity against *S. maltophilia* clinical isolates. MXF and TGC may also prove useful in the treatment of infections caused by this pathogen.

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1204. The Novel β-Lactamase Inhibitor, ETX-2514, in Combination with Sulbactam Effectively Inhibits *Acinetobacter baumannii*

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Background. Multidrug resistant (MDR) *Acinetobacter sp*. were deemed a "serious" health threat by the Centers for Disease Control and Prevention with a daunting 63% of infections being nearly untreatable. Underlying this challenging pathogen are the presence of a chromosomal class C β-lactamase, *Acinetobacter*-derived cephalosporinase (ADC), as well as the abundant prevalence of class D OXA β-lactamases that hydrolyze carbapenems in conjunction with a lack of potent β-lactamase inhibitors. Based on the ability of ETX2514, a rationally designed novel diazabicyclooctane inhibitor (Figure 1A), to inhibit class D β-lactamases as well as PBPs, we hypothesized that highly resistant clinical isolates of *A. baumannii* will demonstrate susceptibility to the sulbactam-ETX2514 combination and that *A. baumannii* β-lactamases, ADC-7 and OXA-58 will be readily inactivated by ETX2514.

Methods. Susceptibility testing according to Clinical and Laboratory Standards Institute was performed for sulbactam ±4 mg/L ETX2514 using 72 *A. baumannii* strains. More than half of the isolates are MDR, have ≥ eight resistant determinants, contain an ADC β-lactamase, and have OXA-23 and OXA-58-like β-lactamases in the carbapenem resistant isolates. ADC-7 and OXA-58 β-lactamases were purified and characterized with ETX2514 by steady-state inhibition kinetics and Q-TOF mass spectrometry.

Results. The *A. baumannii* strains demonstrated an MIC_{90} of 32 mg/L for sulbactam and 2 mg/L for the sulbactam-ETX-2514 combination. The addition of ETX2514 lowered the MIC_{50} from 8 to 1 mg/L (Figure 1B). ETX-2514 effectively inhibited purified OXA-58 ($k_2/K = 2.5 \pm 0.3 \times 10^5$ M^{-1} s^{-1} and $K_{i\,appP} = 0.39 \pm 0.01$ µM) and ADC-7 ($k_2/K = 1.0 \pm 0.1 \times 10^6$ M^{-1} s^{-1} and $K_{i\,app} = 0.11 \pm 0.04$ µM). The two β-lactamases displayed similar dissociation constants (K_d =1 ± 0.1 nM), but ADC-7 possessed a faster dissociation rate ($k_{off} = 8 \pm 1 \times 10^{-4}$ s^{-1} for ADC-7 and $1.6 \pm 0.3 \times 10^{-4}$ $s^{-1}$for OXA-58). Using mass spectrometry, ADC-7 and OXA-58 were found to stably bind the ETX-2514 compound for up to 24 hours (Figure 1C).

Conclusion. ETX2514 is a new β-lactamase inhibitor that is strikingly effective at restoring susceptibility to highly drug-resistant *A. baumannii* isolates when combined with sulbactam via inhibition of the ADC-7 and OXA-58 β-lactamases.

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1205. Ceftobiprole Activity When Tested Against Contemporary Bacteria Causing Bloodstream Infections in the US (2016)

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Background. Ceftobiprole medocaril (prodrug of ceftobiprole) is an advanced cephalosporin, approved for adults in multiple European countries for the treatment of hospital-acquired pneumonia (excluding ventilator-associated pneumonia) or community-acquired pneumonia. It is not approved in the US; however, it has achieved qualified infectious disease product status and two phase 3 studies supported by BARDA are planned to begin in the US in 2017.

Methods. A total of 2,787 Gram-positive (GP) and -negative (GN) isolates from bloodstream infections (BSI) from 30 medical centers in the SENTRY Antimicrobial Surveillance Program were evaluated. Isolates were collected in the US during 2016. Susceptibility (S) testing was performed by reference broth microdilution method against ceftobiprole and comparators. Isolates included 693 *Staphylococcus aureus* (SA), 216 coagulase-negative staphylococci (CoNS), 244 enterococci, 63 *Streptococcus pneumoniae* (SPN), 74 viridans group streptococci (VGS), 138 β-haemolytic streptococci (BHS), 1,105 *Enterobacteriaceae* (ENT), 129 *Pseudomonas aeruginosa* (PSA), 41 *Acinetobacter* spp. (ASP), 30 *Stenotrophomonas maltophila*, 19 *Haemophilus* spp. and 35 miscellaneous bacteria.

Results. Methicillin-resistant *S. aureus* (MRSA) S rates were lower than for methicillin-susceptible *S. aureus* (MSSA) for most agents. For levofloxacin (LEV) and erythromycin (ERY), the S rates were LEV: MRSA, 23.2%; MSSA, 86.1%; ERY: MRSA, 9.0%; MSSA, 69.3%. All MSSA and 99.0% of MRSA were S to ceftobiprole, while all MSSA and 96.5% of MRSA were S to ceftaroline (CPT). For CoNS, 98.1% of ceftobiprole MIC values were ≤2mg/L. Ceftobiprole was active against *Enterococcus faecalis* (96.1% ≤2mg/L) and not against *E. faecium* (18.9% ≤2mg/L). Against ENT, ceftobiprole (85.0%S) was similar in activity to ceftazidime (CAZ, 87.2%S) and cefepime (FEP, 88.9%S). The $MIC_{50/90}$ values for ceftobiprole, FEP, and CAZ against PSA were identical at 2/16 mg/L.

Conclusion. Ceftobiprole exhibited potent *in vitro* activity against GP and GN isolates from contemporary BSI in the US. These results support further clinical evaluation of ceftobiprole for the treatment of BSI.

Organism	$MIC_{50/90}$ in mg/L (%S)			
	Ceftobiprole	CPT	CRO	LEV
MRSA (289)	1/2 (99.0)	0.5/1 (96.5)	>8/>8 (0.0)	4/>4 (23.2)
MSSA (404)	0.5/0.5 (100.0)	0.25/0.25 (100.0)	4/4 (100.0)	0.12/4 (86.1)
CoNS (216)	0.5/1 (-)	0.25/0.5 (-)	8/>8 (34.3)	0.5/>4 (51.9)
BHS (138)	0.015/0.03 (-)	≤0.008/0.015 (100.0)	0.06/0.06 (100.0)	0.5/1 (100.0)
VGS (74)	0.03/0.5 (-)	0.03/0.12 (-)	0.12/1 (91.9)	1/>4 (89.2)
E. faecalis (153)	0.5/2 (-)	2/8 (-)	NT	1/>4 (73.9)
SPN (63)	0.015/0.06 (100.0)	≤0.008/0.03 (100.0)	0.03/0.12 (100.0)	1/1 (100.0)
ENT (1,105)	0.03/>16 (85.0)	0.12/>32 (77.9)	≤0.06/>8 (83.8)	0.06/>4 (80.2)
PSA (129)	2/16 (-)	16/>32 (-)	NT	0.5/>4 (79.1)

Ceftobiprole (S using EUCAST breakpoints), CPT, ceftaroline, CRO, ceftriaxone, LEV, levofloxacin; NT, not tested; (-), no susceptibility interpretive criteria available

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1206. Assessment of the *In Vitro* Antifungal Activity of SCY-078 Against a Collection of *C. parapsilosis* Clinical Isolates

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Background. Global rates of candidemia caused by *C. parapsilosis* are increasing with differences detected between neonates and adult patients (50% vs. 12%, respectively) and across geographic regions (5% vs. 25% in Iceland and Spain, respectively). SCY-078 is a novel, oral and intravenous, triterpenoid glucan synthase inhibitor under