	% C-T susceptible					
US divisions	ENT	ESBL, nonCRE	PSA	MER-NS PSA	CAZ-NS PSA	TZP-NS PSA
All	94.2%	86.3%	97.4%	89.1%	82.4%	87.5%
1: New England	96.9%	86.4%	97.3%	85.5%	80.9%	86.6%
2: Mid-Atlantic	87.4%	84.9%	96.6%	88.9%	81.9%	87.4%
3: East North Central	95.3%	88.6%	97.6%	90.9%	83.0%	88.1%
4: West North Central	98.1%	93.8%	99.6%	98.4%	96.3%	97.4%
5: South Atlantic	95.6%	83.4%	97.4%	87.1%	81.8%	85.7%
6: East South Central	94.8%	91.3%	98.0%	94.7%	86.8%	90.4%
7: West South Central	92.7%	79.8%	97.3%	90.4%	84.3%	89.5%
8: Mountain	95.5%	90.0%	97.7%	92.0%	83.3%	90.0%
9: Pacific	95.8%	89.0%	94.9%	77.5%	70.0%	77.5%

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1217. In Vitro Activity of Ceftolozane-Tazobactam vs. Antimicrobial Non-Susceptible *Pseudomonas aeruginosa* Clinical Isolates Obtained from Across Canada as Part of the CANWARD Study, 2008–2016

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Background. Ceftolozane-tazobactam (C/T) is a novel β-lactam β-lactamase inhibitor combination with a broad spectrum of activity that includes *Pseudomonas aeruginosa*. The purpose of this study was to evaluate the in vitro activity of C/T and relevant comparators vs. a large collection of antimicrobial non-susceptible (NS) *P. aeruginosa* clinical isolates obtained from patients across Canada (CANWARD, 2008–2016).

Methods. From January 2008 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, respiratory, urine, and wound infections. Susceptibility testing was performed using broth microdilution as described by CLSI. Multidrug-resistant (MDR) *P. aeruginosa* were defined as isolates that tested NS to at least one antimicrobial from ≥3 classes. Extensively drug-resistant (XDR) *P. aeruginosa* were defined as isolates that tested NS to at least one antimicrobial from ≥5 classes.

Results. 3229 *P. aeruginosa* isolates were obtained as a part of CANWARD. The in vitro activity of C/T and relevant comparators is presented below.

Conclusion. C/T demonstrated excellent in vitro activity vs. antimicrobial NS *P. aeruginosa* clinical isolates, including MDR, XDR, and meropenem NS subsets. It may prove useful in the treatment of infections caused by these organisms.

	C/T		Ceftazidime		Meropenem		Piperacillin-Tazobactam	
	MIC50/ MIC90	%S	MIC50/ MIC90	%S	MIC50/ MIC90	%S	MIC50/ MIC90	%S
All Isolates (*n* = 3229)	0.5/1	98.3	4/32	83.0	0.5/8	81.0	4/64	84.1
Ceftazidime NS (*n* = 550)	1/4	90.5	32/>32	0.0	4/32	47.6	64/256	20.0
Ciprofloxacin NS (*n* = 735)	1/4	94.8	8/>32	63.0	2/16	55.1	16/128	64.5
Colistin NS (*n* = 155)	0.5/2	92.9	4/32	76.8	0.5/16	78.7	4/128	81.9
Gentamicin NS (*n* = 535)	1/4	93.8	4/>32	67.3	1/32	59.6	8/128	69.3
Meropenem NS (*n* = 615)	1/4	94.6	8/>32	53.2	8/32	0.0	16/256	54.5
Piperacillin-tazobactam NS (*n* = 515)	1/4	92.0	32/>32	14.6	4/32	45.6	64/256	0.0
MDR (*n* = 463)	1/4	90.5	32/>32	19.7	8/32	22.5	64/256	21.4
XDR (*n* = 84)	2/16	78.6	>32/>32	0.0	16/>32	0.0	128/512	0.0

%S = percent susceptible

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1218. *In Vitro* Activity of Lefamulin against *S. aureus* Collected Worldwide from Hospitalized Patients with Bacterial Pneumonia

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Background. *S. aureus* (SA) is a well-recognized cause of pneumonia from both the community and hospital settings. The clinical management of SA pneumonia is complicated by the invasive infection it can cause and the high prevalence of methicillin-resistance (MR). Lefamulin (LEF) is the first semi-synthetic pleuromutilin antibiotic for IV and oral use in humans. LEF is the first semi-synthetic pleuromutilin antibiotic for IV and oral use in humans and it specifically inhibits bacterial protein synthesis. LEF is currently in Phase 3 trials for the treatment of community-acquired bacterial pneumonia (CABP). This study investigated the *in vitro* activity of LEF and comparators against SA strains collected from patients hospitalized with pneumonia in 2015.

Methods. 1273 unique SA isolates were collected from hospitalized patients with pneumonia worldwide in 28 countries (33 sites) in 2015 as part of the SENTRY surveillance program. Isolates included 401 hospital-acquired (HA) SA (259 from ICU, 152 from ventilator associated pneumonia, VAP). Susceptibility testing was conducted using the CLSI broth microdilution method and susceptibility was interpreted per CLSI 2017 breakpoint criteria.

Results. LEF was the most potent compound tested, with 99.7% of all SA isolates being inhibited at a concentration of ≤0.25 mg/L ($MIC_{50/90}$ values of 0.06/0.12 mg/L) and irrespective of the collection source (ICU/non-ICU, VAP/non-VAP). 31.6% of isolates (n = 402) were MRSA of which 99.3% were inhibited at a LEF concentration of ≤0.25 µg/mL ($MIC_{50/90}$, 0.06/0.12 mg/L). Susceptibility rates for all SA isolates were >90% for ceftaroline, vancomycin, linezolid and doxycycline. Susceptibility to azithromycin, levofloxacin and clindamycin was limited, particularly among MRSA (see Table).

Conclusion. SA strains collected from patients hospitalized with pneumonia including HAP and VAP were highly susceptible to LEF regardless of the resistance phenotype to the other antibiotics tested. Due to its potent activity against resistant SA and the most prevalent typical and atypical respiratory pathogens, as well as the availability of IV and oral formulations, LEF has the potential to play a role in the empiric treatment of CABP and supports evaluation in HAP and VAP caused by SA.

Table: Antibacterial activity of lefamulin and comparators against *S. aureus* (mg/L)

Compound	*S. aureus*, total (*n*=1273)		MSSA (*n*=871)		MRSA (*n*=402)	
	MIC_{50}	MIC_{90}	% S	% R	% S	% R
Lefamulin	0.06	0.12	-	-	-	-
Azithromycin	0.5	>4	73.9	**23.9**	19.2	**79.9**
Ceftaroline	0.25	1	100.0	0.0	78.9	0.2
Clindamycin	≤0.25	>2	100.0	0.0	57.0	**43.0**
Doxycycline	≤0.06	0.25	99.4	0.1	93.8	0.2
Levofloxacin	0.25	>4	93.8	**5.5**	22.4	**77.1**
Oxacillin	0.5	>2	100.0	0.0	0.0	**100.0**
Linezolid	1	2	99.9	0.1	100.0	0.0
Vancomycin	0.5	1	100.0	0.0	100.0	0.0

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1219. Effects of Iclaprim and Trimethoprim on Exotoxin Production by Methicillin-resistant *Staphylococcus aureus*

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Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) causes serious, often life-threatening, infections. Exotoxins such as alpha-hemolysin (AH), Panton Valentine leukocidin (PVL), and Toxic shock syndrome toxin 1 (TSST-1) mediate pathogenesis and inhibition of toxin production is an important consideration in choosing appropriate treatments. Vancomycin is recommended for severe MRSA infections; however, increasing vancomycin resistance, poor clinical outcomes and nephrotoxicity are serious concerns. Thus newer agents are needed,