SUNDAY - 8

Activity of Ceftobiprole Against Pathogens Isolated from Patients in Canadian Hospitals: CANWARD Study 2015-2016

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ABSTRACT

Background: Ceftobiprole is a broad-spectrum cephalosporin with anti-MRSA activity approved for adults in several countries for the treatment of hospital-acquired pneumonia (excluding ventilator-associated pneumonia) and community-acquired pneumonia. We compared the activity of ceftobiprole, ceftaroline, ceftriaxone, cefepime and other comparators against pathogens causing infections in hospitalized patients across Canada.

Methods: From January 2015 to December 2016, bacterial pathogens were collected by clinical laboratories in tertiary-care hospitals across Canada. Antimicrobial susceptibility testing was performed using CLSI broth microdilution methods (M07-A10, 2015; M100-S26, 2016).

Results: 6340 isolates were collected from blood (40.0%), respiratory tract (39.6%), wound/IV sites (10.2%), and urine (10.2%). The activities (MIC_{50} and MIC_{90}) of ceftobiprole and comparators against selected pathogens are detailed in the table below:

Organism [#]	MIC_{50}/MIC_{90} (µg/mL)			
	Ceftobiprole	Ceftaroline	Ceftriaxone	Cefepime
S.aureus [1414]	0.5/1	0.25/0.5	4/>64	2/64
MRSA (all) [253]	1/2	1/1	>64/>64	>64/>64
- MRSA (HA) [114]	1/2	1/1	>64/>64	64/>64
- MRSA (CA) [95]	1/1	1/1	64/>64	64/>64
S. epidermidis [170]	0.5/1	0.12/0.5	4/>64	2/64
S. pneumoniae [260]	≤0.03/≤0.03	≤0.03/0.03	≤0.12/≤0.12	≤0.12/≤0.12
- Pen-R [10]	0.12/0.25	0.12/0.12	0.5/1	1/2
E. coli (AmpC) [10]	0.25/0.05	1/8	8/32	≤0.25/1
E. coli (ESBL) [69]	>32/>32	>16/>16	64/>64	4/32
K. pneumoniae [382]	≤0.06/0.12	0.12/0.5	≤0.25/≤0.25	≤0.25/≤0.25
P. aeruginosa [695]	2/8	16/>16	16/>64	4/16

HA - healthcare-associated; CA - community-acquired; Pen-R - penicillin-resistant [≥2 µg/mL]; and ESBL- extended spectrum β-lactamase.

Conclusions: Ceftobiprole was more active than ceftriaxone versus *S.aureus*, *E. coli* (including AmpC strains), *P.aeruginosa*, MRSA (HA and CA) and *S. epidermidis*. Ceftobiprole is more active than cefepime versus *S. aureus*, MRSA (HA and CA), and *S. epidermidis.* These data demonstrate the breadth of ceftobiprole's spectrum of activity.

INTRODUCTION

Ceftobiprole is a broad-spectrum IV antibiotic with rapidly bactericidal activity against Gram-positive and Gram-negative organisms including methicillin-resistant *Staphylococcus aureus* (MRSA) and susceptible *Pseudomonas aeruginosa* (1-5). Health Canada has approved ceftobiprole for the treatment of patients 18 years of age and older with hospital-acquired pneumonia (HAP), excluding ventilator-associated pneumonia (VAP), and for the treatment of community-acquired pneumonia (CAP). Ceftobiprole is also available for use in several European and non-european countries.

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Participating Centres and Site Investigators

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MATERIALS AND METHODS

Study Background - CANWARD

The isolates tested in this study were obtained from January 2015 to December 2016, inclusive, from an ongoing cross-Canada surveillance study (CANWARD study; 13 participant sites, www.can-r.ca) (5). The goal of the CANWARD 2015-2016 study was to assess pathogens and antimicrobial resistance patterns associated with lower respiratory tract, skin/skin structure, urinary, and bacteremias due to any cause in Canadian patients on medical wards, surgical wards, intensive care units, and presenting to emergency rooms and hospital clinics (5).

Bacterial Isolates

From January 2015 through December 2016, inclusive, each study site was asked to submit clinical isolates (consecutive, one per patient, per infection site) from inpatients and outpatients with respiratory, urine, wound, and bloodstream infections. The medical centres submitted "clinically significant" isolates from patients with a presumed infectious disease. Surveillance swabs, eye, ear, nose and throat swabs were excluded. We also excluded anaerobic organisms. Isolate identification was performed by the submitting site and confirmed at the reference site as required, based on morphological characteristics and antimicrobial susceptibility patterns. Isolates were shipped on Amies semi-solid transport media to the coordinating laboratory (Health Sciences Centre, Winnipeg, Canada), subcultured onto appropriate media, and stocked in skim milk at -80°C until minimum inhibitory concentration (MIC) testing was carried out.

Antimicrobial Susceptibilities

Following two subcultures from frozen stock, the *in vitro* activities of selected antimicrobials were determined by broth microdilution in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines (CLSI, 2015 M7-A10). Antimicrobial minimum inhibitory concentration (MIC) interpretive standards were defined according to CLSI breakpoints (M100S, 2015). Antimicrobial agents were obtained as laboratory grade powders from their respective manufacturers. Stock solutions were prepared and dilutions made as described by CLSI (M7-A10, 2015). The MICs of the antimicrobial agents for the isolates were determined using 96-well custom designed microtitre plates. These plates contained doubling antimicrobial dilutions in 100 µL/well of cation adjusted Mueller-Hinton broth and inoculated to achieve a final concentration of approximately 5×10^5 CFU/mL then incubated in ambient air for 24 hours prior to reading. Colony counts were periodically performed to confirm inocula. Quality control was performed using ATCC QC organisms including; *S. pneumoniae* 49619, *S. aureus* 29213, *E. faecalis* 29212, *E. coli* 25922, and *P. aeruginosa* 27853.

CONCLUSIONS

- Against methicillin-susceptible and methicillin-resistant *S. aureus*, ceftobiprole was more active than ceftriaxone.
- Against methicillin-susceptible and methicillin-resistant *S. epidermidis,* ceftobiprole was more active than ceftriaxone.
- Against penicillin-resistant *S. pneumoniae* and *E. faecalis*, ceftobiprole was more active than ceftriaxone.
- Ceftobiprole was more active than ceftriaxone against AmpC *E. coli*.
- Ceftobiprole was more active than cefepime against *P. aeruginosa*.

REFERENCES

1. Zhanel GG, Lam A, Schweizer F, Thompson K, Walkty A, Rubinstein E, Gin AS, Hoban DJ, Noreddin AM and Karlowsky JA. Ceftobiprole: A review of a broad spectrum and anti-MRSA cephalosporin. American Journal Clinical Dermatology 2008;9(4):245-254.
2. Walkty A, DeCorby M, Nichol K, Karlowsky JA, Hoban DJ, the Canadian Antimicrobial Resistance Alliance (CARA) and Zhanel GG. In vitro activity of ceftobiprole against clinical isolates of *Pseudomonas aeruginosa* obtained from intensive care units (ICU) patients a part of the CAN-ICU study. Journal of Antimicrobial Chemotherapy 2008;62(1):206-208.
3. Karlowsky JA, DeCorby M, Hoban DJ and Zhanel GG. In vitro activities of ceftobiprole and doripenem tested against frequently encountered aerobic and facultative Gram-positive and Gram-negative bacterial pathogens isolated from patients in Canadian hospitals in 2007. Canadian Journal of Infectious Diseases and Medical Microbiology 2009;20 (Suppl A):59-66.
4. Zhanel GG, Voth D, Nichol K, Karlowsky JA, Noreddin AM and Hoban DJ. Pharmacodynamic activity of ceftobiprole to vancomycin versus methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-intermediate *Staphylococcus aureus* (VISA) and vancomycin-resistant *Staphylococcus aureus* (VRSA) using an in vitro model. Journal of Antimicrobial Chemotherapy 2009;64:364-369.
5. Walkty A, Adam HJ, Laverdiere M, Karlowsky JA, Hoban DJ, the Canadian Antimicrobial Resistance Alliance (CARA), Zhanel GG. In vitro activity of ceftobiprole against frequently encountered aerobic and facultative Gram-positive and Gram-negative bacterial pathogens: Results of the CANWARD 2007-2009 Study. Diagnostic Microbiology and Infectious Diseases 2011;69:348-355.

RESULTS

Table 1. Ceftobiprole *in vitro* activity against 2,291 aerobic gram-positive bacteria isolated from patients in Canadian hospitals in 2015/2016

Organism and phenotype (no. of isolates)	Antimicrobial Agent	µg/mL MIC Range	MIC_{50}	MIC_{90}	% S
Methicillin-susceptible *S. aureus* (1,156)	Cefazolin	≤0.5-1	≤0.5	≤0.5	-
	Cefepime	≤0.25-8	2	4	-
	Ceftaroline	≤0.03-1	0.25	0.25	100[a]
	Ceftobiprole	**≤0.06-2**	**0.5**	**0.5**	**100**
	Ceftriaxone	≤0.25-8	4	4	-
	Ertapenem	≤0.03-32	0.25	0.25	-
	Meropenem	≤0.03-16	0.12	0.25	-
Methicillin-resistant *S. aureus* (256)	Cefazolin	≤0.5->128	64	> 128	-
	Cefepime	2->64	64	> 64	-
	Ceftaroline	0.06-2	0.5	1	99.6
	Ceftobiprole	**0.25-4**	**1**	**2**	**99.6**
	Ceftriaxone	8->64	> 64	> 64	-
	Ertapenem	0.25->32	8	> 32	-
	Meropenem	0.12->32	4	32	-
Methicillin-susceptible *S. epidermidis* (159)	Cefazolin	≤0.5-8	≤0.5	4	-
	Cefepime	≤0.25-64	1	16	-
	Ceftaroline	≤0.03-1	0.12	0.25	NA[b]
	Ceftobiprole	**≤0.06-4**	**0.5**	**1**	**NA**
	Ceftriaxone	≤0.25->64	4	32	-
	Ertapenem	≤0.03->32	1	16	-
	Meropenem	≤0.03-16	0.5	8	-
Methicillin-resistant *S. epidermidis* (9)	Cefazolin	32-128	64	128	-
	Cefepime	64->64	>64	>64	-
	Ceftaroline	0.25-0.5	0.5	0.5	NA
	Ceftobiprole	**1-2**	**1**	**2**	**NA**
	Ceftriaxone	>64->64	>64	>64	-
	Ertapenem	> 32->32	>32	>32	-
	Meropenem	16->32	16	>32	-
Penicillin-susceptible[c] *S. pneumoniae* (206)	Cefuroxime	≤0.25-0.5	≤0.25	≤0.25	100
	Ceftaroline	≤0.008-0.03	≤0.008	≤0.008	100
	Ceftobiprole	**≤0.03-0.06**	**≤0.03**	**≤0.03**	**100**
	Ceftriaxone	≤0.12	≤0.12	≤0.12	100
	Ertapenem	≤0.06-0.12	≤0.06	≤0.06	100
	Meropenem	≤0.06-0.12	≤0.06	≤0.06	100
Penicillin-intermediate[d] *S. pneumoniae* (40)	Cefuroxime	≤0.25-4	≤0.25	4	65
	Ceftaroline	≤0.008-0.12	0.03	0.06	100
	Ceftobiprole	**≤0.03-0.5**	**0.06**	**0.25**	**100**
	Ceftriaxone	≤0.12-1	≤0.12	0.5	100
	Ertapenem	≤0.06-1	≤0.06	1	100
	Meropenem	≤0.06-0.5	≤0.06	0.5	80
Penicillin-resistant[e] *S. pneumoniae* (4)	Cefuroxime	4-8	4	8	0
	Ceftaroline	0.06-0.12	0.06	0.12	100
	Ceftobiprole	**0.25**	**0.25**	**0.25**	**100**
	Ceftriaxone	0.25-1	0.5	1	100
	Ertapenem	0.5-1	1	1	100
	Meropenem	0.5-1	0.5	1	0
S. pyogenes (94)	Cefuroxime	≤0.25	≤0.25	≤0.25	NA
	Ceftaroline	≤0.008-0.03	≤0.008	≤0.008	100
	Ceftobiprole	**≤0.03-0.06**	**≤0.03**	**≤0.03**	**NA**
	Ceftriaxone	≤0.12-0.25	≤0.12	≤0.12	100
	Ertapenem	≤0.06-0.12	≤0.06	≤0.06	100
	Meropenem	≤0.06-≤0.06	≤0.06	≤0.06	100
S. agalactiae (91)	Cefuroxime	≤0.25	≤0.25	≤0.25	NA
	Ceftaroline	≤0.008-0.03	≤0.008	0.015	100
	Ceftobiprole	**≤0.03-0.06**	**≤0.03**	**≤0.03**	**NA**
	Ceftriaxone	≤0.12-0.5	≤0.12	≤0.12	100
	Ertapenem	≤0.06	≤0.06	≤0.06	100
	Meropenem	≤0.06-0.12	≤0.06	≤0.06	100
E. faecalis (195)	Cefazolin	8-128	32	32	NA
	Cefepime	4->64	32	>64	NA
	Ceftaroline	0.12-16	1	4	NA
	Ceftobiprole	**≤0.06-8**	**0.5**	**1**	**NA**
	Ceftriaxone	0.5->64	>64	>64	NA
	Ertapenem	0.5->32	16	16	NA
	Meropenem	0.25-16	4	8	NA
E. faecium (81)	Cefazolin	16->128	>128	>128	NA
	Cefepime	2->64	>64	>64	NA
	Ceftaroline	0.25->16	>16	>16	NA
	Ceftobiprole	**0.5->32**	**>32**	**>32**	**NA**
	Ceftriaxone	2->64	>64	>64	NA
	Ertapenem	4->32	>32	>32	NA
	Meropenem	1->32	>32	>32	NA

[a] Ceftobiprole MICs interpreted using EUCAST breakpoints: *S. aureus* - susceptible (S) ≤2 µg/mL, resistant (R) >2 µg/mL; *S. pneumoniae* - (S) ≤0.5 µg/mL, resistant (R) >0.5 µg/mL; [b] NA - not available; [c] Penicillin-susceptible, MIC ≤0.06 µg/mL; [d] Penicillin-intermediate, MIC 0.12-1 µg/mL; [e] Penicillin-resistant, MIC ≥2 µg/mL

Table 2. Ceftobiprole *in vitro* activity against 2,874 aerobic gram-negative bacteria isolated from patients in Canadian hospitals in 2015/2016

Organism and phenotype (no. of isolates)	Antimicrobial Agent	µg/mL MIC Range	MIC_{50}	MIC_{90}	% S
E. coli (1,170)	Amoxicillin-clavulanate	0.5->32	4	16	77.4
	Cefazolin	≤0.5->128	2	>128	73.2
	Cefepime	≤0.25->64	≤0.25	1	92.9
	Cefoxitin	0.5->32	4	8	93
	Ceftaroline	≤0.03->16	0.06	16	85.2
	Ceftobiprole	**≤0.06->32**	**≤0.06**	**8**	**87.6[a]**
	Ceftriaxone	≤0.25->64	≤0.25	32	87.2
	Ertapenem	≤0.03-1	≤0.03	≤0.03	99.8
	Meropenem	≤0.03-0.12	≤0.03	≤0.03	100
	Piperacillin-tazobactam	≤1->512	2	4	97.3
E. coli ESBL-negative (1,033)	Amoxicillin-clavulanate	0.5->32	4	16	82.4
	Cefazolin	≤0.5->128	1	4	82.9
	Cefepime	≤0.25-32	≤0.25	≤0.25	99.9
	Cefoxitin	0.5->32	4	8	94.4
	Ceftaroline	≤0.03-16	0.06	0.25	96.4
	Ceftobiprole	**≤0.06->32**	**≤0.06**	**≤0.06**	**98.9[a]**
	Ceftriaxone	≤0.25->64	≤0.25	≤0.25	98.6
	Ertapenem	≤0.03-1	≤0.03	≤0.03	99.9
	Meropenem	≤0.03-0.12	≤0.03	≤0.03	100
	Piperacillin-tazobactam	≤1->512	≤1	4	97.6
E. coli ESBL-positive (137)	Amoxicillin-clavulanate	2->32	16	32	40.2
	Cefazolin	8->128	>128	>128	0
	Cefepime	≤0.25->64	4	32	40.2
	Cefoxitin	1->32	8	16	82.5
	Ceftaroline	0.5->16	>16	>16	0.7
	Ceftobiprole	**0.25->32**	**>32**	**>32**	**2.2**
	Ceftriaxone	1->64	64	>64	1.5
	Ertapenem	≤0.03-1	≤0.03	0.12	99.3
	Meropenem	≤0.03-0.12	≤0.03	≤0.03	100
	Piperacillin-tazobactam	≤1-512	4	16	95.6
E. coli AmpC positive (16)	Amoxicillin-clavulanate	2->32	>32	>32	12.5
	Cefazolin	1->128	>128	>128	6.2
	Cefepime	≤0.25-32	≤0.25	2	93.7
	Cefoxitin	8->32	>32	>32	6.2
	Ceftaroline	0.06->16	4	>16	31.2
	Ceftobiprole	**≤0.06->32**	**0.12**	**1**	**81.2**
	Ceftriaxone	≤0.25->64	2	>64	43.7
	Ertapenem	≤0.03-1	≤0.03	0.25	93.7
	Meropenem	≤0.03-0.06	≤0.03	0.06	100
	Piperacillin-tazobactam	≤1-128	4	64	81.2
K. pneumoniae (382)	Amoxicillin-clavulanate	≤0.06->32	2	8	90
	Cefazolin	≤0.5->128	1	8	83.5
	Cefepime	≤0.25->64	≤0.25	≤0.25	93.2
	Cefoxitin	0.5->32	2	8	91.4
	Ceftaroline	≤0.03->16	0.12	0.5	90.3
	Ceftobiprole	**≤0.06->32**	**≤0.06**	**0.12**	**91.9**
	Ceftriaxone	≤0.25->64	≤0.25	≤0.25	92.4
	Ertapenem	≤0.03->32	≤0.03	≤0.03	98.2
	Meropenem	≤0.03-16	≤0.03	0.06	98.9
	Piperacillin-tazobactam	≤1->512	2	8	94.8
K. pneumoniae ESBL-negative (354)	Amoxicillin-clavulanate	≤0.06->32	2	4	96.3
	Cefazolin	≤0.5->128	1	2	90.1
	Cefepime	≤0.25-64	≤0.25	≤0.25	99.4
	Cefoxitin	0.5->32	2	8	94.1
	Ceftaroline	≤0.03->16	0.12	0.25	97.2
	Ceftobiprole	**≤0.06->32**	**≤0.06**	**≤0.06**	**98.9**
	Ceftriaxone	≤0.25->64	≤0.25	≤0.25	98.9
	Ertapenem	≤0.03-32	≤0.03	≤0.03	99.7
	Meropenem	≤0.03-8	≤0.03	≤0.03	99.7
	Piperacillin-tazobactam	≤1->512	2	8	97.7
K. pneumoniae ESBL-positive (28)	Amoxicillin-clavulanate	8->32	16	>32	10.7
	Cefazolin	8->128	>128	>128	0
	Cefepime	≤0.25- 64	8	>64	14.3
	Cefoxitin	2-> 32	8	>32	57.1
	Ceftaroline	0.5->16	>16	>16	3.6
	Ceftobiprole	**0.12->32**	**>32**	**>32**	**3.6**
	Ceftriaxone	≤0.25->64	>64	>64	10.7
	Ertapenem	≤0.03->32	0.12	8	78.6
	Meropenem	≤0.03-16	≤0.03	2	89.3
	Piperacillin-tazobactam	2->512	16	>512	57.1

Organism and phenotype (no. of isolates)	Antimicrobial Agent	µg/mL MIC Range	MIC_{50}	MIC_{90}	% S
K. oxytoca (112)	Amoxicillin-clavulanate	1-32	2	4	92
	Cefazolin	1->128	4	32	36.6
	Cefepime	≤0.25-16	≤0.25	≤0.25	98.2
	Cefoxitin	0.5->32	2	4	95.5
	Ceftaroline	≤0.03->16	0.12	0.5	90.2
	Ceftobiprole	**≤0.06->32**	**0.12**	**1**	**80.4**
	Ceftriaxone	≤0.25->64	≤0.25	≤0.25	94.6
	Ertapenem	≤0.03-0.12	≤0.03	≤0.03	100
	Meropenem	≤0.03-0.12	≤0.03	≤0.03	100
	Piperacillin-tazobactam	≤1->512	≤1	4	94.6
E. cloacae (181)	Amoxicillin-clavulanate	1->32	>32	>32	3.3
	Cefazolin	2->128	>128	>128	0.6
	Cefepime	≤0.25-64	≤0.25	1	95.6
	Cefoxitin	1->32	>32	>32	5
	Ceftaroline	≤0.03->16	0.25	>16	71.8
	Ceftobiprole	**≤0.06->32**	**≤0.06**	**2**	**84**
	Ceftriaxone	≤0.25->64	≤0.25	>64	72.4
	Ertapenem	≤0.03-16	0.06	0.5	92.3
	Meropenem	≤0.03-4	≤0.03	0.06	98.9
	Piperacillin-tazobactam	≤1->512	2	32	85.6
P. mirabilis (91)	Amoxicillin-clavulanate	0.5->32	1	8	93.4
	Cefazolin	2->128	4	16	7.7
	Cefepime	≤0.25-16	≤0.25	≤0.25	98.9
	Cefoxitin	≤0.06->32	2	4	94.5
	Ceftaroline	0.06->16	0.12	0.5	92.3
	Ceftobiprole	**≤0.06-16**	**≤0.06**	**≤0.06**	**98.9**
	Ceftriaxone	≤0.25->64	≤0.25	≤0.25	95.6
	Ertapenem	≤0.03-0.12	≤0.03	≤0.03	100
	Meropenem	≤0.03-0.25	0.06	0.12	100
	Piperacillin-tazobactam	≤0.12-64	≤1	≤1	98.9
S. marcescens (93)	Amoxicillin-clavulanate	16->32	>32	>32	0
	Cefazolin	>128->128	>128	>128	0
	Cefepime	≤0.25-1	≤0.25	≤0.25	100
	Cefoxitin	8->32	16	>32	16.1
	Ceftaroline	0.25-16	0.5	2	72
	Ceftobiprole	**≤0.06-2**	**≤0.06**	**0.12**	**96.8**
	Ceftriaxone	≤0.25-4	≤0.25	0.5	96.8
	Ertapenem	≤0.03-0.25	≤0.03	0.06	100
	Meropenem	≤0.03-0.12	0.06	0.06	100
	Piperacillin-tazobactam	≤1-16	≤1	4	100
P. aeruginosa (690)	Cefepime	≤0.25->64	2	16	87.7
	Ceftaroline	0.25->16	8	>16	NA[b]
	Ceftobiprole	**0.12->32**	**4**	**16**	**NA**
	Ceftriaxone	≤0.25->64	16	>64	NA
	Ertapenem	0.06->32	8	>32	NA
	Meropenem	≤0.03->32	0.5	8	80.7
	Piperacillin-tazobactam	≤1->512	4	64	83.3
S. maltophilia (129)	Amoxicillin-clavulanate	2->32	>32	>32	NA
	Cefepime	0.5->64	32	>64	NA
	Ceftaroline	2->16	>16	>16	NA
	Ceftobiprole	**8->32**	**>32**	**>32**	**NA**
	Ceftriaxone	2->64	>64	>64	NA
	Ertapenem	2->32	>32	>32	NA
	Meropenem	1->32	>32	>32	NA
	Piperacillin-tazobactam	4->512	256	>512	NA
A. baumannii (26)	Amoxicillin-clavulanate	4-32	16	32	NA
	Cefepime	1-16	2	8	92.3
	Ceftaroline	1-16	2	8	NA
	Ceftobiprole	**0.12-1**	**0.25**	**1**	**NA**
	Ceftriaxone	4-32	8	32	65.4
	Ertapenem	1-16	4	16	NA
	Meropenem	0.12-2	0.25	1	100
	Piperacillin-tazobactam	≤ 1-32	2	32	88.5

[a] Ceftobiprole MICs interpreted using EUCAST breakpoints: Enterobacteriaceae - susceptible (S) ≤0.25 µg/mL, resistant (R) >0.25 µg/mL ESBL - extended spectrum ß-lactamase; [b] NA - not available