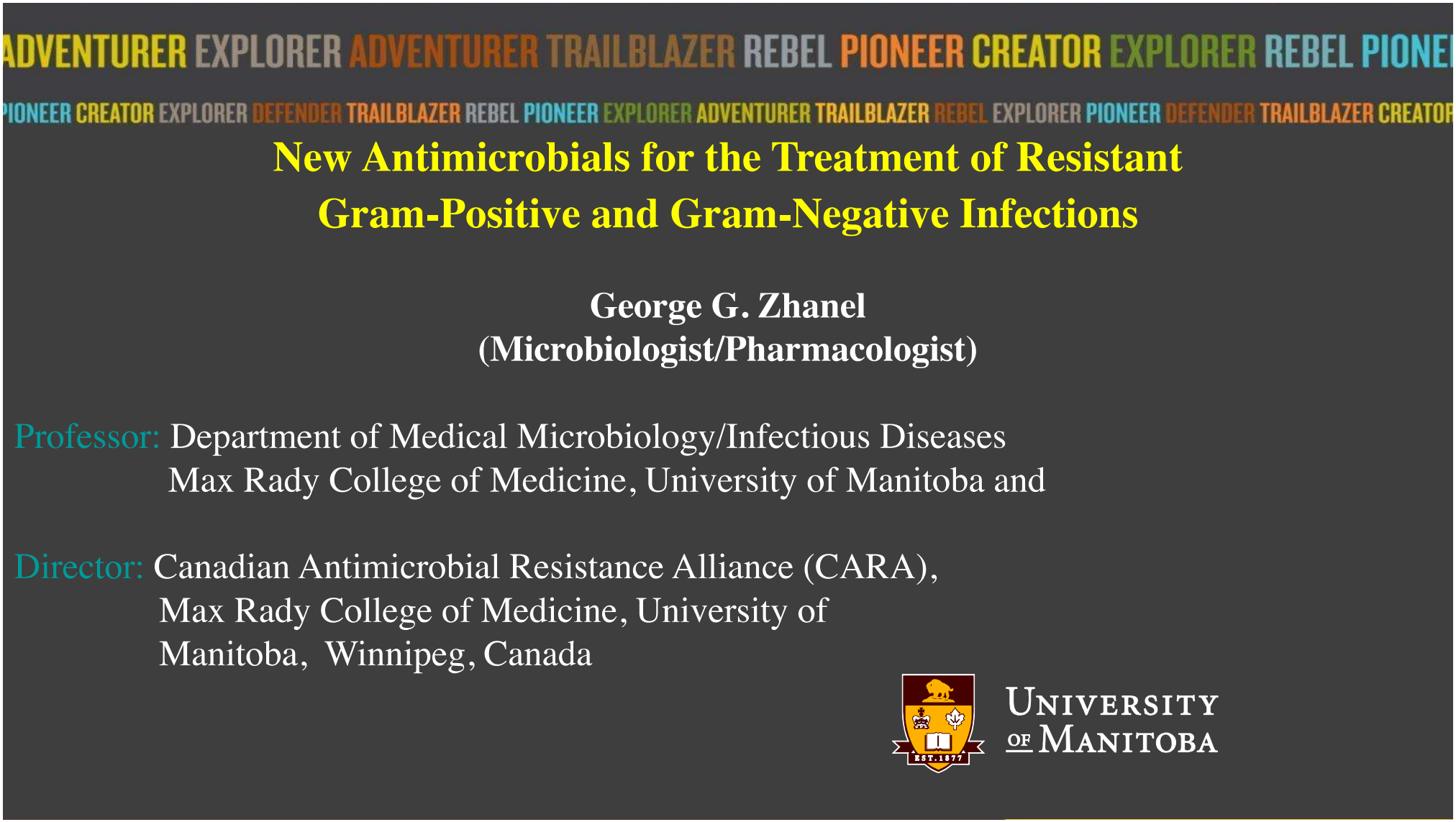
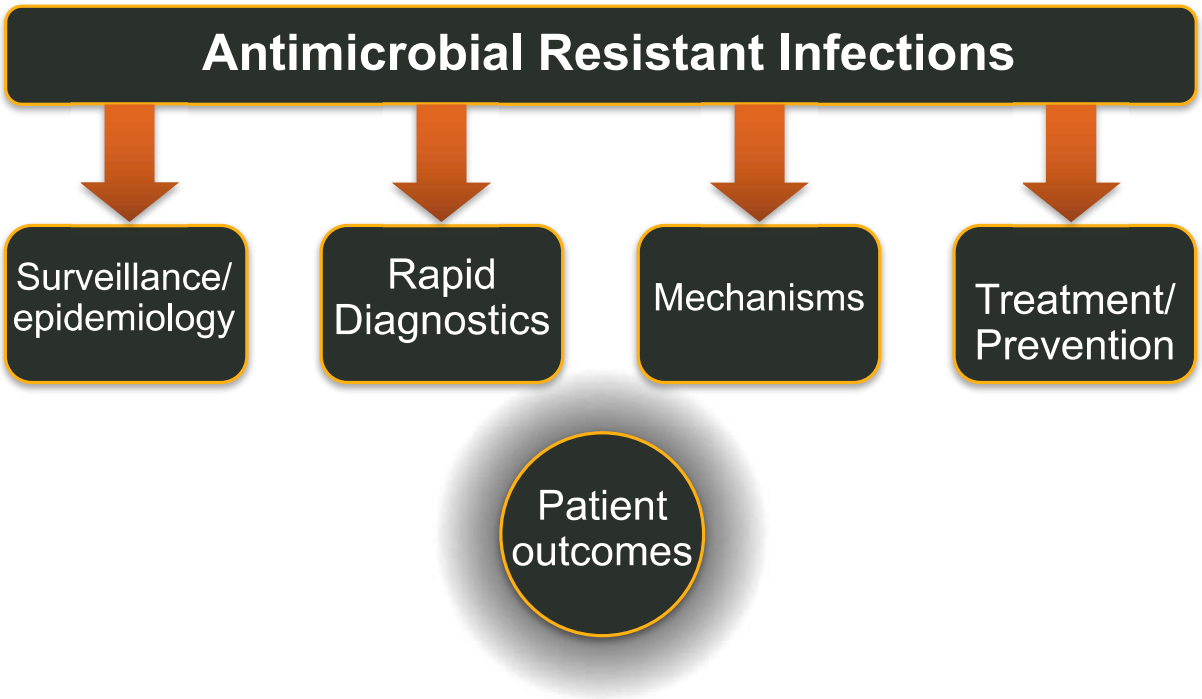

ADVENTURER EXPLORER ADVENTURER TRAILBLAZER REBEL PIONEER CREATOR EXPLORER REBEL PIONE
PIONEER CREATOR EXPLORER DEFENDER TRAILBLAZER REBEL PIONEER EXPLORER ADVENTURER TRAILBLAZER REBEL EXPLORER PIONEER DEFENDER TRAILBLAZER CREATOR
New Antimicrobials for the Treatment of Resistant Gram-Positive and Gram-Negative Infections
George G. Zhanel
(Microbiologist/Pharmacologist)
Professor: Department of Medical Microbiology/Infectious Diseases
Max Rady College of Medicine, University of Manitoba and
Director: Canadian Antimicrobial Resistance Alliance (CARA),
Max Rady College of Medicine, University of
Manitoba, Winnipeg, Canada
EST. 1877
UNIVERSITY OF MANITOBA

Canadian Antimicrobial Resistance Alliance (CARA)



www.can-r.ca

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

Objectives:

1. Understand current treatments of MRSA, VRE and MDR Gram-negative bacilli

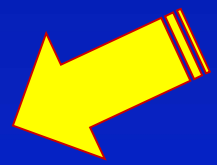
2. Review **new/investigational** agents for the **resistant Gram-negative bacilli**

3. Review **new/investigational** agents for **MRSA and VRE infections**

Potential Solutions to Infections Caused By Resistant Superbugs

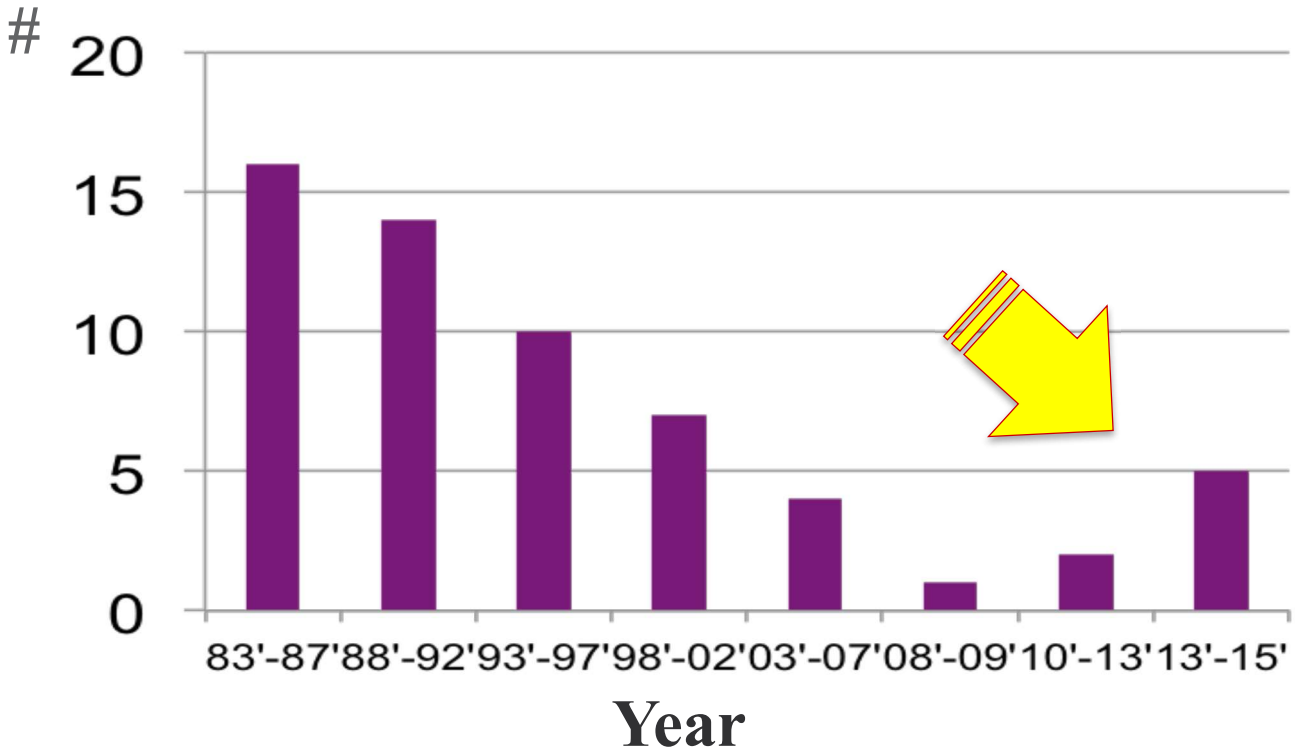
(Adapted from WHO 2014; UK 2014 and US 2015)

- Surveillance of resistant pathogens (www.can-r.ca)
- Infection control (wash those hands !)
- Rapid diagnostics
- Treatment guidelines
- Antimicrobial stewardship
- **New antimicrobials/new therapies**
- Probiotics/Bacteriotherapy
- Vaccination
- Bacteriophages (lytic)



Iredell et al. BMJ 2015

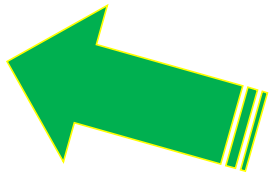
Some New Antimicrobials Are Coming



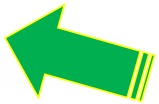
IDSA. http://www.idsociety.org/BBND/.
Deak et al. Ann Intern Med 2016;165:363-372.

New Antimicrobials

- Recently marketed in Canada/US



- New/old antimicrobials



- Older antimicrobials
  - Optimizing pharmacodynamics
  - Combinations

CANWARD 2007- Present

George Zhanel, Heather Adam, Mel Baxter, Melissa McCracken, Laura Mataseje, Michael R Mulvey, Matt Gilmour, Karen Wake, Barbara Weshnoweski, Ravi Vashisht, Sali Biju, Nancy Laing, James Karlowsky, Kim Nichol, Andrew Denisuik, Alyssa Golden, Philippe Lagacé-Wiens, Andrew Walkty, Frank Schweizer, Jack Johnson, the Canadian Antimicrobial Resistance Alliance (CARA)
and Daryl J Hoban

University of Manitoba, Health Sciences Centre,
National Microbiology Lab, Winnipeg, Canada and International Health Management Associates (IHMA), Chicago, USA

Supplements in CJIDMM 2009, DMID 2011 and JAC 2013.
www.can-r.ca

Bacteriology of Top 10 Organisms in Canada CANWARD 2007-2015 (*BLOOD* n=17,421)

Ranking	Organism	% of Total
1.	***Escherichia coli***	**23.0**
2.	*Staphylococcus aureus,* MSSA	13.9
3.	***Klebsiella pneumoniae***	**7.4**
4.	***Enterococcus* spp.**	**6.5**
5.	*Streptococcus pneumoniae*	4.9
6.	***Pseudomonas aeruginosa***	**3.9**
7.	***Staphylococcus aureus,* MRSA**	**3.8**
8.	*Candida albicans*	2.5
9.	*Enterobacter cloacae*	2.4
10.	*Streptococcus agalactiae*	1.9
Total	**-**	**70.3**

Zhanel et al. ICAAC/ICC 2015.
Zhanel et al. JAC 2013.

CNS / *S. epidermidis* 7.6%

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

NEW/Investigational Agents vs. MDR Gram-negative Pathogens

- Ceftolozane/tazobactam
- Ceftobiprole
- Ceftazidime-avibactam
- Ceftaroline-avibactam
- Imipenem/relebactam
- Meropenem/vaborbactam
- Eravacycline/Omadacycline
- Plazomicin
- Aztreonam-avibactam
- Delafloxacin
- Refamulin
- Oral/IV Fosfomycin
- Cefiderocol

ICAAC/ICC 2015, ASM Microbe 2016.
Deak et al. Ann Intern Med 2016;165:363-372.
Butler, Blaskovich and Cooper. J Antibiot 2017;70:3-24.

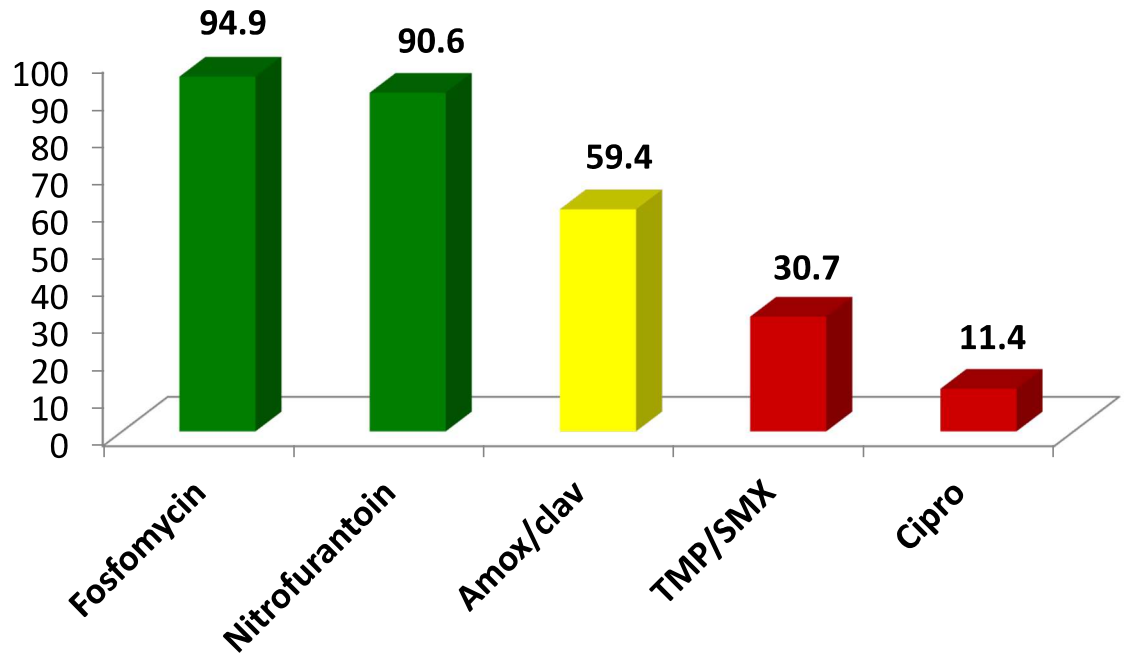
NEW/Investigational Agents vs. MDR Gram-negative Pathogens

Oral Fosfomycin

Activity of Antimicrobials vs ESBL *E. coli* Causing UTIs (Canada 2007-2013)

% Susceptibility

n=254

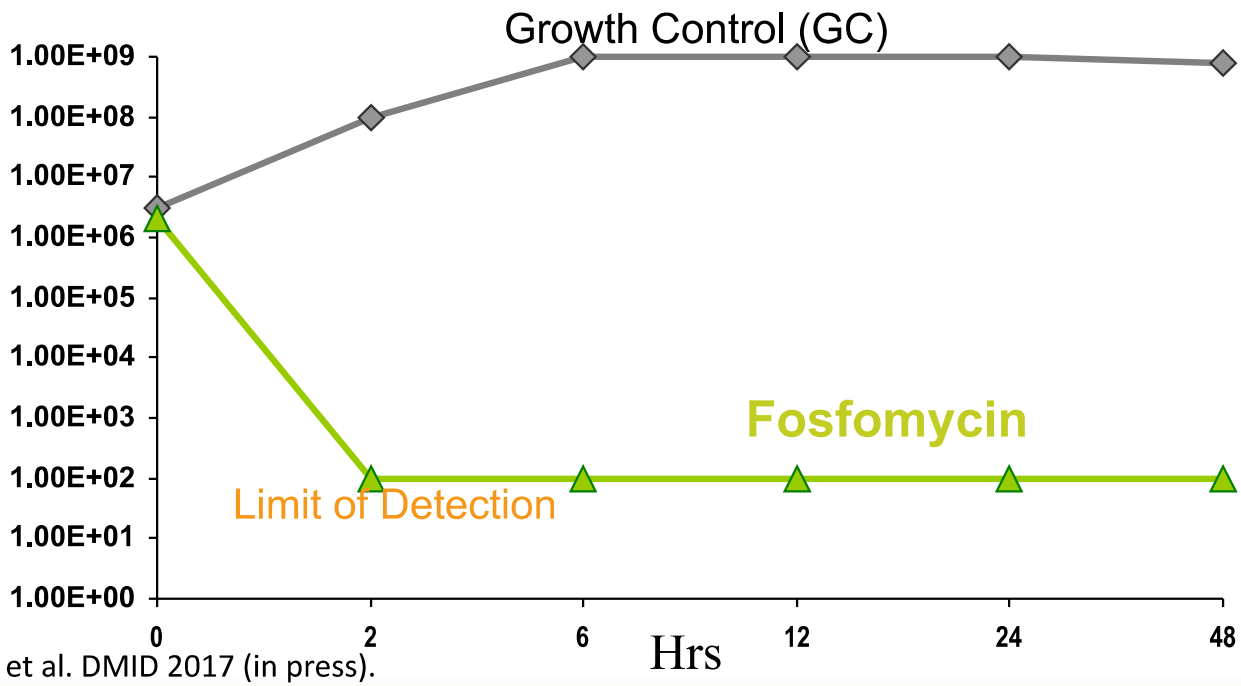


Karlowsky, Adam, Denisuik, Lagace-Wiens, Baxter and Zhanel. AAC 2014;58:1252-1256.

Fosfomycin Kills ESBL *E. coli*

Simulating 3g PO, fCmax 4000 μg/mL, $t_{1/2}$ 6 hrs)

Strain #87164 CTX-M-15, TEM-1; Fosfomycin MIC 1 μg/mL



Zhanel et al. DMID 2017 (in press).

NEW/Investigational Agents vs. MDR Gram-negative Pathogens

Ceftolozane-Tazobactam

Ceftolozane-Tazobactam

- **Antipseudomonal cephalosporin plus beta-lactamase inhibitor**
- **Spectrum of activity: Gram-negatives, including MDR *Pseudomonas aeruginosa* and ESBL-producing strains**
- **FDA approval in December 2014 (Canada 2015)**
  - **Complicated urinary tract infections, including pyelonephritis**
  - **Complicated intraabdominal infections (plus metronidazole)**
  - **IV dose: 1.5 g (1 g ceftolozane; 0.5 g tazobactam) q8h (1-h infusion)**

Zhanel GG, et al. *Drugs.* 2014;74:31-51.
Liscio JL, et al. *Int J Antimicrob Agents.* 2015;46:266-271.

Ceftolozane/tazobactam Activity

(CANWARD 2011-2014, n=10,272, MIC_{90})

Organism (#)	Ceftol/tazo	Imipenem
***E. coli* (1322)**	**0.25**	**0.25**
***E. coli* ESBL (218)**	**1**	**0.25**
***P. aeruginosa* (322)**	**1**	**16**
K. pneumoniae 809	0.5	0.5
E. cloacae 344	8	0.5
S. marcescens 209	1	1
P. mirabilis 187	0.5	4
E. aerogenes 93	2	1
A. baumannii 52	2	0.5

Zhanel et al. Drugs. 2014;74:31-51.; Zhanel et al. ICAAC/ICC 2015.

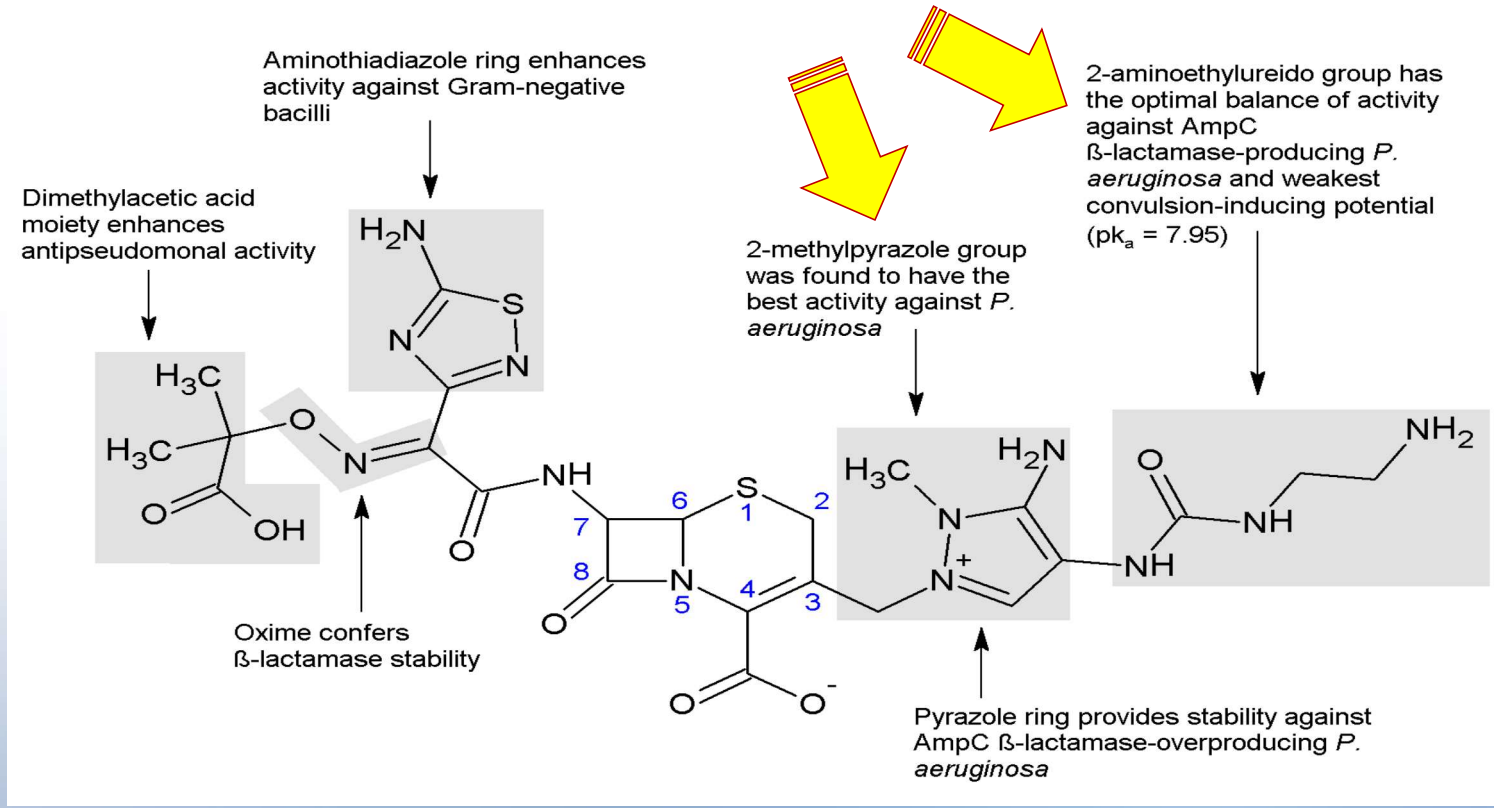
Clinical Efficacy of Ceftolozane/Tazobactam in the Treatment of

ESBL cUTI and cIAI

97.4% clinical cure rate

Popejoy et al. JAC 2017;72(1):268-272.

Ceftolozane Structure



Zhanel et al. Drugs 2014:Jan;74(1):31-51.

Ceftolozane-Tazobactam: Activity Against *P. aeruginosa*

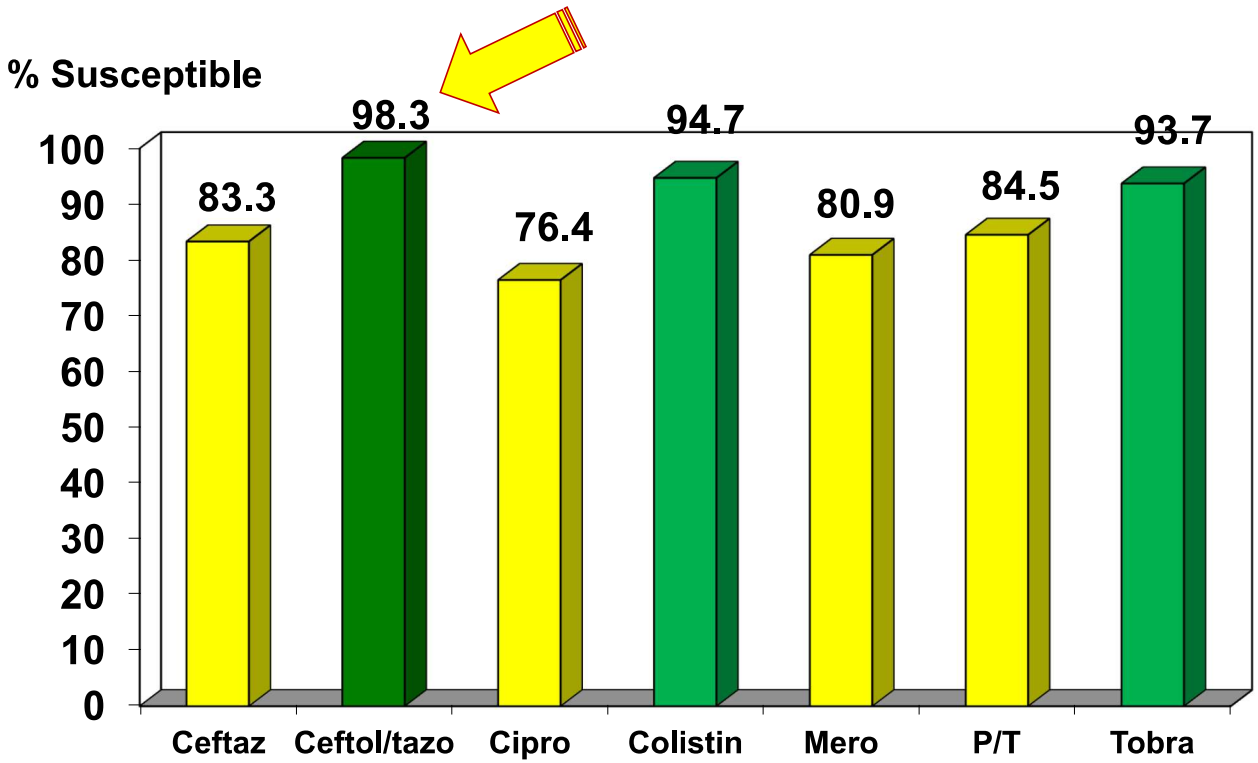
- ***In vitro* activity against *P. aeruginosa* that had:**
  - **Chromosomal AmpC *or***
  - **Loss of outer membrane porin (OprD) *or***
  - **Up-regulation of efflux pumps (MexXY, MexAB)**
- **Not active against bacteria producing metallo-β-lactamases**

Current FDA susceptibility interpretive criteria:

	Minimum Inhibitory Concentrations (µg/mL)		
Pathogen	Susceptible (S)	Intermediate (I)	Resistant (R)
Pseudomonas aeruginosa	≤4 / 4*	8 / 4*	≥16 / 4*

Cabot et al. *Antimicrob Agents Chemother.* 2014;58:6:3091-3099.
Takeda S, et al. *Antimicrob Agents Chemother.* 2007;51:826-830.
Castanheira M, et al. *Antimicrob Agents Chemother.* 2014;58:6844-6850.

Antibiotic Susceptibility of *P. aeruginosa* (CANWARD 2007-2015) [n=3036]

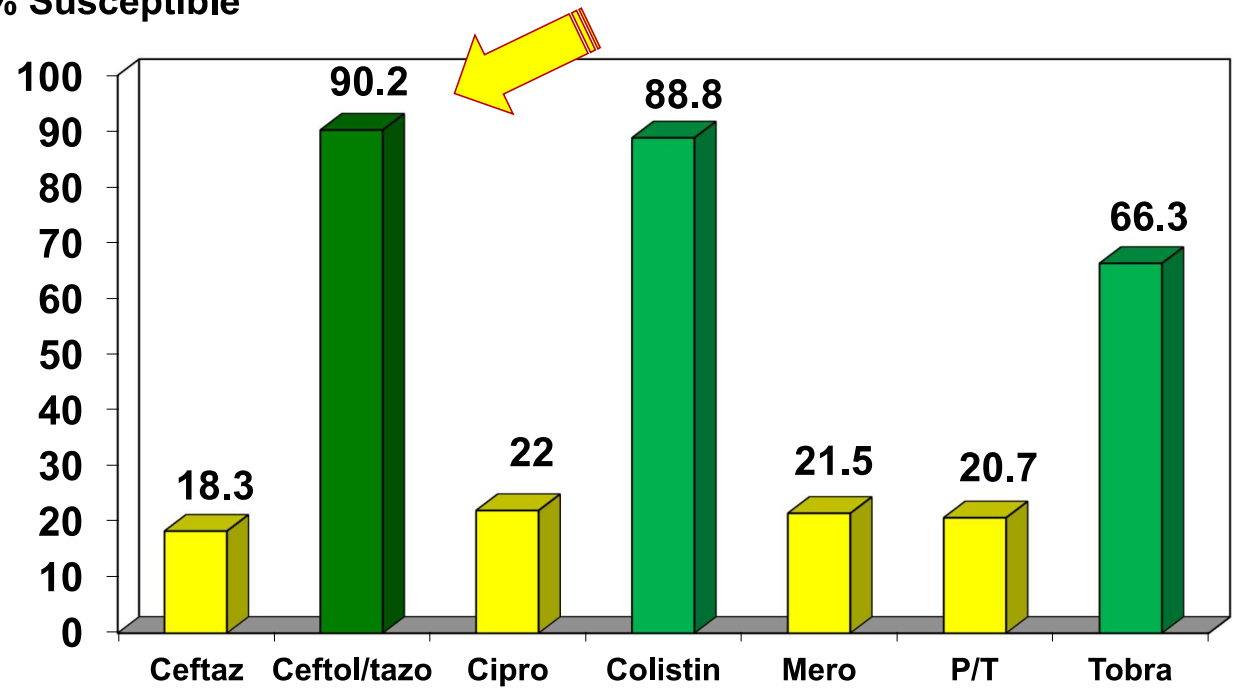


Zhanel et al. ASA 2017 (P033).
Walkty et al. AAC 2013;57:5707-5709.

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

Antibiotic Susceptibility of Versus MDR *P. aeruginosa* (CANWARD 2007-2015) [n=410 or 13.5%]

(MDR Resistance 3 or more antibiotic classes)

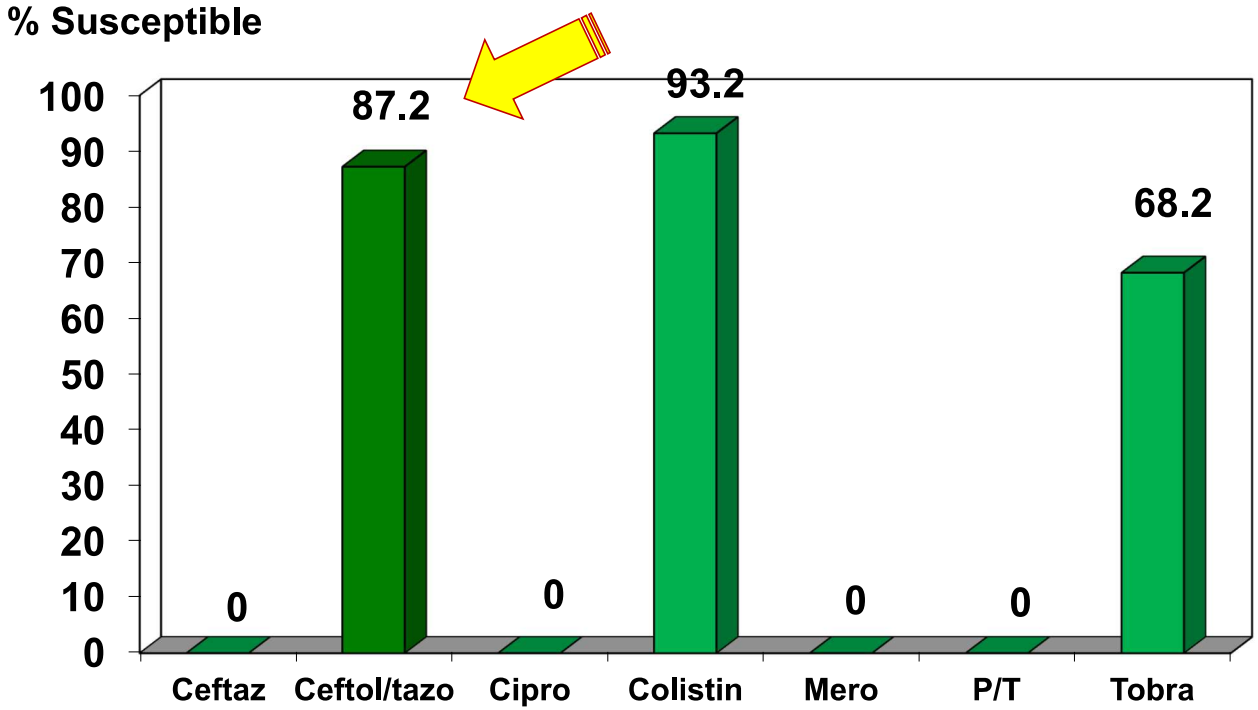


Zhanel et al. ASA 2017 (P033).
Walkty et al. AAC 2013;57:5707-5709.

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

Antibiotic Susceptibility of Versus XDR *P. aeruginosa* (CANWARD 2007-2015) [n=148 or 4.9%]

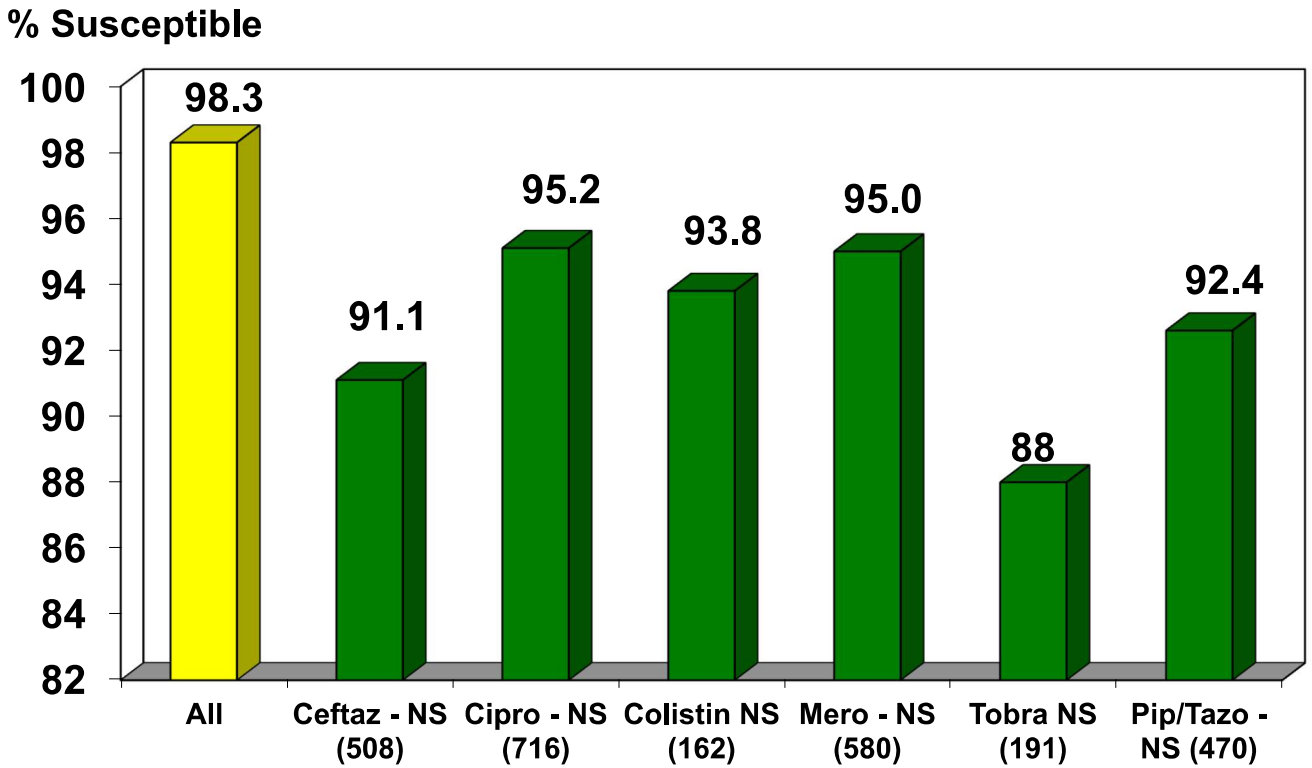
(XDR Resistance to Ceftaz + Cipro + Mero + Pip/Tazo



Zhanel et al. ASA 2017 (P033).
Walkty et al. AAC 2013;57:5707-5709.

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

Ceftolozane-tazobactam Susceptibility of *P. aeruginosa* (CANWARD 2007-2015) [n=3036]



Zhanel et al. ASA 2017.
Walkty et al. AAC 2013;57:5707-5709.

CLSI 2016 BP :≤ 4, 8, ≥ 16 ug/ml

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

Ceftolozane/Tazobactam Conclusions Today…

Versus other anti-Pseudomonal agents…

- **Bactericidal versus *P. aeruginosa***
  - **In vitro**
  - **In vivo**
  - **Clinical trials**

- **Alternative to ? Resistant (or MDR) *P. aeruginosa* ?**

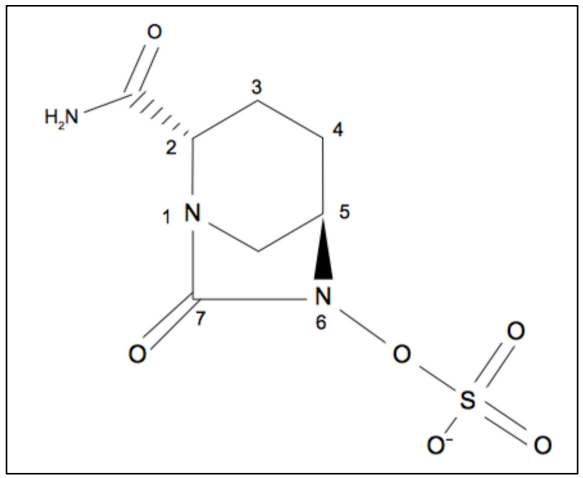
- **Need to get the drug on automated susceptibility testing (eg. Vitek 2)**

NEW/Investigational Agents vs. MDR Gram-negative Pathogens

Ceftazidime-Avibactam

Ceftazidime/Avibactam

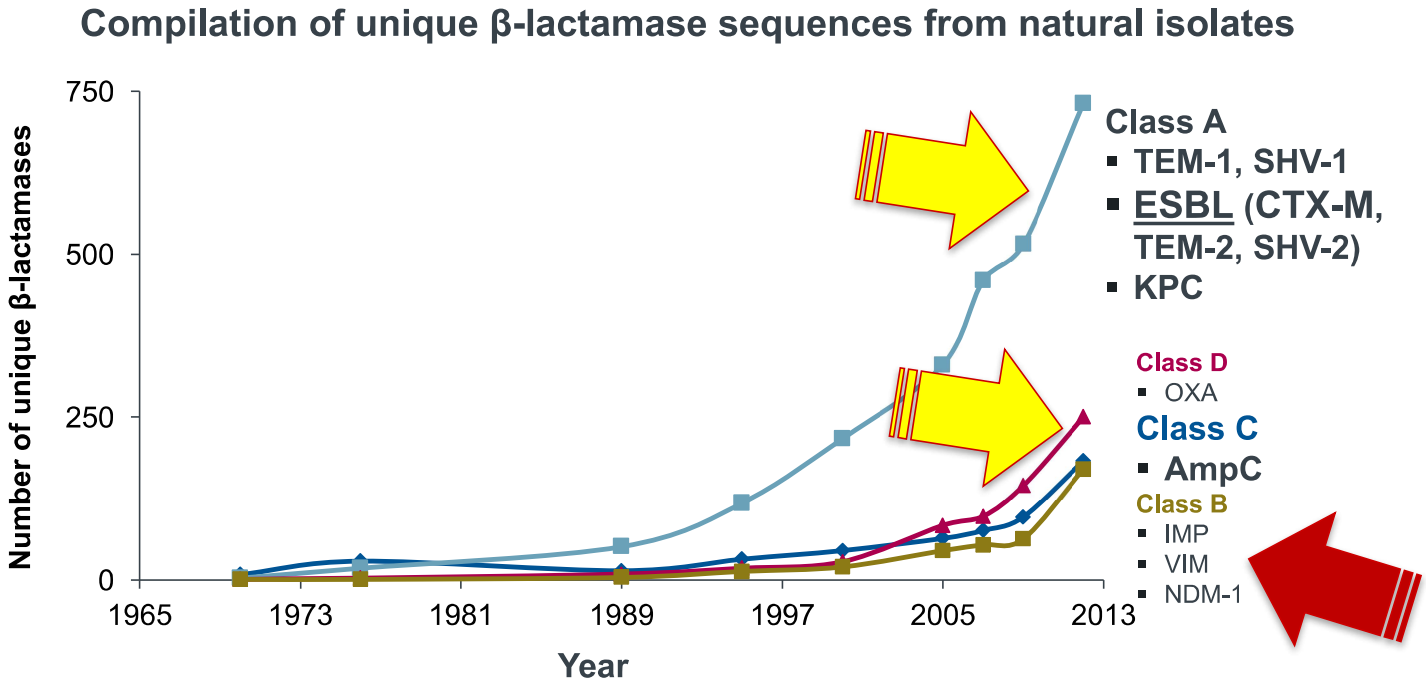
- **Non-β-lactam** β-lactamase inhibitor
  - Ambler **class A (ESBL, KPC), class C** and some class D (OXA-48) enzymes
- FDA approved in US 2015
  - **cUTI and cIAI**
- Active against:
  - Most Enterobacteriaceae (including MDR strains)
  - *P. aeruginosa*



Zhanel GG et al. Drugs. 2013 Feb;73(2):159-77.

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

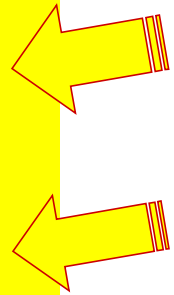
Increasing Numbers of β-Lactamases by Class



Bush K, Fisher JF. *Ann Rev Microbiol* 2011;65:455–478.

CAZ-AVI vs. Enterobacteriaceae

Gram negative aerobe	Ceftazidime			Ceftazidime-avibactam[a]			Ceftazidime-avibactam MIC_{90} reduction (fold)
	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	Range	
Citrobacter freundii			≤0.25–>64			≤0.06–2	
Citrobacter spp.			NA			≤0.06–4	
Ceftazidime non-susceptible			NA			≤0.06–4	
Enterobacter aerogenes			≤0.25–>32			≤0.06–2	
Enterobacter cloacae			≤0.25–>32			≤0.06–2	
Enterobacter spp.			NA			≤0.03–>32	
Ceftazidime-resistant[b]			NA			0.06–>32	
AmpC producing + porin loss			64–256			0.25–1	
Escherichia coli			≤0.03–>32			≤0.03–2	
ESBL producing			0.5–>64			<0.008–2	
AmpC hyper-producing			0.12–>64			≤0.004–4	
ESBL producing and AmpC hyper-producing			2–>64			0.015–0.12	
Klebsiella oxytoca			≤0.25–>64			≤0.06–1	
Klebsiella pneumoniae			≤0.5–>32			≤0.06–2	
ESBL producing			0.12–256			0.06–2	
OXA-48 carbapenemase-producing			≤0.12–512			<0.008–1	
KPC-producing			32–≥512			≤0.06–1	
ESBL-producing plus porin loss			126–512			0.5–2	
Klebsiella spp.			NA			≤0.03–32	
ESBL			NA			≤0.03–32	
Carbapenem non-susceptible[c]			NA			≤0.03–32	



CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

Zhanel GG et al. Drugs. 2013 Feb;73(2):159-77.

Ceftazidime-Avibactam Salvage Therapy for Infections Caused by Carbapenem Resistant Organisms

- Case series of patients with Carbapenem-Resistant Enterobacteriaceae (**CRE**) and Carbapenem-Resistant *P. aeruginosa* (**CRPa**) infections
- **36 patients** with CRE and 2 CRPa (mostly IAI)
- 60.5% were life threatening infections
- 94% received antibiotics prior to CAZ-AVI (median 13 days)
- Median duration of CAZ-AVI treatment 16 days
- 65.8% (25/36) concurrent Ab with resistance

Temkin et al. AAC 2017 Jan 24;61(2)

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

Ceftazidime-Avibactam Salvage Therapy for Infections Caused by Carbapenem Resistant Organisms

- **Clinical/Microbiological cure**
  - **73.7%** (28/36)
- 20.8% (5/36) with microbiological **CURE** died

CAZ-AVI resistance on therapy-KPC3 (Shields et al AAC Dec 2016)

- **Conclusion:**
  - **CAZ-AVI +/- other antibiotics an option for Carbapenem-Resistant Organisms**

85% cure CRE bacteremia (septic shock) [Caston IJID 2017]

Temkin et al. AAC 2017 Jan 24;61(2)

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

NEW/Investigational Agents vs. MDR Gram-negative Pathogens

Imipenem (cilastatin) - Relebactam

Imipenem/Relebactam

Phase II Clinical Trials

- cUTI (versus imipenem)
- cIAI (versus imipenem)

Strengths

- Gram-positives AND negatives and anaerobes
- **Relebactam inhibits ESBL, KPC and AmpC**

- *Enterobacteriaceae*
  - ESBL (*E. coli* and *Klebsiella* spp)
  - KPC (*E. coli* and *Klebsiella* spp)
  - MDR (*E. coli* and *Klebsiella* spp)
  - Imipenem-R *P. aeruginosa*

Paschke A, et al. ASM Microbe 2016.

Activity of Imipenem/Relebactam Versus Gram-negative Bacilli (MIC_{90} ug/ml)

Organism	Imipenem	Imipenem/ Relebactam
Klebsiella pneumoniae (n=891)	4	0.25
Klebsiella pneumoniae Bla KPC (n=111)	>16	1
Pseudomonas aeruginosa (n=490)	16	2
Pseudomonas aeruginosa Imipenem-R (n=490)	>16	2

Lapuebla et al. AAC 2015 Aug;59(8):5029-31.

Imipenem/Relebactam

Current Phase III Clinical Trials

HAP/VAP: Imipenem/relebactam versus piperacillin/tazobactam

Imipenem-Resistant infections: Imip/ relebactam versus

colistin + imipenem - HAP/VAP, cIAI, cUTI

Clinical trials.gov (accessed April 2017)

NEW/Investigational Agents vs. MDR Gram-negative Pathogens

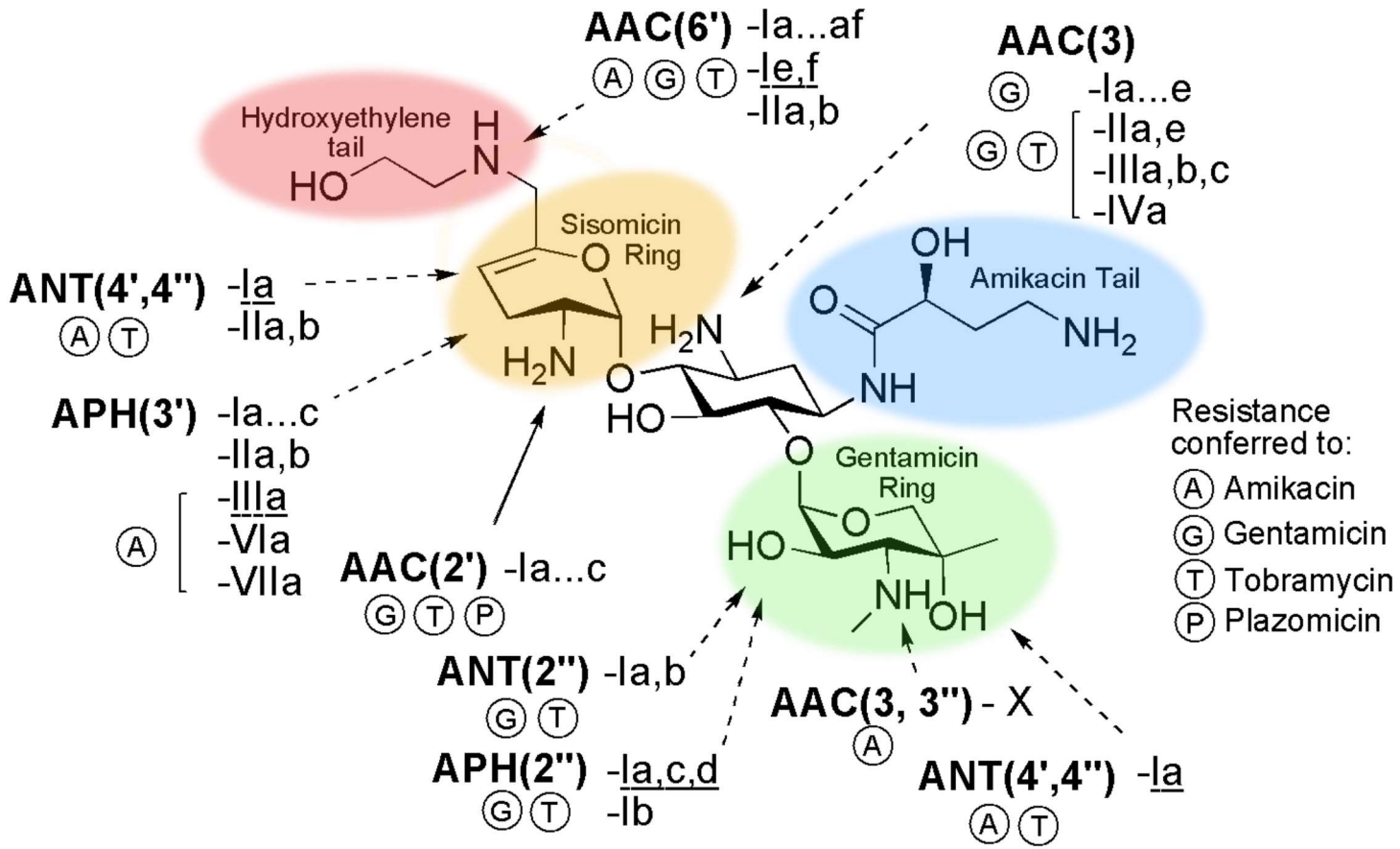
Plazomicin

Current Aminoglycosides…

Agent	Year
Streptomycin	1944
Neomycin	1949
Kanamycin	1957
Paromomycin	1959
Spectinomycin	1961
Gentamicin	**1963**
Tobramycin	**1967**
Sisomicin	1970
Amikacin	**1976**

Zhanel et al. Expert Reviews in Antiinfective Therapy 2012;10(4):459-473.

Structure/Activity of Plazomicin



Zhanel et al. Expert Reviews in Antiinfective Therapy 2012;10(4):459-473.

Activity of Plazomicin vs. Gram-negative bacilli (MIC ug/ml)

Organisms	Plazomicin MIC_{90}	Gentamicin MIC_{90}
Acinetobacter baumannii	16	>64
Citrobacter spp.	1	>64
Escherichia coli	2	32
Enterobacter spp.	1	>64
Klebsiella pneumoniae	1	64
Proteus mirabilis	8	>64
Indole+ Proteus	16	>64
Pseudomonas aeruginosa	16	>64
Serratia spp.	4	>64

Zhanel et al. Expert Reviews in Antiinfective Therapy 2012;10(4):459-473.

RESISTANCE ALLIANCE CARA

Activity of Plazomicin vs. Organisms With Defined Aminoglycoside Resistance Mechanisms

Species	Resistance Phenotype	MIC_{90} (µg/ml)	
		Plazomicin	Gent
Escherichia coli (includes ESBL)	ATCC 25922	0.25	0.5
	AAC(3)-II	2	>64
	AAC(3)-IV	1	32
	AAC(6')-I	0.25	2
	ANT(2")-I	1	>64
	APH(3')-I	0.25	0.25
	AAC(3)-II; ANT(3")-I	1	>32
	AAC(3)-II; AAC(6')-I	2	>32
	AAC(3)-II, APH(3)-I/II	1	>16

Zhanel et al. Expert Reviews in Antiinfective Therapy 2012;10(4):459-473.

RESISTANCE ALLIANCE CARA

Plazomicin Clinical Trials

- **Phase 2:** (15mg/kg IV)
  - cUTI (versus levofloxacin)

- **Phase 3:**
  - **EPIC** (**E**valuating **P**lazomicin **I**n **c**UTI), **609 patients** versus meropenen
  - **CARE** (**C**ombating **A**ntibiotic **R**esistant **E**nterobacteriaceae) **69 patients** with serious bacterial infections due to CRE. …**lower** rate of mortality **or** serious disease-related complications observed for plazomicin compared to colistin therapy

Conclusions - Plazomicin

- Promising new agent versus MDR GNB
- Appeal of new agent in a well described class
- Need MORE human efficacy and safety data
- Monitor spread of rRNA methylases (NDM-1)
- Clinical trials continue…
  - **nephrotoxicity and/or ototoxicity versus legacy aminoglycosides ?**

… Submit to FDA Later 2017 ?

López-Diaz et al. AAC 2017 Jan 24;61(2).
Zhanel et al. Exp Rev Antiinf Ther 2012;10(4):459-473.

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

New/Investigational Agents vs. MDR Gram-positive Pathogens (eg. MRSA)

- Ceftobiprole
- Telavancin

- Oritavancin
- Dalbavancin

- High Dose Daptomycin
- Tedizolid
- Eravacycline/omadacycline
- Solithromycin
- Ceftaroline
- Delafloxacin
- AFN-1252

ICAAC/ICC 2015, ASM Microbe 2016.
Deak et al. Ann Intern Med 2016;165:363-372.
Butler, Blaskovich and Cooper. J Antibiot 2017;70:3-24.

Ceftobiprole

- Gram-positive cocci:
  - *S. aureus*/**MRSA**/MRSE/**PRSP**/*E. faecalis*
- Gram-negative bacilli:
  - **Enterobacteriaceae**
  - AmpC but not ESBL
  - ***P. aeruginosa***

- **Indications:**
  - **CAP (ceftriaxone +/- linezolid)** **[Nicholson et al. IJAA 2012]**
  - **HAP (ceftazidime + linezolid)** **[Awad et al. CID 2014]**

Walkty et al. DMID 2011; 66(2):343-349.;
Zhanel et al. Am J Clin Derm 2008;9(4):245-254.; Walkty et al. JAC 2008; Jul;62(1):206-8.

Ceftobiprole Activity vs. GPC

(CANWARD 2015-2016, $MIC_{50/90;}$ Eucast BP: *S. aureus* ≤2 ug/ml)

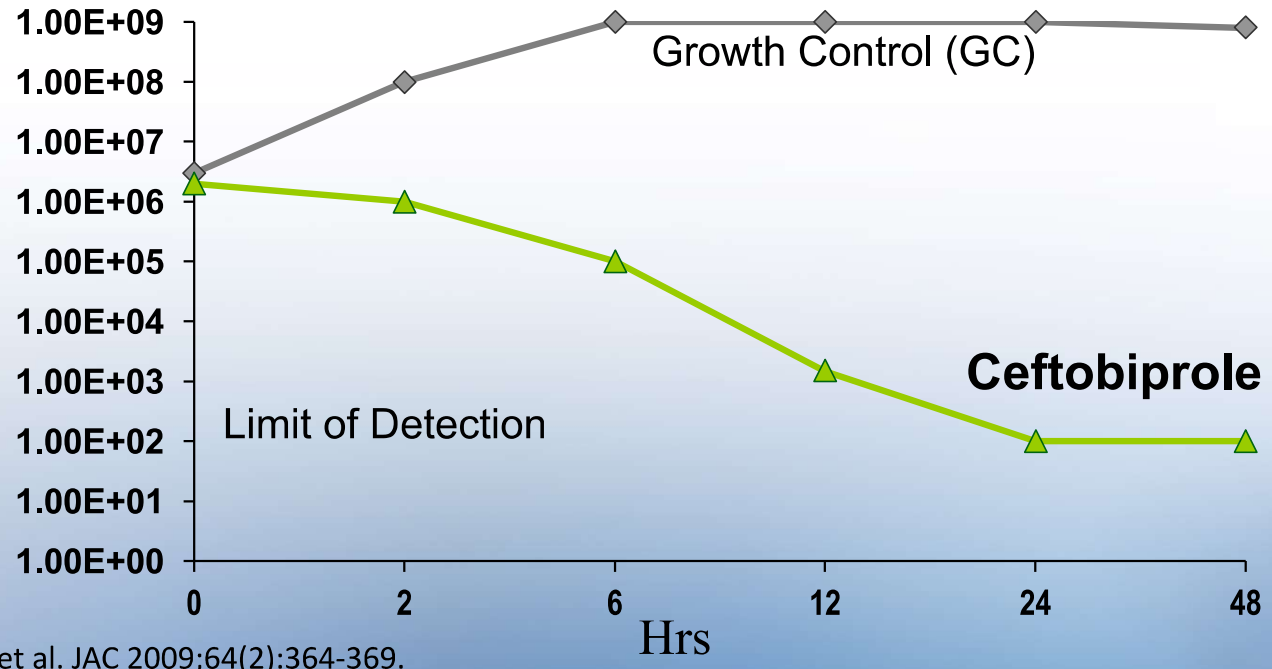
Organism (#)	Ceftobiprole	Vancomycin	Ceftriaxone
S. aureus (1414)	0.5/1	1/1	4/>64
MRSA (253)	1/2	1/1	>64/>64
HA-MRSA (114)	1/2	1/1	>64/>64
CA-MRSA (95)	1/1	1/1	64/>64
S. epidermidis (170)	0.5/1	1/2	4/>64
S. pneumoniae (260)	≤0.03/≤0.03	≤0.25/0.25	≤0.12/≤0.12
Pen-R SPN (10)	0.12/0.25	≤0.25/0.25	0.5/1

Zhanel et al. ASM Microbe 2017.; Zhanel et al. JAC 2013.; Walkty et al. DMID 2011.

Ceftobiprole Kills MRSA

(Simulating 1g IV, (*f*Cmax 35 μg/mL, $t_{1/2}$ 3.5 hrs)

(Strain #61592, Ceftobiprole MIC 1 μg/mL)



Zhanel et al. JAC 2009;64(2):364-369.

Ceftobiprole Activity vs. GNB

(CANWARD 2015-2016, $MIC_{50/90;}$ Eucast BP: Enterobacteriaceae ≤0.25 ug/ml)

Organism (#)	Ceftobiprole	Vancomycin	Ceftriaxone
E. coli ALL (1172)	≤0.06/2	>64/>64	≤0.06/32
E. coli AmpC (10)	0.25/0.5	>64/>64	8/32
E. coli ESBL (69)	>32/>32	>64/>64	64/>64
K. pneumoniae (382)	≤0.06/0.12	>64/>64	≤0.25/≤0.25
P. aeruginosa (695)	2/8	>64/>64	16/>64

Zhanel et al. ASM Microbe 2017.; Zhanel et al. JAC 2013.;
Walkty et al. DMID 2011.; Walkty et al. JAC 2008.

Ceftobiprole Conclusions Today…

- **Bactericidal Gram-positive activity (MRSA) as good as or better than vancomycin**
- **Bactericidal Gram-negative (Enterobacteriaceae) activity better than ceftriaxone**
- ***P. aeruginosa* activity similar to ceftazidime**
- **?? HAP instead of ceftriaxone + vancomycin**
- **?? CAP when worried about CA-MRSA**
- **?? MRSA instead of vancomycin/linezolid/daptomycin**

Telavancin
(10mg/kg IV OD)

Indications

- **HAP/VAP (MRSA)**
- **cSSSI**

Strengths

- **Kills MRSA better than vancomycin**
  - **In vitro**
  - **In vivo**
  - **Clinical trials**

Zhanel et al. Drugs 2010;70(7):859-886.
Karlowsky, Nichol and Zhanel CID 2015;61(Suppl2):58-68.

Telavancin is Active vs All MRSA (CANWARD 2013)

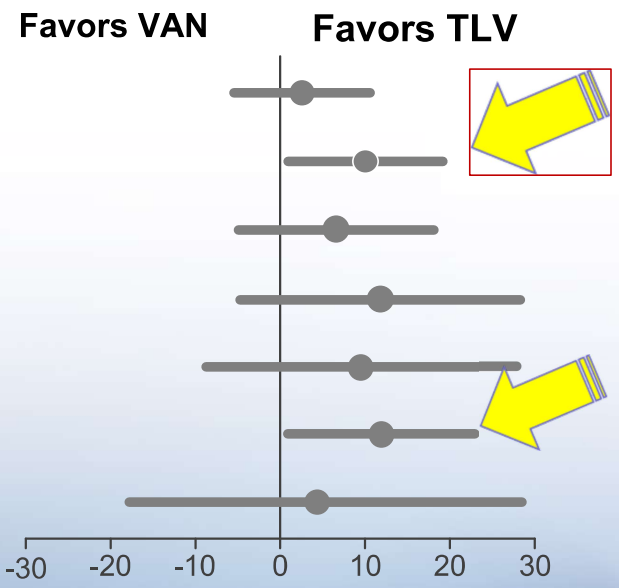
Antibiotic	MIC $_{50}$ (ug/ml)	MIC $_{90}$ (ug/ml)	Fold > Vanco
Vancomycin	0.5	1	
Telavancin	**0.06**	**0.06**	**8-16**
Linezolid	2	2	

Karlowsky, Nichol and Zhanel CID 2015;61(Suppl2):58-68.

Telavancin vs Vancomycin in HAP/VAP

ATTAIN 1, ATTAIN				
	TLV Cured/n	VAN Cure/n	Delta	95% CI
All *S. aureus*	171/219	161/214	3.00	(-5.00, 11.00)
Mono *S. aureus*	123/146	113/152	9.9	(0.7, 19.1)
Mono MRSA	72/88	86/116	7.9	(-3.5, 19.3)
Mono MSSA	51/58	27/36	12.2	(-4.2, 28.8)
VAN MIC<=0.5	33/37	22/28	10.1	(-9.00, 28.8)
VAN MIC>=1	74/85	78/105	12.5	(0.5, 23.0)
Mono *S. pneumonaie*	18/20	18/21	5.9	(-19.1, 29.7)

Mono = monomicrobial.



Adapted from:
Sandrock & Shorr, 2015, CID, 61(Suppl2): 79-86
Rubinstein et al., 2011, CID 52:31-9

Telavancin Conclusions Today…

Versus vancomycin…

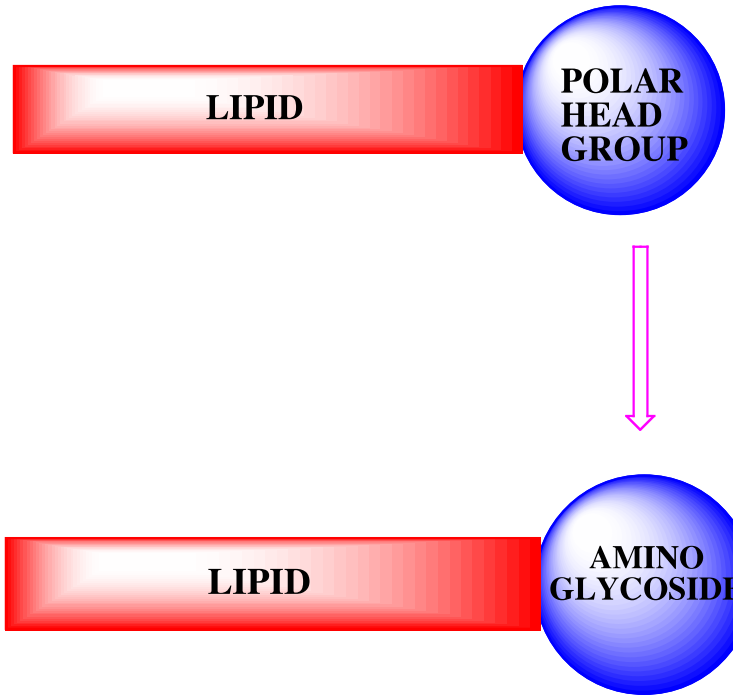
- **Kills MRSA better than vancomycin**
  - **In vitro**
  - **In vivo**
  - **Clinical trials**
- **? Alternative to vancomycin in MRSA HAP/VAP when vancomycin:**
  - **Adverse effects**
  - **Intolerance**
  - **Failure**
  - **MRSA MIC ≥ 1 ug/ml**

Oritavancin
(Single dose therapy-SSTI)

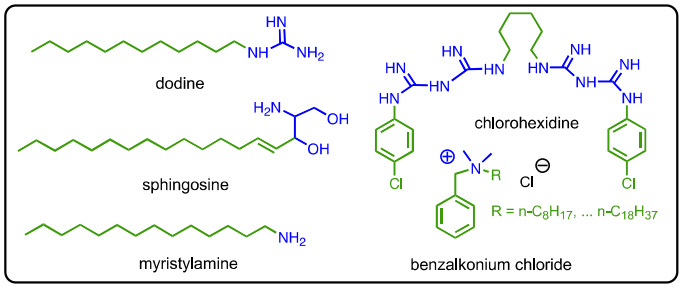
- Gram-positive cocci (**MRSA**), **VRE**
- t ½ ~ 390 hours (~16.3 days)
- **1 IV dose treatment regimen for skin/soft tissue infections (vs. vancomycin)**

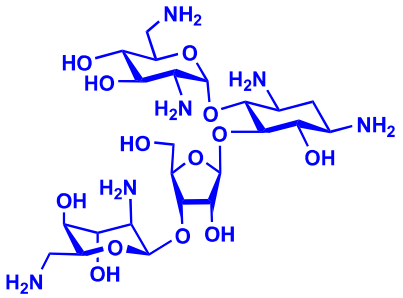
Zhanel et al. ERAT 2008;6:67-81.
Zhanel et al. Drugs 2010;70:859-886.
Zhanel et al. CID 2012;54 (Suppl 3):214-218.

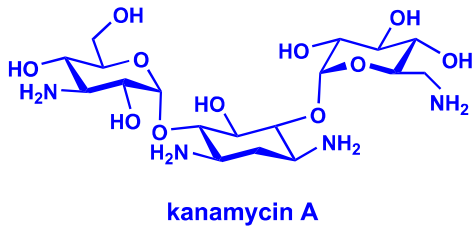
Aminoglycoside Hybrids



Aminoglycoside Antibiotics-derived Amphiphiles (AADAs)







Findlay, Zhanel and Schweizer. Antimicrobial Agents Chemother. 54, 4049-4058 (2010)

Conclusions – Good News !

- **We have new agents for resistant Gram-negative Bacilli (ESBL + CRE Enterics, MDR *P. aeruginosa*)**

- **We have new agents for resistant Gram-positive cocci (MRSA, VRE)**

Conclusions – Bad News

- Not all agents coming to Canada !
- cSSTI, cUTI/cIAI indications
- Need to do MIC testing (disks/Etest) in lab
- Need to get onto Vitek 2, Microscan