Infections à l'hôpital

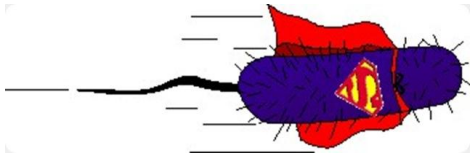
Vendredi 9 novembre 2012

INSTITUT MAURICE RAPIN

SANOFI

Quel avenir pour les carbapénémases ?

Perspectives du traitement antibiotique



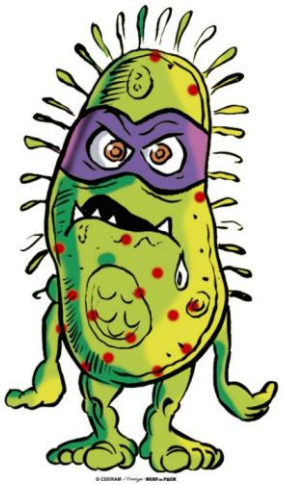
Benoit Guery

CHRU Lille

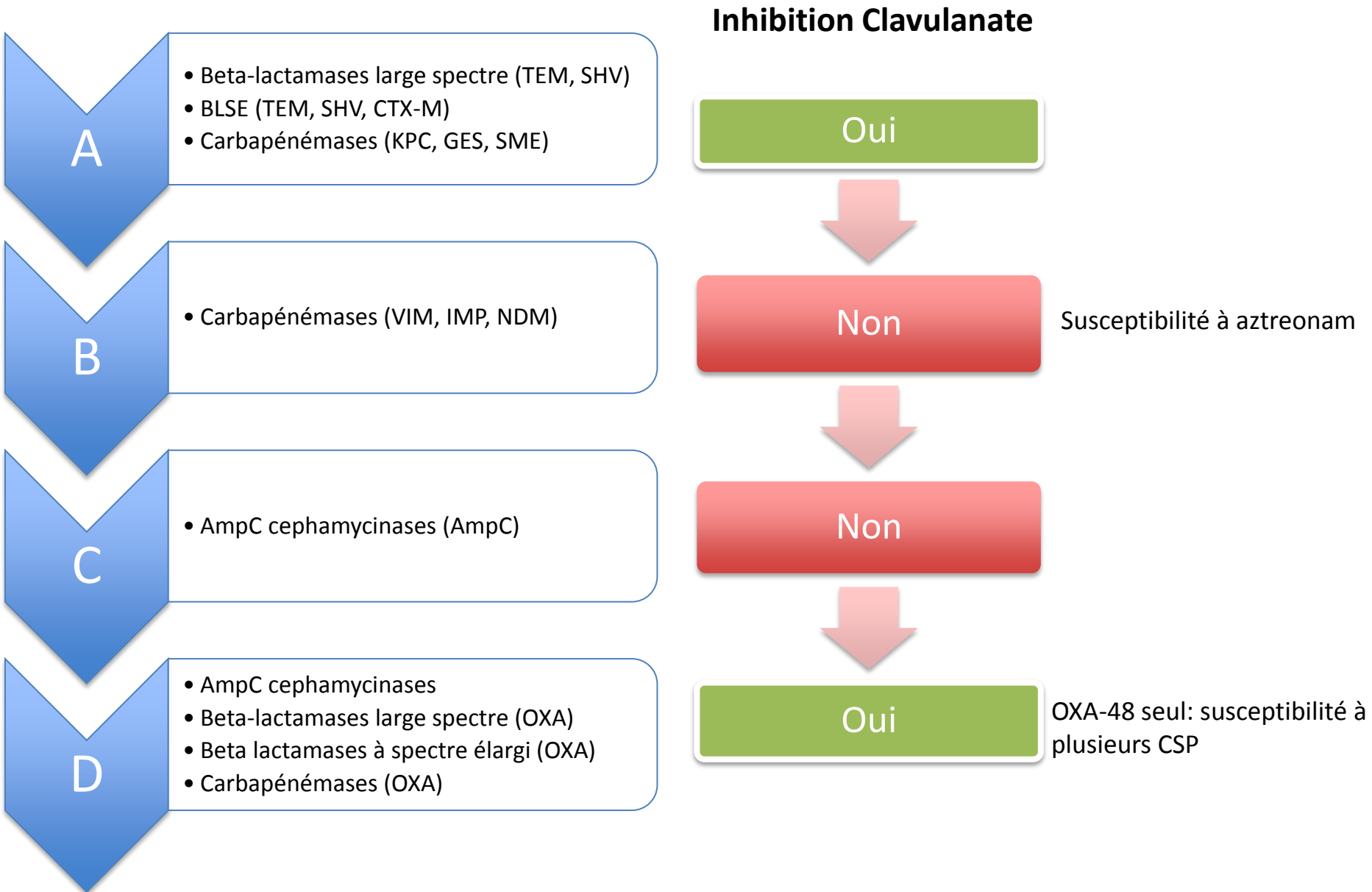
La Résistance

- ESKAPE pathogens
  - *Enterococcus faecium ,*
  - *Staphylococcus aureus,*
  - *Klebsiella pneumoniae ,*
  - *Acinetobacter species,*
  - *Pseudomonas aeruginosa,*
  - *Enterobacter species*

Carbapénémases



Classification des beta-lactamases

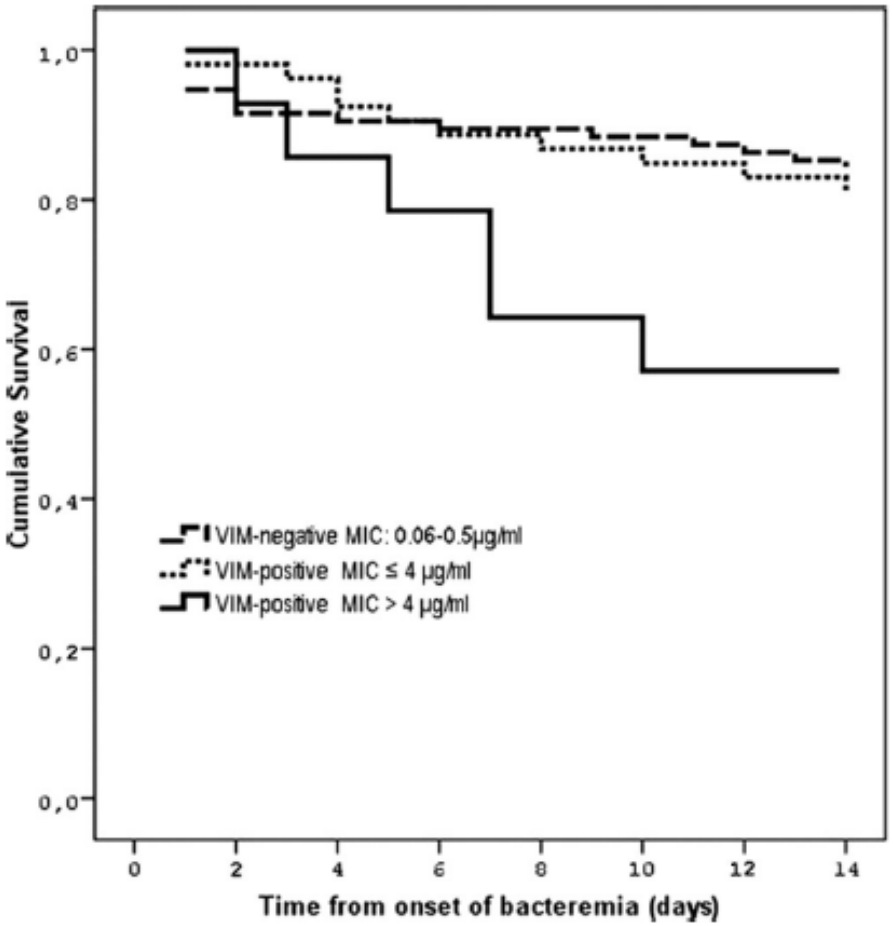


Prospective Observational Study of the Impact of VIM-1 Metallo-β-Lactamase on the Outcome of Patients with *Klebsiella pneumoniae* Bloodstream Infections[▽]

George L. Daikos,[1*] Panayiotis Petrikkos,[1] Mina Psichogiou,[1] Chris Kosmidis,[1] Evangelos Vryonis,[2] Athanasios Skoutelis,[2] Kleoniki Georgousi,[3] Leonidas S. Tzouvelekis,[4] Panayotis T. Tassios,[4] Christina Bamia,[5] and George Petrikkos[1]

A total of 162 patients were included in the analysis; 67 (41.4%) were infected with VPKP, and 95 were infected with non-VPKP.

OR: 2.83



Antimicrobial Agents and Chemotherapy, May 2009, p. 1868–1873

Attributable Mortality Rate for Carbapenem-Resistant *Klebsiella pneumoniae* Bacteremia

Abraham Borer, MD; Lisa Saidel-Odes, MD; Klaris Riesenberg, MD; Seada Eskira, RN, MPH; Nejama Peled, MSc; Ronit Nativ, RN, MPH; Francisc Schlaeffer, MD; Michael Sherf, MD

32 patients developed bacteremia due to carbapenem-resistant *K. pneumoniae*

TABLE 3. Mortality Rates and Risk of Death Associated with Carbapenem-Resistant *Klebsiella pneumoniae* Bacteremia

Variable	No. (%) of subjects
Case subjects ($n = 32$)	
Crude mortality rate	23 (71.9)
Attributable mortality rate[a]	16 (50)
Control subjects ($n = 32$)	
Crude mortality rate	7 (21.9)

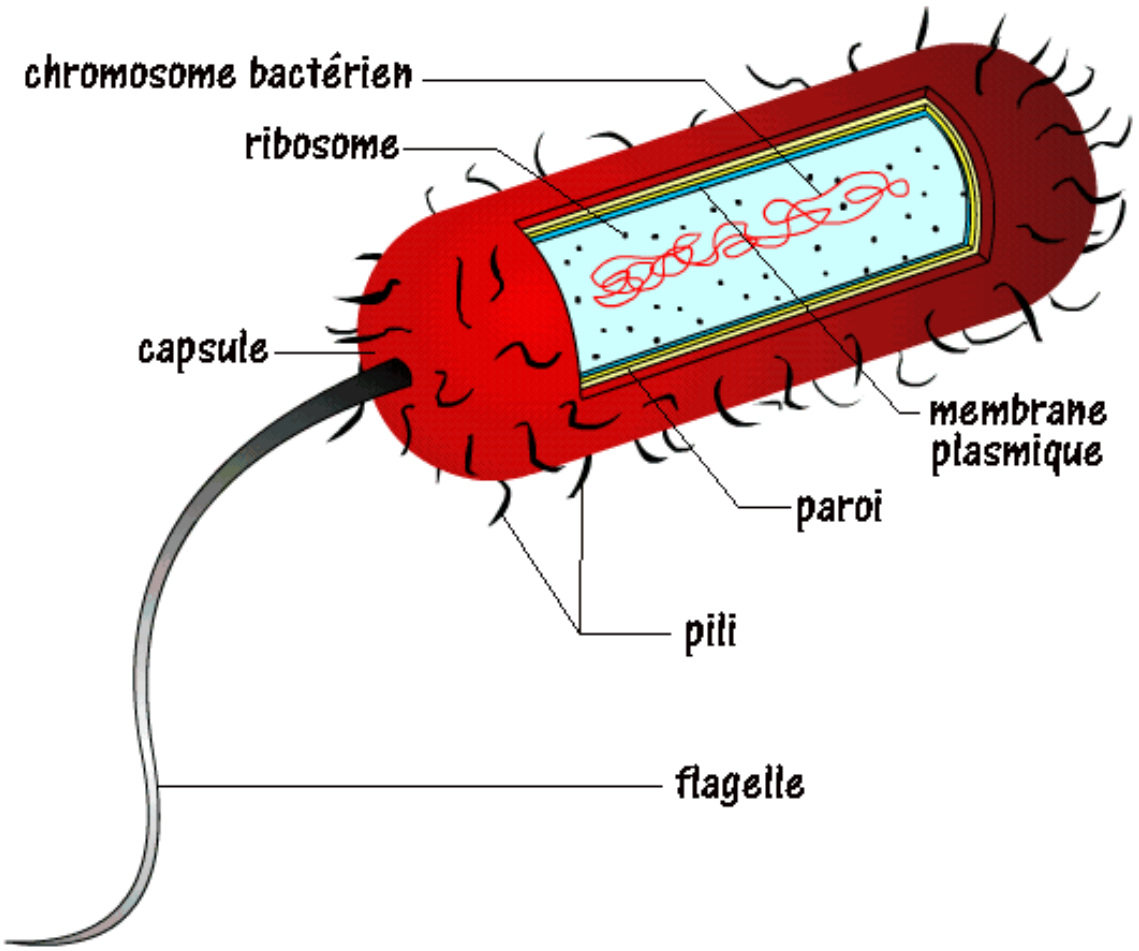
[a] 95% confidence interval, 15.3%–98.6%; the risk ratio was 3.3 (95% confidence interval, 2.9–28.5.

Mode de fonctionnement des antibiotiques

Inhibition de la synthèse paroi/membrane
Beta-lactamines
Fosfo

Inhibition de la synthèse protéique
Aminosides
Cyclines

Inhibition de la synthèse ADN
Quinolones



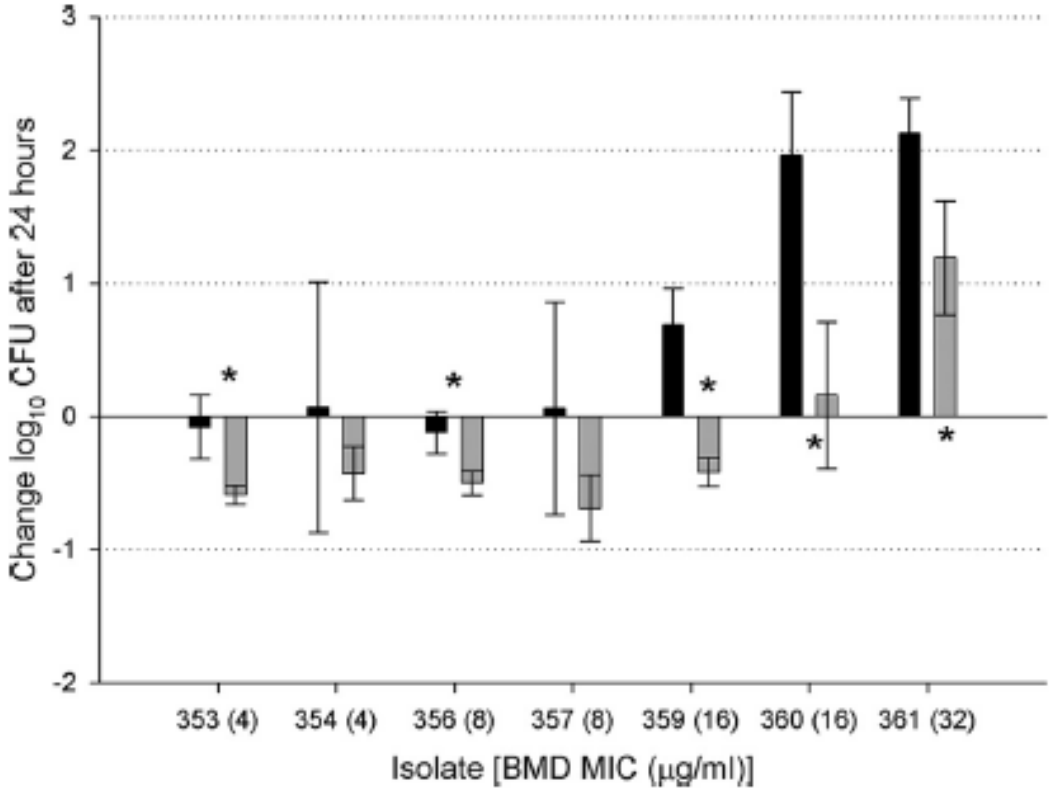
Plus haut….?

In Vivo Efficacy of Simulated Human Dosing Regimens of Prolonged-Infusion Doripenem against Carbapenemase-Producing *Klebsiella pneumoniae*[▽]

Catharine C. Bulik[1] and David P. Nicolau[1,2]*

Modèle murin d'infection de cuisse sur souris neutropénique
Modélisation de l'administration prolongée de doripénème 1g/2g sur 4h/8h

Isolate	MIC (μg/ml) by:	
	BMD	Etest
KPC 353	4	3
KPC 354	4	4
KPC 356	8	12
KPC 357	8	6
KPC 359	16	>32
KPC 360	16	16
KPC 361	32	>32



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Oct. 2010, p. 4112–4115

En clinique

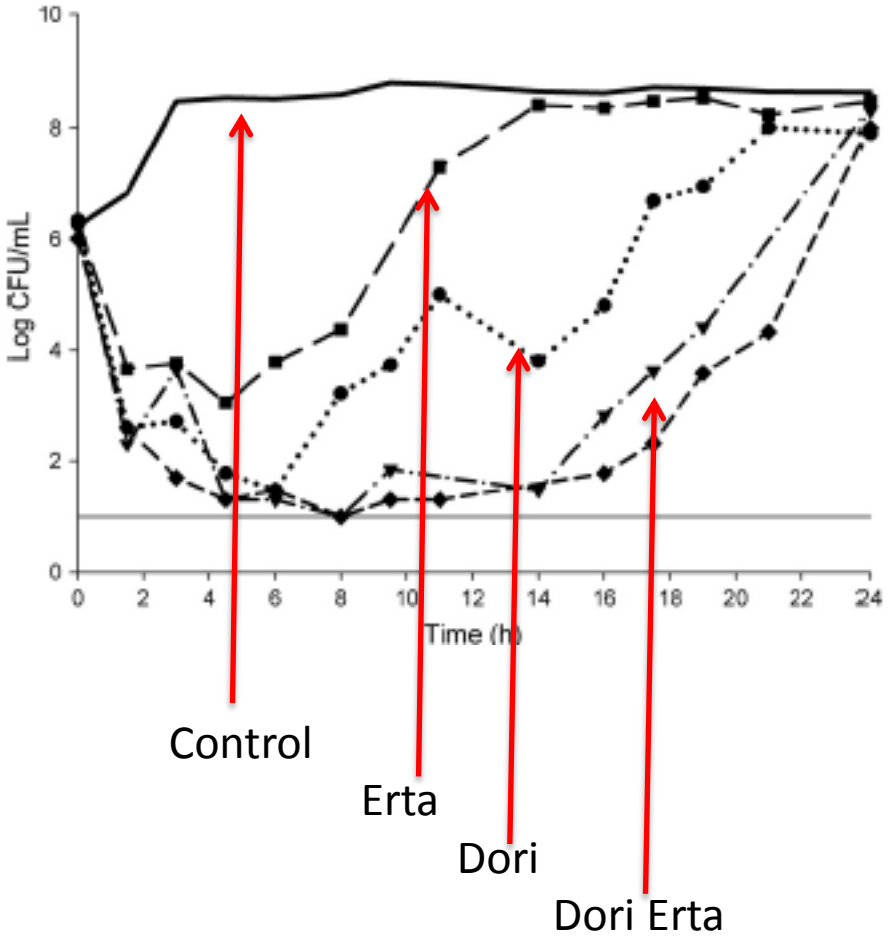
- Les CMI sont variables
- Possibilité d'utilisation si CMI très basses (imipénème, méropénème)
- Possibilité d'acquisition de résistance sous traitement
- Monothérapie par carbapénème n'est pas supérieure à une antibiothérapie inadaptée en terme mortalité (Falagas et al, JAC 2007)
- Pour KPC: échec dans 56% des cas avec imipénème et méropénème avec imipénème sensible

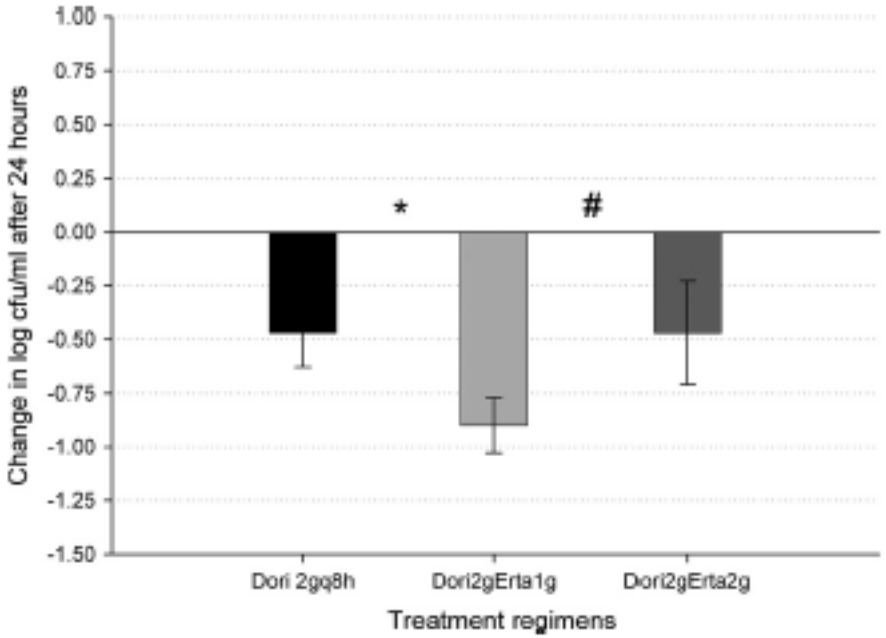
	CLSI		EUCAST	
	S	R	S	R
Imipénème	4	8	2	8
Méropénème	4	8	2	8
Ertapénème	4	4	0,5	1
Doripénème	ND	ND	1	4

Double-Carbapenem Therapy for Carbapenemase-Producing *Klebsiella pneumoniae*[▽]

Catharine C. Bulik[1] and David P. Nicolau[1,2]*

Modèle murin d'infection de cuisse sur souris neutropénique





ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, June 2011, p. 3002–3004

Journal of Antimicrobial Chemotherapy (2009) **64**, 326–329
doi:10.1093/jac/dkp197
Advance Access publication 2 June 2009

JAC

In vitro activity of the β-lactamase inhibitor NXL104 against KPC-2 carbapenemase and Enterobacteriaceae expressing KPC carbapenemases

Thérèse Stachyra, Premavathy Levasseur, Marie-Claude Péchereau, Anne-Marie Girard, Monique Claudon, Christine Miossec* and Michael T. Black

Short communication

International Journal of Antimicrobial Agents 39 (2012) 86–89

In vitro activity of avibactam (NXL104) in combination with β-lactams against Gram-negative bacteria, including OXA-48 β-lactamase-producing *Klebsiella pneumoniae*☆

Z. Aktaş[a,*], C. Kayacan[a], O. Oncul[b]

MIC90 values for the combination of avibactam 4 mg/L with imipenem, cefepime and ceftazidime were in the susceptible range for all strains (MIC90 ≤ 0.5 mg/L).

Evaluation of Ceftazidime and NXL104 in Two Murine Models of Infection Due to KPC-Producing *Klebsiella pneumoniae*▽

Andrea Endimiani,[1,2] Kristine M. Hujer,[1,2] Andrea M. Hujer,[1,2] Mark E. Pulse,[3] William J. Weiss,[3] and Robert A. Bonomo[1,2,4]*

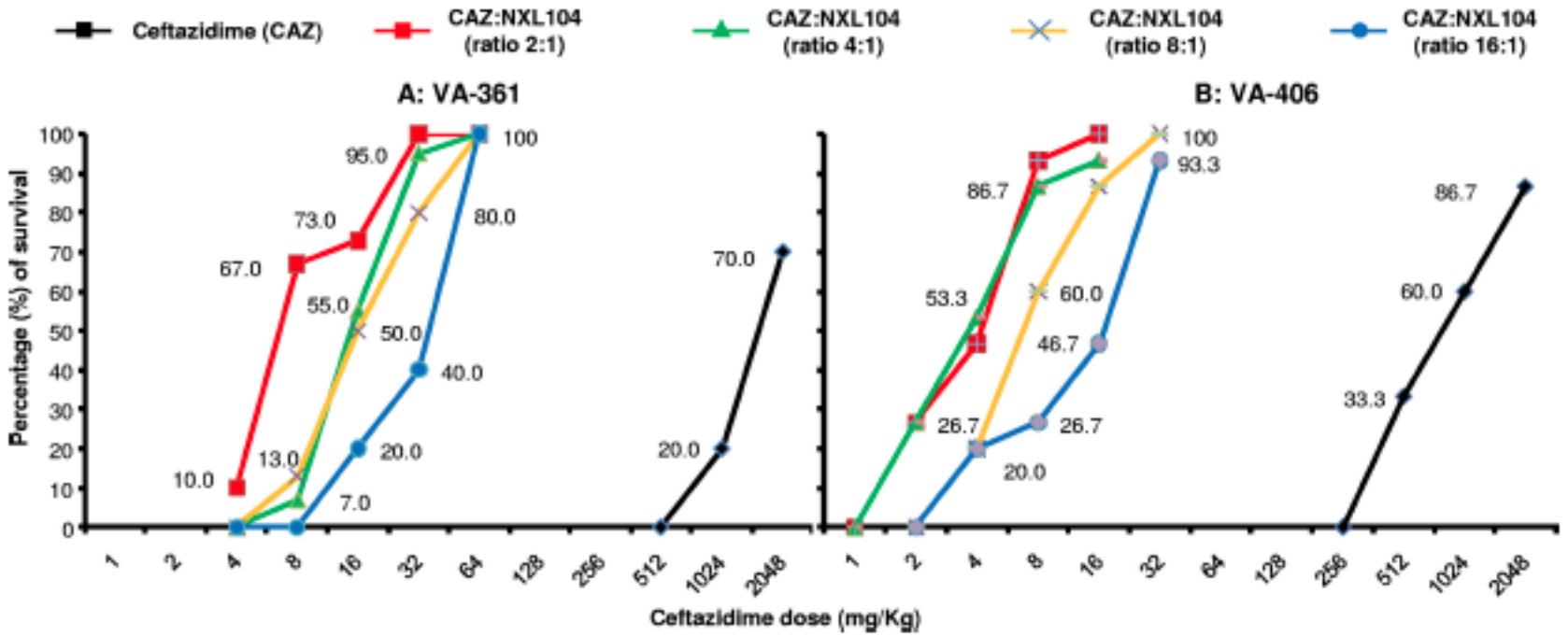


FIG. 1. Survival curves for mice treated with ceftazidime (CAZ) with and without NXL104 in the murine septicemia model due to KPC-producing *K. pneumoniae*. (A) Data regarding KPC-producing *K. pneumoniae* strain VA-361. (B) Data regarding KPC-producing *K. pneumoniae* strain VA-406.

Résistances croisées

- Quinolones
  - IMP-4 sensibilité conservée (Australie), 4 patients
- Aminosides, succès variables
- Associations à d'autres mécanismes touchant les beta-lactamines
  - BLSE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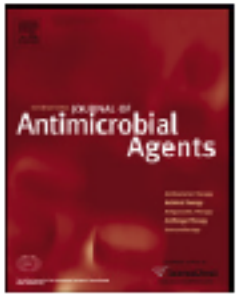
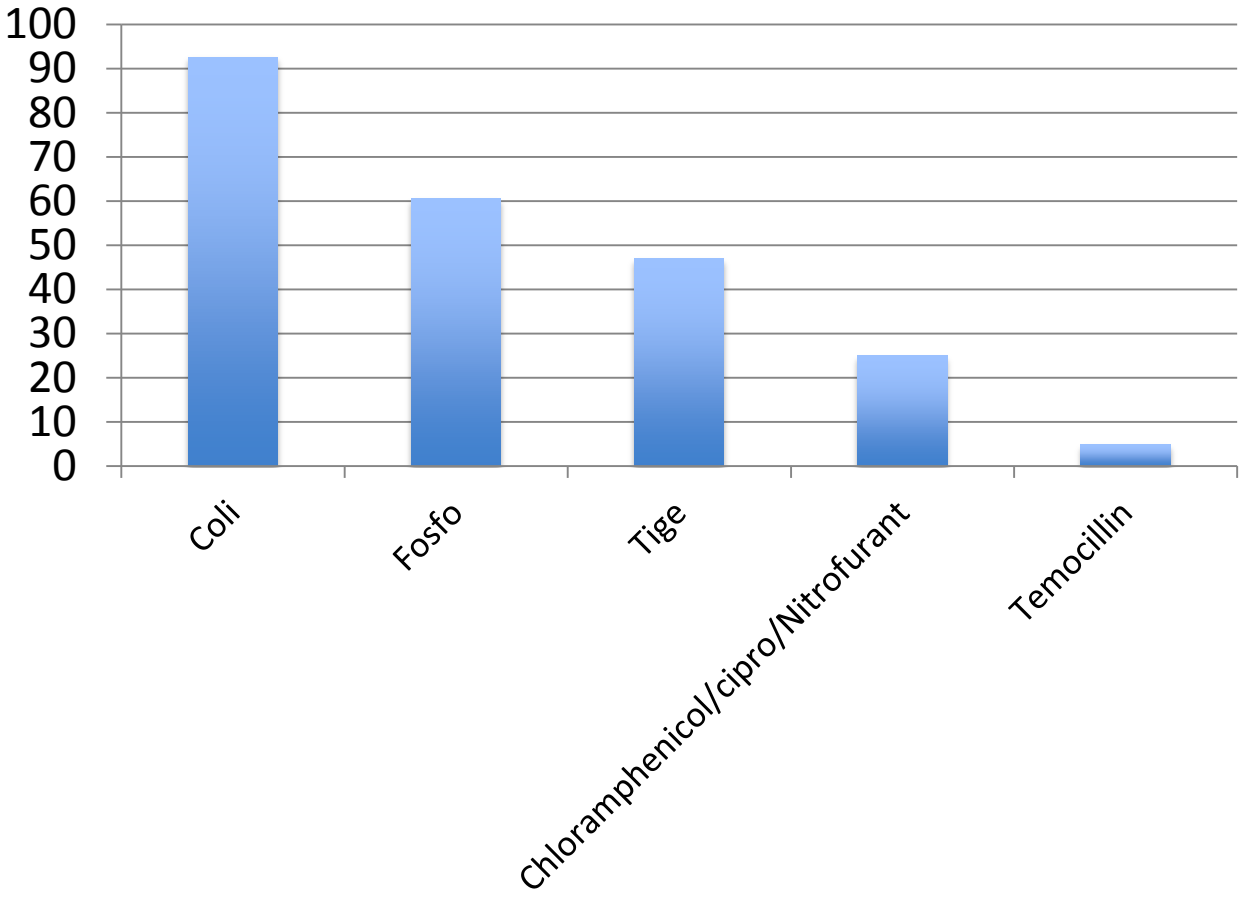
What remains against carbapenem-resistant Enterobacteriaceae? Evaluation of chloramphenicol, ciprofloxacin, colistin, fosfomycin, minocycline, nitrofurantoin, temocillin and tigecycline

David M. Livermore*, Marina Warner, Shazad Mushtaq, Michel Doumith, Jiancheng Zhang, Neil Woodford





International Journal of Antimicrobial Agents 37 (2011) 415–419

Colistin: The Revival of Polymyxins for the Management of Multidrug-Resistant Gram-Negative Bacterial Infections

Matthew E. Falagas[1,2,3] and Sofia K. Kasiakou[1]

REVIEWS OF ANTI-INFECTIVE AGENTS • **CID 2005:40 (1 May)** • 1333

Review

The revival of fosfomycin

Argyris S. Michalopoulos *, Ioannis G. Livaditis, Vassilios Gougoutas

Intensive Care Unit, Henry Dunant Hospital, 107 Mesogeion Ave, 11526 Athens, Greece

International Journal of Infectious Diseases 15 (2011) e732–e739


Colistin®
Colistimethate sodium for injection and inhalation
Taj Pharma India

Ascorbic acid protects against the nephrotoxicity and apoptosis caused by colistin and affects its pharmacokinetics

Jumana M. Yousef[1], Gong Chen[1], Prue A. Hill[2], Roger L. Nation[1]† and Jian Li[1]*†

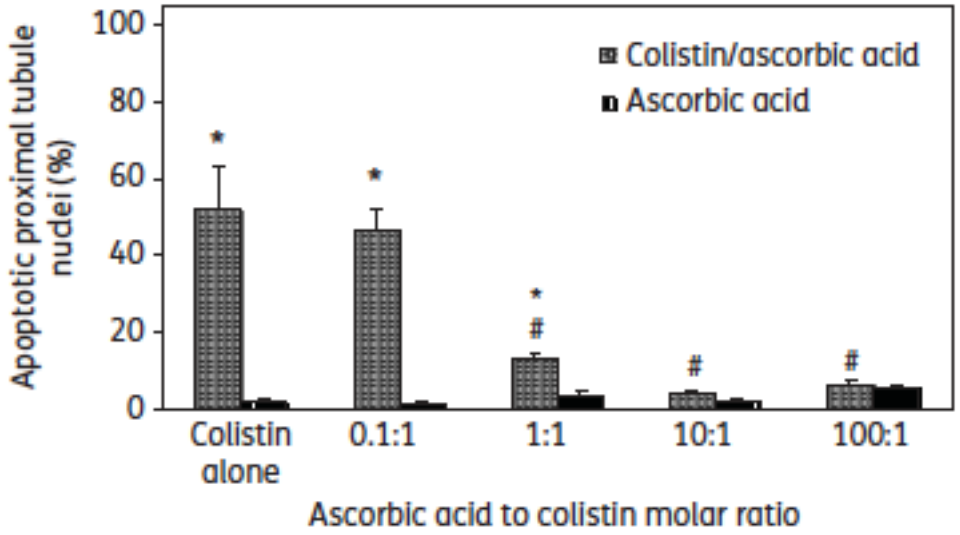
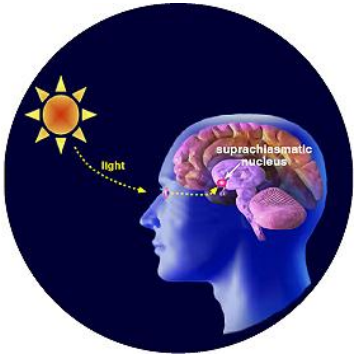


Figure 4. Percentage of TUNEL-positive apoptotic cells in rat proximal tubular cell line treated with 0.1 mM colistin alone or in the presence of various concentrations of ascorbic acid. *$P<0.005$ compared with corresponding control. #$P<0.0001$ compared with colistin alone.

J Antimicrob Chemother 2012; **67**: 452–459

Melatonin Attenuates Colistin-Induced Nephrotoxicity in Rats[▽]

Jumana M. Yousef,[1] Gong Chen,[1] Prue A. Hill,[2] Roger L. Nation,[1]* and Jian Li[1]*



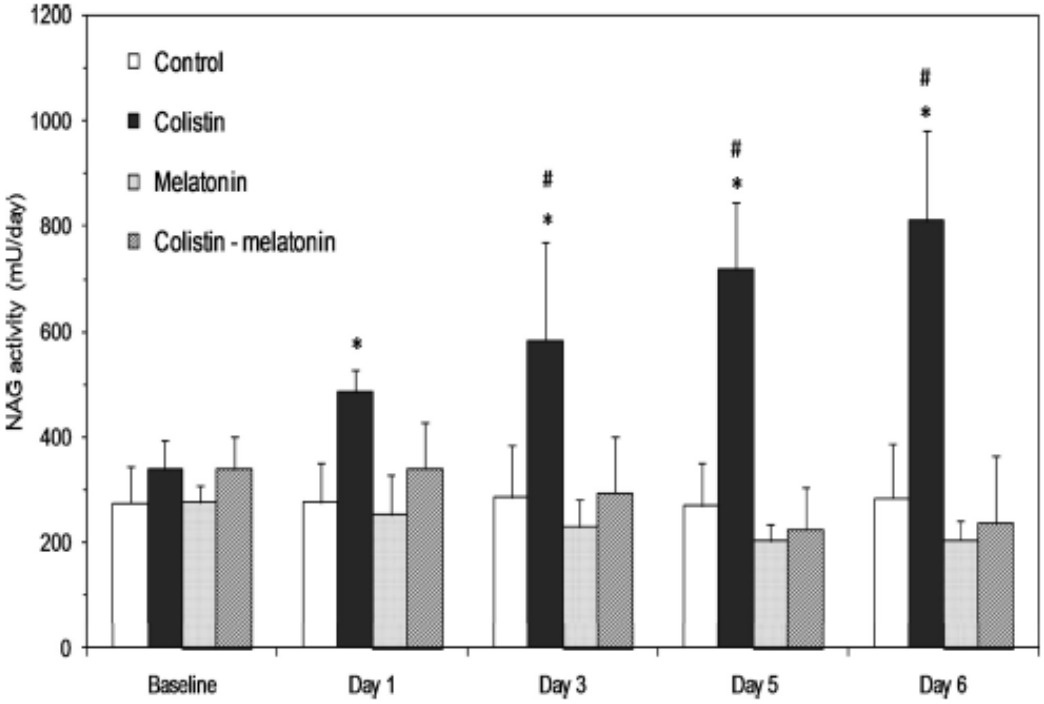
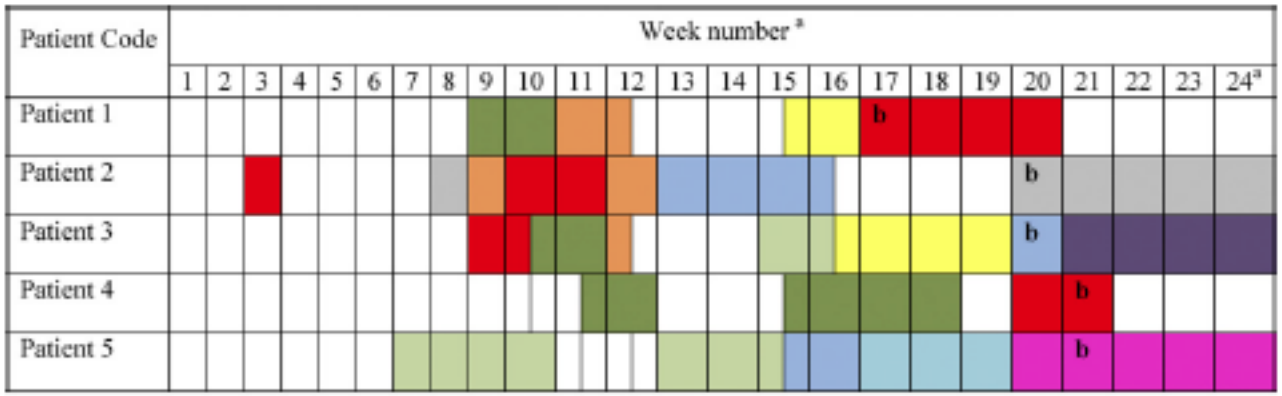


FIG. 1. Mean (±SD) urinary excretion of *N*-acetyl-β-D-glucosaminidase (NAG) in the control, colistin, melatonin, and colistin-melatonin groups. *, Significantly different from control group ($P < 0.0001$); #, significantly different from baseline for the same group ($P < 0.005$).

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Sept. 2011, p. 4044–4049

Outbreak of Colistin-Resistant, Carbapenem-Resistant *Klebsiella pneumoniae* in Metropolitan Detroit, Michigan[▽]

Dror Marchaim,[1]* Teena Chopra,[1] Jason M. Pogue,[2] Federico Perez,[3] Andrea M. Hujer,[3] Susan Rudin,[3] Andrea Endimiani,[3] Shiri Navon-Venezia,[4] Jatinder Hothi,[1] Jessica Slim,[1] Christopher Blunden,[1] Maryann Shango,[1] Paul R. Lephart,[5] Hossein Salimnia,[5] Deborah Reid,[1] Judy Moshos,[1] Wasif Hafeez,[1] Suchitha Bheemreddy,[1] Ting-Yi Chen,[1] Sorabh Dhar,[1] Robert A. Bonomo,[3,6] and Keith S. Kaye[1]



Legend to figure colors:

Medicine 1
Medicine 2
Medicine 3
Medicine 4
LTAC
Medicine 5
Medicine 6
Medicine 7
Surgery 1
Medicine 8

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Feb. 2011, p. 593–599


FOS
RA

Intravenous fosfomycin for the treatment of nosocomial infections caused by carbapenem-resistant *Klebsiella pneumoniae* in critically ill patients: a prospective evaluation

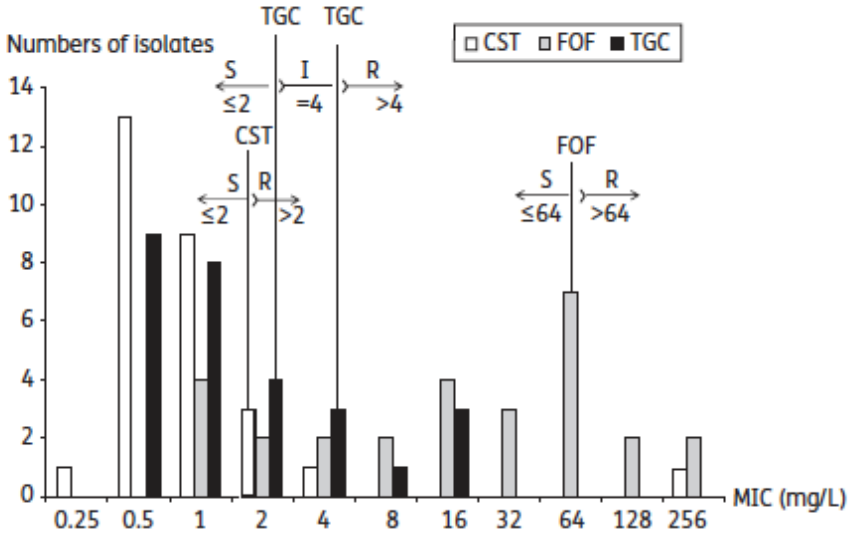
A. Michalopoulos[1,2], S. Virtzili[1], P. Rafailidis[2,3], G. Chalevelakis[2], M. Damala[4] and M. E. Falagas[2,3,5]

- Fosfomycin was administered in combination with
  - ✓ colistin (n = 6),
  - ✓ gentamicin (n = 3) and
  - ✓ piperacillin/tazobactam (n = 1), based on sensitivities.
- The mean ± SD duration of IF administration was 14.0 ± 5.6 days.
- There was a good bacteriological and clinical outcome of infection for all patients.
- All-cause hospital mortality was 18.2%.

Clinical Microbiology and Infection, Volume 16 Number 2, February 2010

In vitro evaluation of antibiotic synergy for NDM-1-producing Enterobacteriaceae

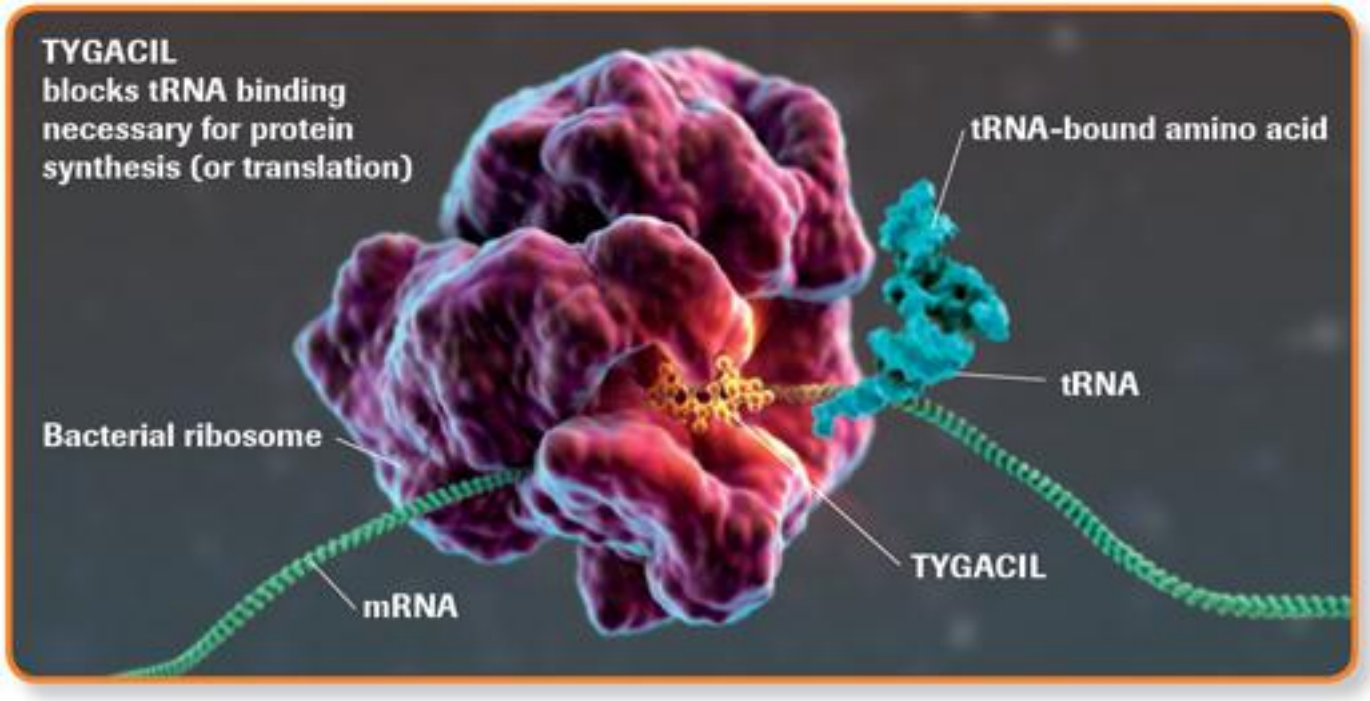
Béatrice Berçot[1,2]*, Laurent Poirel[1], Laurent Dortet[1] and Patrice Nordmann[1]



		Chequerboard synergy testing		
	Country of isolation	CST + FOF	CST + TGC	FOF + TGC
Susceptible isolates				
E. coli A	Australia	NI	NI	NI
E. cloacae D	India	synergy/NI	synergy/NI	NI
K. pneumoniae A	Kenya	NI	NI	NI
K. pneumoniae C	Sultanate of Oman	NI	NI	NI
K. oxytoca A	India	synergy/NI	NI	NI
E. coli J53 transconjugant (with *E. coli* A as donor)		NI	NI	NI
Resistant isolates[a]				
E. cloacae A	India	NI	NI	NI
K. pneumoniae E	India	synergy/NI	NI	NI
P. rettgeri	India	NI	NI	NI

J Antimicrob Chemother 2011; **66**: 2295–2297

Cyclines


TYGACIL
blocks tRNA binding
necessary for protein
synthesis (or translation)
tRNA-bound amino acid
tRNA
Bacterial ribosome
TYGACIL
mRNA

Treatment and Clinical Outcomes of Urinary Tract Infections Caused by KPC-Producing Enterobacteriaceae in a Retrospective Cohort

Bryan T. Alexander, PharmD[1,*]; Jonas Marschall, MD[2]; Robert J. Tibbetts, PhD[3,†]; Elizabeth A. Neuner, PharmD[1,‡]; W. Michael Dunne, Jr, PhD[3,§]; and David J. Ritchie, PharmD[1,4]

- 21 patients
- 76% de succès clinique et microbiologique
- Prise en charge
  - Pas antibiotiques 7/21
  - Aminosides: 7/21, 7 succès
  - Cipro: 3/21, 3 succès
  - Doxi: 3/21, 3 succès
  - Coli, Nitrofurant, Tigé

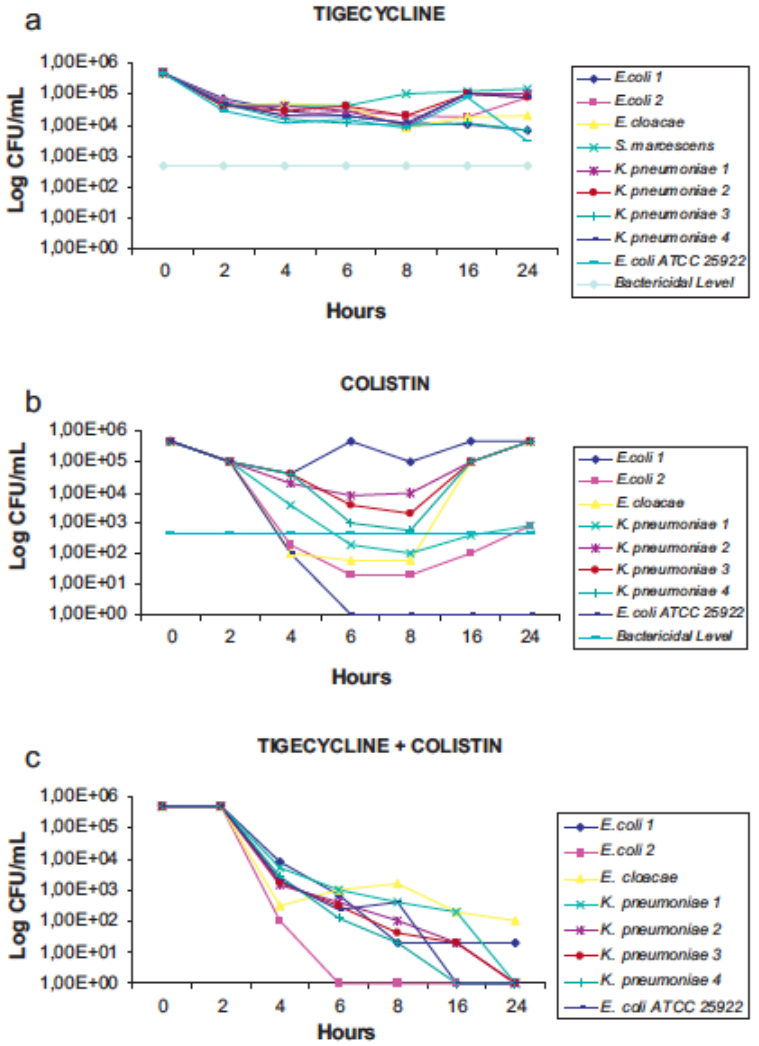
Clinical Therapeutics/Volume 34, Number 6, 2012

Activity of tigecycline alone and in combination with colistin and meropenem against *Klebsiella pneumoniae* carbapenemase (KPC)-producing Enterobacteriaceae strains by time–kill assay

Spyros Pournaras[a], Georgia Vrioni[b], Evangelia Neou[a], John Dendrinos[b], Evangelia Dimitroulia[b], Aggeliki Poulou[c], Athanassios Tsakris[b,*]

- L'association Tigé-mero jamais synergique sur les 8 souches testées

- Tigecycline alone might be a therapeutic option for infections caused by KPC-producers when bacteriostatic activity is adequate or combined with colistin when bactericidal activity is necessary



International Journal of Antimicrobial Agents 37 (2011) 244–247

In vitro activity of tigecycline against clinical isolates of carbapenem resistant *Acinetobacter baumannii* complex in Pretoria, South Africa

BMC Research Notes

Nahid H Ahmed[1*], Kamaldeen Baba[1,2], Cornelis Clay[1], Ruth Lekalakala[1,2] and Anwar A Hoosen[1,2]

A total of 232 carbapenem resistant clinical isolates of *A. baumannii* complex were collected over the six months study period.

Table 1 Patient and specimen information (N = 232)

Age groups	
≤ 30 years	87 (37.5%)
31–59 years	113 (48.7%)
≥ 60 years	32 (13.8%)
Gender	
Male	139 (59.9%)
Females	93 (40.1%)
Wards	
ICUs	145 (62.5%)
Non-ICUs	87 (37.5%)
Specimen type	
ETAs*	149 (64.2%)
Blood Culture	20 (8.6%)
Urine	15 (6.5%)
CVP tips**	11 (4.7%)
Other***	37 (15.9%)

*ETA = Endo-Tracheal Aspirates.
**CVP = Central Venous Puncture.
***Other = includes wound swabs, tissues and effusions.

Table 2 Antimicrobial susceptibility profile* of carbapenem resistant *A. baumannii* complex isolates (N = 232)

Antibiotic	Susceptible (µg/ml)	Intermediate (µg/ml)	Resistant (µg/ml)
Ampicillin	-	-	100.0% (≥ 32)
Amoxicillin/clavulanic acid	-	-	100.0% (≥ 32)
Piperacillin/tazobactam	-	-	100.0% (≥ 32)
Cefuroxime	-	-	100.0% (≥ 32)
Cefuroxime Axetil	-	-	100.0% (≥ 32)
Cefoxitin	-	-	100.0% (≥ 32)
Cefotaxime	-	-	100.0% (≥ 32)
Nitrofurantoin	-	-	100.0% (≥ 32)
Meropenem	-	-	100.0% (≥ 16)
Imipenem	-	-	100.0% (≥ 16)
Cefepime	-	0.4% (9 - 31)	99.6% (≥ 32)
Nalidixic acid	8.1% (≤ 2)	-	91.9% (≥ 32)
Ciprofloxacin	9.0% (≤ 1)	-	91.0% (≥ 4)
Trimethoprim/ Sulfamethoxazole	12.6% (≤ 20)	-	87.4% (≥ 320)
Ceftazidime	7.6% (≤ 8)	12.6% (9-31)	79.8% (≥ 64)
Gentamicin	9.4% (≤ 1)	12.6% (2-15)	78.0% (≥ 16)
Amikacin	78.0% (≤ 16)	11.7% (17-63)	10.3% (≥ 64)
Tigecycline	75.8% (≤ 0.25)	16.6% (1-7)	7.6% (≥ 8)
Colistin	100.0% (≤ 2)	-	-

* According to CLSI guidelines 2010 (MIC values in µg/ml).
- = none.

In Vivo Emergence of Tigecycline Resistance in Multidrug-Resistant *Klebsiella pneumoniae* and *Escherichia coli*

Teresa Spanu,[a] Giulia De Angelis,[b] Michela Cipriani,[b] Barbara Pedruzzi,[b] Tiziana D'Inzeo,[a] Maria Adriana Cataldo,[b]* Gabriele Sganga,[c] and Evelina Tacconelli[b]

Although resistance to tigecycline has been reported in surveillance studies, very few reports have described the emergence of resistance in vivo.

We report two cases of patients with infections due to SHV-12-producing Klebsiella pneumoniae and K. pneumoniae carbapenemase-3 (KPC-3)-producing Escherichia coli, which developed tigecycline resistance in vivo after treatment.

The reported limited experience underlines the risk of occurrence of a tigecycline MIC increase under treatment pressure

Antimicrob. Agents Chemother. 2012, 56(8):4516.

Treatment Outcome of Bacteremia Due to KPC-Producing *Klebsiella pneumoniae*: Superiority of Combination Antimicrobial Regimens

Zubair A. Qureshi,[a] David L. Paterson,[a,b] Brian A. Potoski,[a,c] Mary C. Kilayko,[d] Gabriel Sandovsky,[d] Emilia Sordillo,[d,e] Bruce Polsky,[d,e] Jennifer M. Adams-Haduch,[a] and Yohei Doi[a]

- A total of 41 unique patients with blood cultures growing KPC-producing K. pneumoniae were identified at two medical centers in the United States

- In the multivariate analysis,
  - ✓ definitive therapy with a combination regimen was independently associated with survival (odds ratio, 0.07, **P**0.02).
  - ✓ The 28-day mortality was 13.3% in the combination therapy group compared with 57.8% in the monotherapy group (**P**0.01).
  - ✓ The most commonly used combinations were colistin-polymyxin B or tigecycline combined with a carbapenem.

AAC April 2012 Volume 56 Number 4

ACHN-490, a Neoglycoside with Potent In Vitro Activity against Multidrug-Resistant *Klebsiella pneumoniae* Isolates[▽]

Andrea Endimiani,[1,2]* Kristine M. Hujer,[1,2] Andrea M. Hujer,[1] Eliana S. Armstrong,[3] Yuvraj Choudhary,[1] James B. Aggen,[3] and Robert A. Bonomo[1,2,4,5]*

MIC distributions of amikacin, gentamicin, tobramycin, and ACHN-490 against the overall collection of MDR K. pneumoniae isolates (n = 102) and the subgroup of KPC-producing strains (n = 25).

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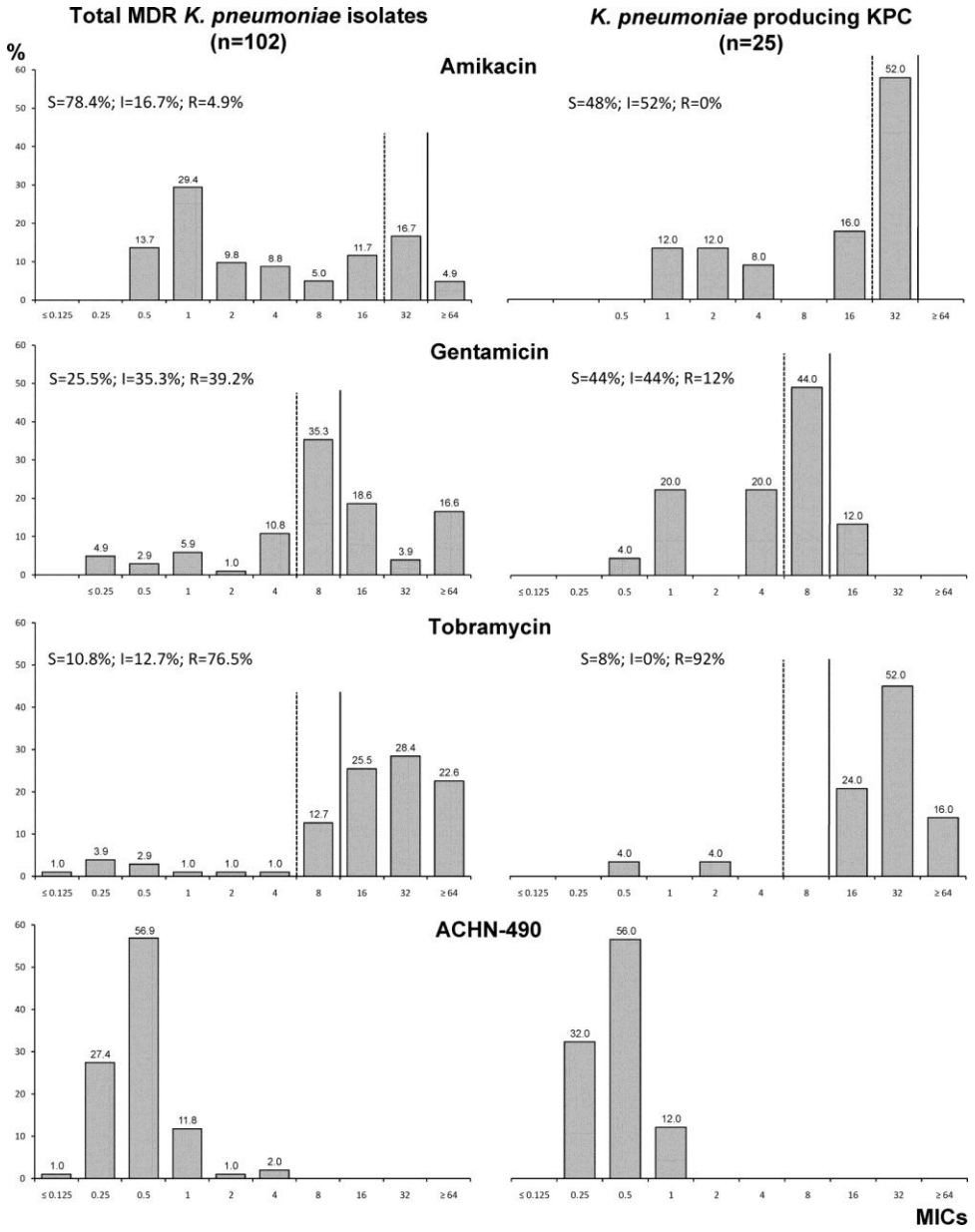

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Oct. 2009, p. 4504–4507

In Vivo Efficacy of the Novel Aminoglycoside ACHN-490 in Murine Infection Models[▽]

Noe Reyes, James B. Aggen, Corwin F. Kostrub*

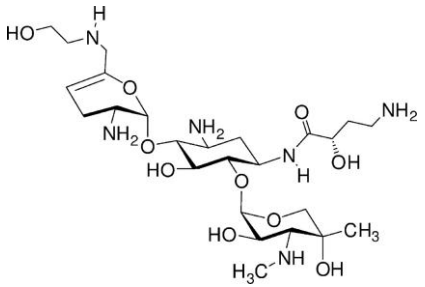

TABLE 4. Relationship between *in vitro* activity and *in vivo* efficacy for ACHN-490 and gentamicin in the mouse neutropenic thigh model

Organism	Phenotype	Strain no.	Gentamicin		ACHN-490	
			Static dose (mg/kg)	Static dose/MIC	Static dose (mg/kg)	Static dose/MIC
Escherichia coli	Susceptible	ATCC 25922	7.8 (5.9–14)[a]	16	11 (8.5–13)	11
	MDR	AECO1003	>64	NA[b]	25 (18–34)	25
Klebsiella pneumoniae	Susceptible	ATCC 43816	15 (13–17)	30	7.8 (6.2–9.7)	16
	MDR	AKPN1073	>64	NA	12 (8.4–16)	24
	KPC	AKPN1109	>64	NA	64 (23–130)	110
Serratia marcescens	KPC	ASMA1030	>64	NA	37 (31–44)	37
Staphylococcus aureus	Methicillin resistant	ATCC 33591	52 (41–67)	13	54 (44–56)	14

[a] Values in parentheses are 95% CIs.
[b] NA, not applicable.

However, gentamicin-resistant *Enterobacteriaceae* strains and those harboring the ***Klebsiella pneumoniae*** **carbapenemase** responded to ACHN-490 but not gentamicin, with static doses ranging from 12 mg/kg to 64 mg/kg for ACHN-490.

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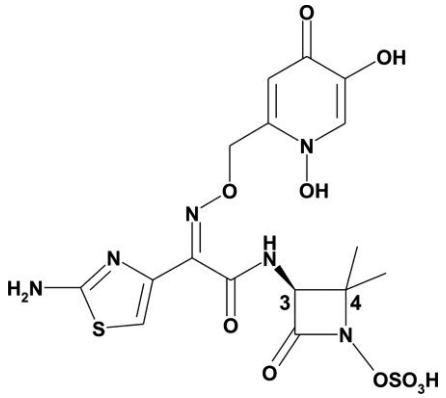
Journal of Antimicrobial Chemotherapy

In vitro activity of the siderophore monosulfactam BAL30072 against meropenem-non-susceptible *Acinetobacter baumannii*

Paul G. Higgins[1], Danuta Stefanik[1], Malcolm G. P. Page[2], Meredith Hackel[3] and Harald Seifert[1]*



Detection of synergy using the combination of polymyxin B with either meropenem or rifampin against carbapenemase-producing *Klebsiella pneumoniae*☆

George A. Pankey*, Deborah S. Ashcraft

Abstract

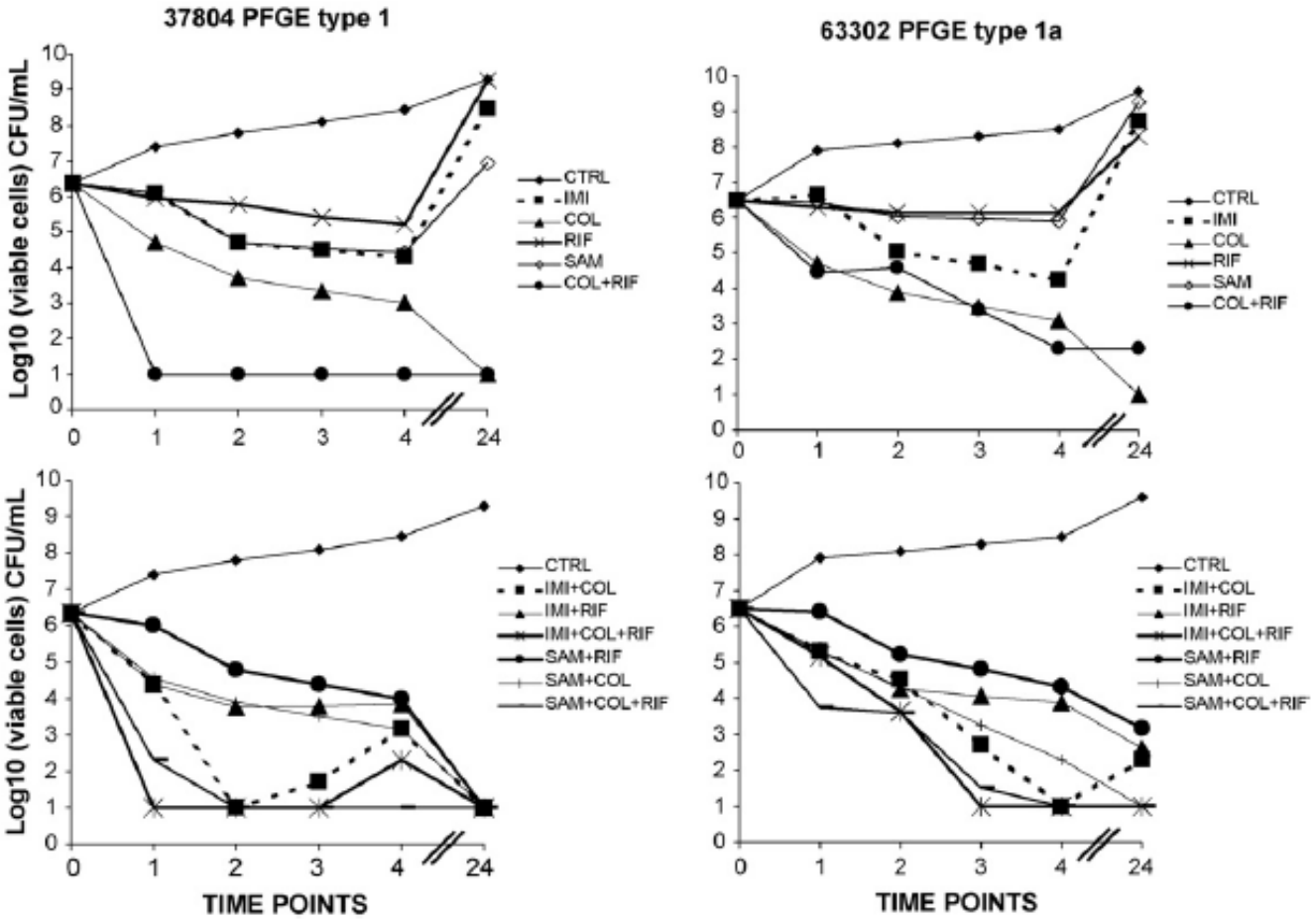
Polymyxin B (PB) plus meropenem (MER) or rifampin (RIF) was tested by Etest® method and time-kill assay (TKA) against 14 genetically unique clinical *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae*. PB + MER: Etest, 43% synergy; TKA, 64% synergy. Concordance between methods was 79%. For PB + RIF: Etest, 21% synergy; TKA, 100% synergy. Concordance between methods was 21%.

Keywords: *Klebsiella*; KPC; Meropenem; Polymyxin B; Rifampin; Synergy

Short communication

Comparative activities of colistin, rifampicin, imipenem and sulbactam/ampicillin alone or in combination against epidemic multidrug-resistant *Acinetobacter baumannii* isolates producing OXA-58 carbapenemases

Marie-Francoise Tripodi [a,b], Emanuele Durante-Mangoni [a,c], Rosaria Fortunato [a,b], Riccardo Utili [a,c,*], Raffaele Zarrilli [d,e]



International Journal of Antimicrobial Agents 30 (2007) 537–540

In Vivo Efficacy of Glycopeptide-Colistin Combination Therapies in a *Galleria mellonella* Model of *Acinetobacter baumannii* Infection

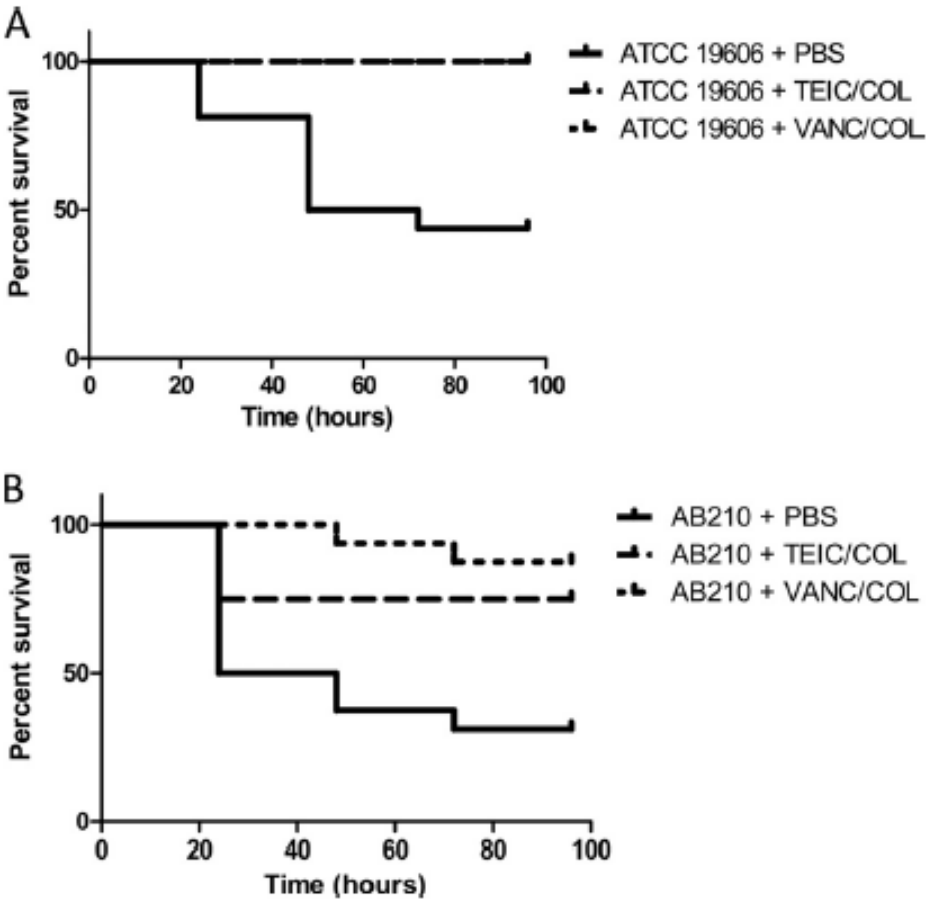
M. Hornsey and D. W. Wareham
Antimicrob. Agents Chemother. 2011, 55(7):3534. DOI: 10.1128/AAC.00230-11.
Published Ahead of Print 18 April 2011.

In Vivo Efficacy of Glycopeptide-Colistin Combination Therapies in a *Galleria mellonella* Model of *Acinetobacter baumannii* Infection▽

M. Hornsey[1] and D. W. Wareham[1,2]*

ATCC 19606: Antibiotic susceptible
AB210: MDR: OXA23 clone1

The effect is thought to be mediated via a permeabilizing effect of colistin on the outer membrane, facilitating the entry of glycopeptide molecules, which are usually excluded due to their size



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2011, p. 3534–3537

Current Concepts in Antimicrobial Therapy Against Resistant Gram-Negative Organisms: Extended-Spectrum β-Lactamase–Producing Enterobacteriaceae, Carbapenem-Resistant Enterobacteriaceae, and Multidrug-Resistant *Pseudomonas aeruginosa*

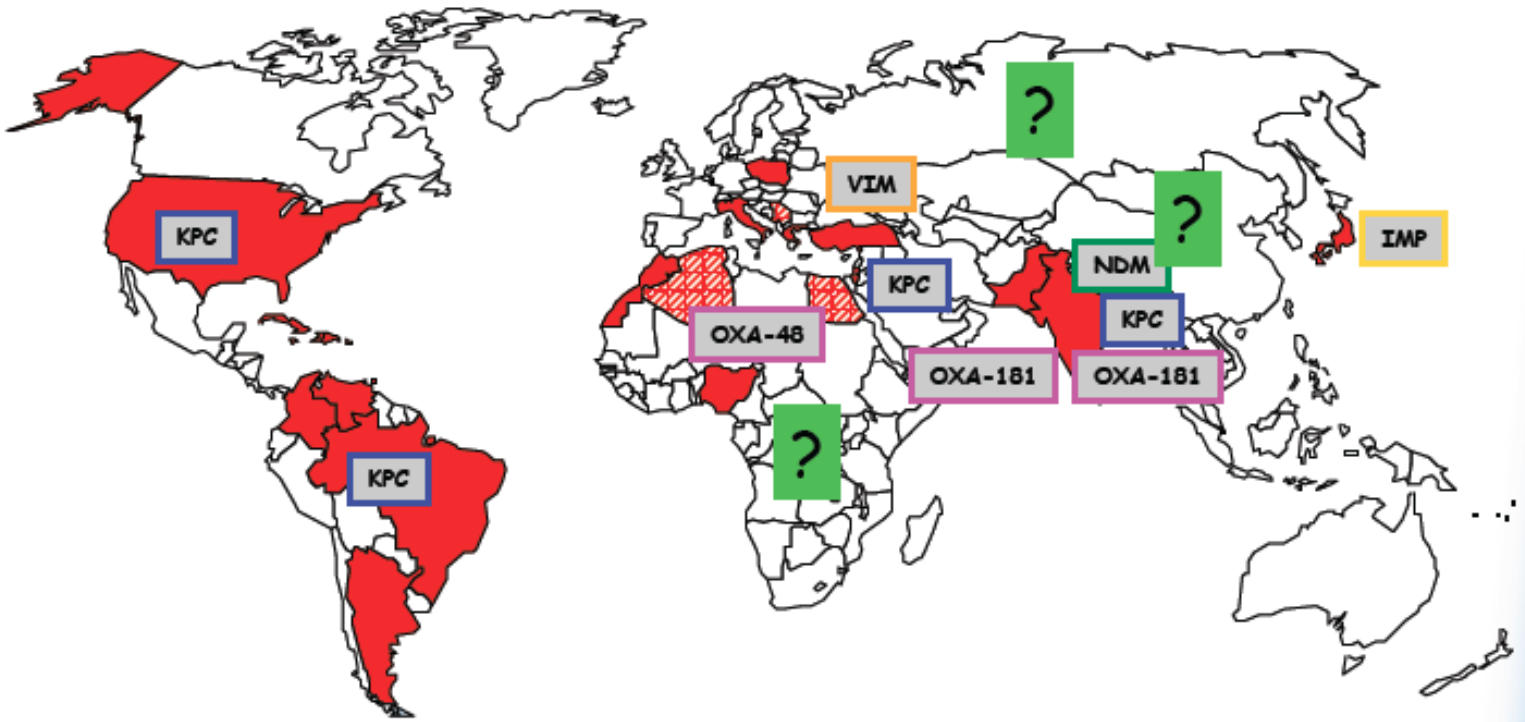
SOUHA S. KANJ, MD, AND ZEINA A. KANAFANI, MD

TABLE 3. **Suggested Approach to the Management of Patients With Serious Infections Due to Multidrug-Resistant Gram-Negative Pathogens**[a]

Organism	First-line therapy	Second-line therapy
Empirical therapy[b]		
Monomicrobial infection	Carbapenem	Piperacillin-tazobactam (low inoculum)
	Tigecycline (not in urinary tract infections) with or without an antipseudomonal agent	Colistin
Mixed gram-positive and gram-negative infection	Anti-MRSA agent plus a carbapenem	Anti-MRSA agent plus piperacillin-tazobactam (low inoculum)
	Tigecycline (not in urinary tract infections) with or without an antipseudomonal agent	Anti-MRSA agent plus colistin
Directed therapy[c]		
ESBL-producing Enterobacteriaceae	Carbapenems	Tigecycline (not in urinary tract infections)
	Piperacillin-tazobactam (low inoculum)	Fluoroquinolone
	Fosfomycin (oral formulation for simple urinary tract infections)	Colistin
Carbapenemase-producing Enterobacteriaceae	Tigecycline	Fosfomycin (parenteral formulation)
	Colistin	
Multidrug resistant *Pseudomonas aeruginosa*	Antipseudomonal agent (among carbapenems, use doripenem or meropenem)	Colistin
		Combination therapy

[a] ESBL = extended-spectrum β-lactamase; MRSA = methicillin-resistant *Staphylococcus aureus*.
[b] Local susceptibility patterns should be taken into consideration before deciding on empirical therapy.
[c] Based on available culture and susceptibility results.

Entérobactéries productrices de carbapénèmases: Réservoirs



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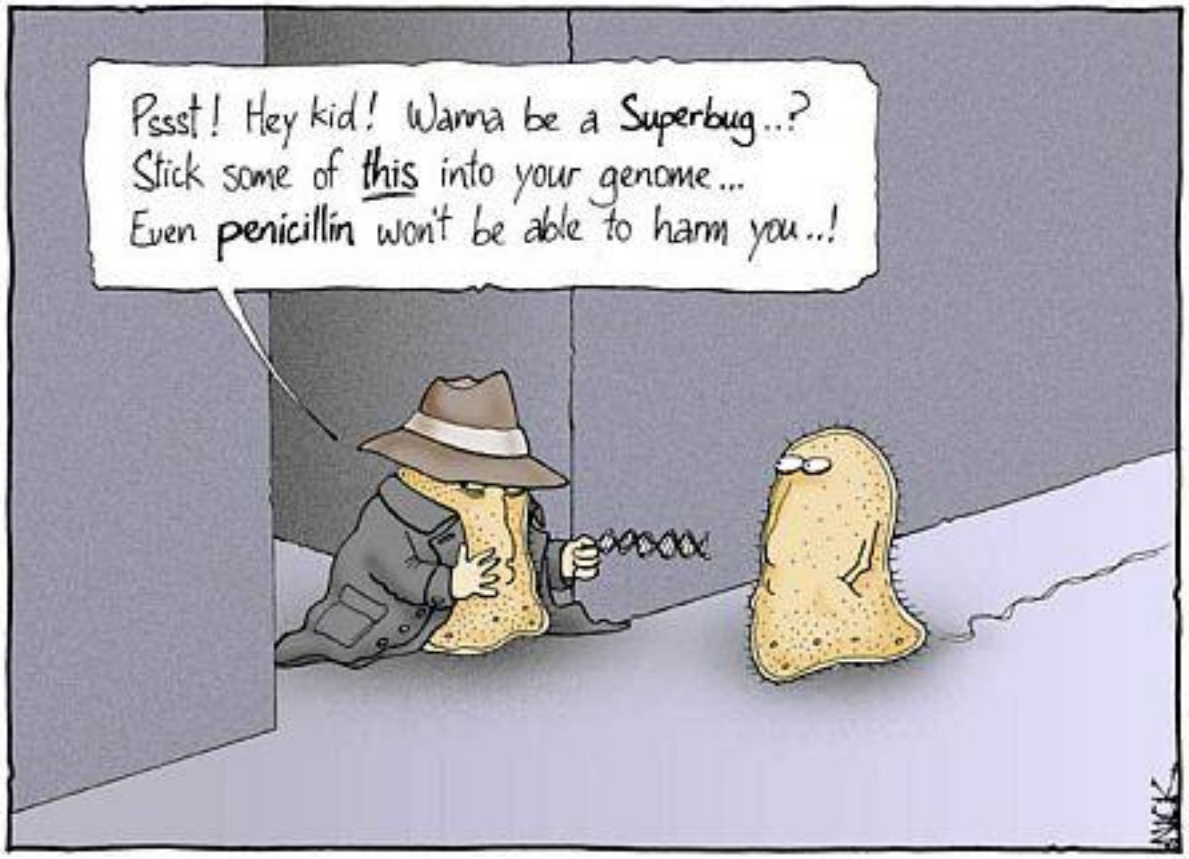
Pssst! Hey kid! Wanna be a Superbug..?
Stick some of this into your genome...
Even penicillin won't be able to harm you..!