XLVII CONGRESSO NAZIONALE AMCLI

10-13 Novembre 2018
Palacongressi Rimini

COMITATO DI STUDIO PER GLI ANTIMICROBICI
CoSA

Corso Precongressuale B:
L'antibiogramma, il biglietto da visita del microbiologo clinico

L'antibiogramma per i batteri MDR: tra esigenze cliniche e criticità diagnostiche

Luigi Principe

U.O.C Microbiologia e Virologia
Azienda Socio Sanitaria Territoriale di Lecco

Pandrug Resistance (P
Extensive Drug Resist
(XDR), and Multidrug
Resistance (MDR) amc
Gram-Negative Bacilli
Need for Internationa
Harmonization in

Matthew E. Falagas[1,2]
and Drosos E. Karageorgopoulos[1]

CORRESPONDENCE • CID 2008:46 (1 April) • 1121

ORIGINAL ARTICLE

Multidrug-resistant, extensively drug-resistant and pandru
bacteria: an international expert proposal for interim stan
definitions for acquired resistance

A.-P. Magiorakos[1], A. Srinivasan[2], R. B. Carey[2], Y. Carmeli[3], M. E. Falagas[4,5], C. G. Giske[6], S. Harbarth

International standard definitions for acquired resistance

CMI
CLINICA
MICROBIOLO
AND INFECTI

PDR = Pan Drug Resistance

Resistance to all possible effective antimicrobial agents

XDR = Extensive Drug Resistance

Resistance to all possible effective antimicrobial agents, except 1 or 2

MDR = Multi Drug Resistance

Resistance to at least 3 classes of potentially effective antimicrobial agents

K. pneumoniae KPC producer

Antibiotico	MIC mg/L(S/I/R)
Pip/Tazo	>64 (R)
Cefotaxime	>32 (R)
Ceftazidime	>32 (R)
Cefepime	>32 (R)
Ertapenem	>4 (R)
Imipenem	>8 (R)
Meropenem	>8 (R)
Amikacina	>64 (R)
Gentamicina	>16 (R)
Ciprofloxacina	>2 (R)
Tigeciclina	>4 (R)
Colistina	>8 (R)

PDR

XDR

Antibiotico	MIC mg/L(S/I/R)
Pip/Tazo	>64 (R)
Cefotaxime	>32 (R)
Ceftazidime	>32 (R)
Cefepime	>32 (R)
Ertapenem	>4 (R)
Imipenem	>8 (R)
Meropenem	>8 (R)
Amikacina	>64 (R)
Gentamicina	>16 (R)
Ciprofloxacina	>2 (R)
Tigeciclina	≤0.5 (S)
Colistina	≤0.5 (S)

XDR

Ceftazidime/Avibactam S

MDR

Antibiotico	MIC mg/L(S/I/R)
Pip/Tazo	>64 (R)
Cefotaxime	>32 (R)
Ceftazidime	>32 (R)
Cefepime	>32 (R)
Ertapenem	>4 (R)
Imipenem	>8 (R)
Meropenem	>8 (R)
Amikacina	>64 (R)
Gentamicina	<=1 (S)
Ciprofloxacina	>2 (R)
Tigeciclina	≤0.5 (S)
Colistina	≤0.5 (S)

MDR

MDR

E. coli

Antibiotico	MIC mg/L(S/I/R)
Amoxi/Clav	4 (S)
Pipera/Taz	4 (S)
Cefotaxime	≤0.25 (S)
Ceftazidime	≤0.25 (S)
Cefepime	≤0.25 (S)
Ertapenem	≤0.5 (S)
Imipenem	≤0.25 (S)
Meropenem	≤0.25 (S)
Amikacina	≤2 (S)
Gentamicina	≤1 (S)
Ciprofloxacina	>2 (R)
Trimet/Sulfam	>160 (R)
Tigeciclina	1 (S)
Colistina	≤0.5 (S)

K. pneumoniae KPC producer

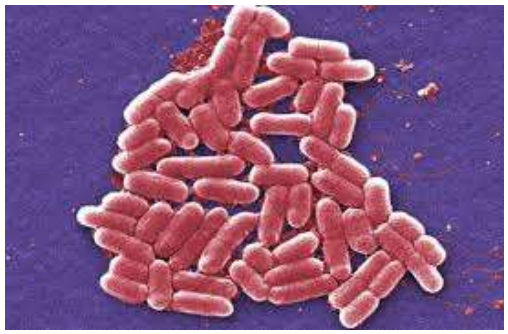
Antibiotico	MIC mg/L(S/I/R)
Amoxi/Clav	>64 (R)
Pipera/Tazo	>64 (R)
Cefotaxime	>32 (R)
Ceftazidime	>32 (R)
Cefepime	>32 (R)
Ertapenem	>4 (R)
Imipenem	>8 (R)
Meropenem	>8 (R)
Amikacina	>64 (R)
Gentamicina	≤1 (S)
Ciprofloxacina	≤0.25 (S)
Trimet/Sulfam	>160 (R)
Tigeciclina	1 (S)
Colistina	≤0.5 (S)

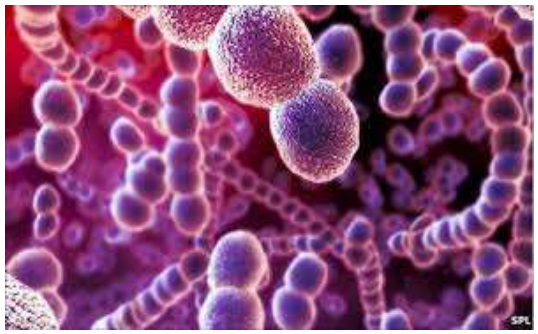
Paziente ambulatoriale con prostatite, allergico ai β-lattamici

La resistenza agli antibiotici è una minaccia globale

33.000 morti/anno EU
700.000 infezioni da MDR/anno EU
[Cassini et al – Lancet, 2018]

Costi relativi ad AMR: in EU 1.5 miliardi di euro/anno





World Health Organization

Health topics | Data | Media centre | Publications | Countries | Programmes | Governance | About WHO | Search

Antimicrobial resistance

- Antimicrobial resistance
- Global action plan on AMR
- Awareness and education
- Surveillance
- Infection, prevention and control
- Optimise use
- R&D and investment
- National action plans
- Resources and publications

United Nations high-level meeting on antimicrobial resistance

Antimicrobial resistance summit to shape the international agenda

Date: 21 September 2016
Place: New York, USA

Related links

- WHO's work on antimicrobial resistance
- Fact sheet on antimicrobial resistance
- At UN, global leaders commit to act on antimicrobial resistance
- Superbugs: Why We Need Action Now

Solo 3 precedenti meeting hanno avuto come tema la Salute Pubblica:
- HIV
- Malattie cronico-degenerative
- Ebola

Italia, terra di santi, poeti e navigatori…

…e di resistenze agli antibiotici

Italian endemic context:

MRSA

KPC-producing *K. pneumoniae*

Carba R-*A. baumannii*

…ma anche di microbiologi!

Piano Nazionale di Contrasto dell'Antimicrobico-Resistenza (PNC

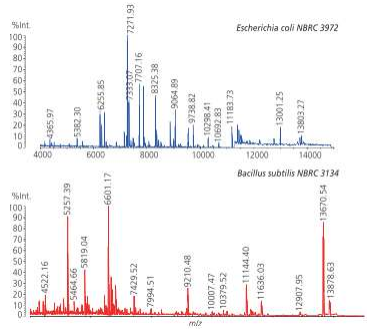
24 ottobre 20-2020

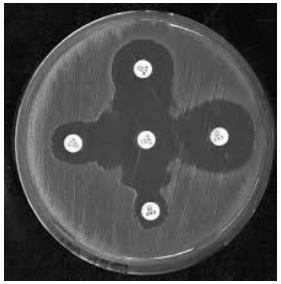
Obiettivi della strategia nazionale:
- Ridurre la frequenza di infezioni da microrganismi resistenti agli antibiotici
- Ridurre la frequenza di infezioni associate all'assistenza sanitaria ospedaliera e comunitaria

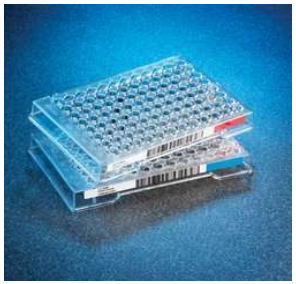
Indicatori:
- Riduzione del consumo di antibiotici in ambito ospedaliero, territoriale e veterinario
- Riduzione della prevalenza di MRSA e CPE
- Sistema di sorveglianza per l'antibiotico-resistenza e per il consumo di soluzione idroalcolica in tutte le Regioni

- individua i principali esiti di salute che si vogliono raggiungere attraverso la sua
- indica le azioni principali da realizzare a livello nazionale e regionale/locale efficace contrasto del fenomeno dell'AMR nei seguenti ambiti:
  - sorveglianza, prevenzione e controllo delle infezioni da microrganismi r
  - uso appropriato e sorveglianza del consumo degli antimicrobici;
  - potenziamento dei servizi diagnostici di microbiologia;
  - formazione degli operatori sanitari;

Cosa ci chiede il clinico?







Tutto e subito

Principali richieste relative agli MDR

1° REFERTAZIONE RAPIDA DELLE RESISTENZE

2° ANTIBIOTICI LAST-RESOURCE

3° VALORI PRECISI DI MIC

4° INTERAZIONI SINERGICHE

5° REFERTAZIONE DI RESISTENZE RARE E INCONSUETE

6° PROBLEMATICHE IRRISOLTE: MDR NON TRATTABILI COI NUOVI ANTIBIOTICI AL MOMENTO DISPONIBILI

Importanza clinica ed epidemiologica (controllo delle infezioni, salute pubblica)

Impostazione terapia basata sull'enzima prodotto

Antibiotico	MIC mg/L (S/I/R)
Ampicillina	> 16 (R)
Amoxi-Clav	> 16 (R)
Piperacillina	> 16 (R)
Pip-Tazo	> 64 (R)
Cefotaxime	> 32 (R)
Ceftazidime	> 32 (R)
Cefepime	> 32 (R)
Imipenem	1 (S)
Meropenem	2 (S)
Ertapenem	> 4 (R)

Antibiotico	MIC mg/L (S/I/R)
Ampicillina	> 16 (R)
Amoxi-Clav	> 16 (R)
Piperacillina	> 16 (R)
Pip-Tazo	> 64 (R)
Cefotaxime	> 32 (R)
Ceftazidime	> 32 (R)
Cefepime	> 32 (R)
Imipenem	1 (S)
Meropenem	1 (S)
Ertapenem	2 (R)

Rilevazione dell'enzima prodotto: requisito base!!!

Nuovi antibiotici e spettro d'azione

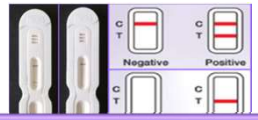
Antibiotico	ESBL	CRE	MDR Pseudomonas	MDR Acinetobacter
Cefiderocol	SI	KPC e NDM	SI	SI
Ceftolozano/Tazobactam	SI	NO	SI	NO
Ceftazidime/Avibactam	SI	KPC e OXA-48 (NO MBL)	SI	NO
Ceftarolina/Avibactam	SI	KPC e OXA-48 (NO MBL)	NO	NO
Aztreonam/Avibactam	SI	MBL	SI	NO
Meropenem/Vaborbactam	SI	KPC	NO	NO
Imipenem/Relebactam	SI	KPC e OXA-48 (NO MBL)	NO	NO
Plazomicina	SI	KPC (NO NDM)	NO	NO
Everacyclina	SI	KPC	NO	SI

1-Refertazione rapida

Perché ridurre i tempi di refertazione:

- Ridurre la mortalità
- Ridurre i tempi di terapia inappropriata
- Ridurre il consumo di antibiotici inutile e ad ampio spettro
- Ridurre le giornate di degenza
- Ridurre i costi correlati all'assistenza
- Ridurre lo sviluppo di resistenze

Lateral flow assay



ABG rapido fenotipico

Sistema perfetto:

Direttamente applicabile su campione clinico
Che mi dia l'identificazione di tutti i microrganismi presenti nel campione
Che mi dia la carica microbica per ogni singolo microrganismo
Che mi dia informazioni sulle resistenze agli antibiotici
Che mi dia informazioni sui fattori di virulenza
Che mi dia tutti i risultati in giornata

PLOS
RESEARCH ARTICI August 21, 2018

Sequencing of *Treponema pallidum* s
pallidum from isolate UZ1974 using *A*
Treponemal Antibodies Enrichment:
complete whole genome sequence c
directly from human clinical materia

JCM July 2015 Volume 53 Number 7
Journals.ASM.org

Rapid Whole-Genome Sequencing of *Mycobacterium tub*
Isolates Directly from Clinical Samples

Amanda C. Brown,[a]* Josephine M. Bryant,[b] Katja Einer-Jensen,[c] Jolyon Holdstock,[a] Darren T. Hounlet,[a]

J Antimicrob Chemother 2017; **72**: 104–114
doi:10.1093/jac/dkw397 Advance Access publication 25 September 2016

Jou
Ant
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**Identification of bacterial pathogens and antimicrobial
directly from clinical urines by nanopore-based meta
sequencing**

JCM January 2014 Volume 52 Number 1
Journals.ASM.org

Rapid Whole-Genome Sequencing for Detection and Cha
of Microorganisms Directly from Clinical Samples

Refertazione emocolture

Metodi tradizionali

24 h **Gram**

48 h ABG diretto in Kirby-Bauer

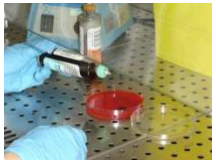
72 h

ID e ABG definitivi

Giorno 1 → Giorno 2 → Giorno 3 → Giorno 4

Prelievo e incubazione dei flaconi

Positivizzazione dei flaconi



Crescita delle colonie

ID biochimica e ABG

Introduzione della spettrometria di massa

24 h

ID e resistenze intrinseche

48 h

ABG definitivo

Giorno 1

Giorno 2

Giorno 3

Prelievo e incubazione dei flaconi

Positivizzazione dei flaconi

ID MALDI-TOF da flacone positivo

ABG

Introduzione della biologia molecolare automatizzata

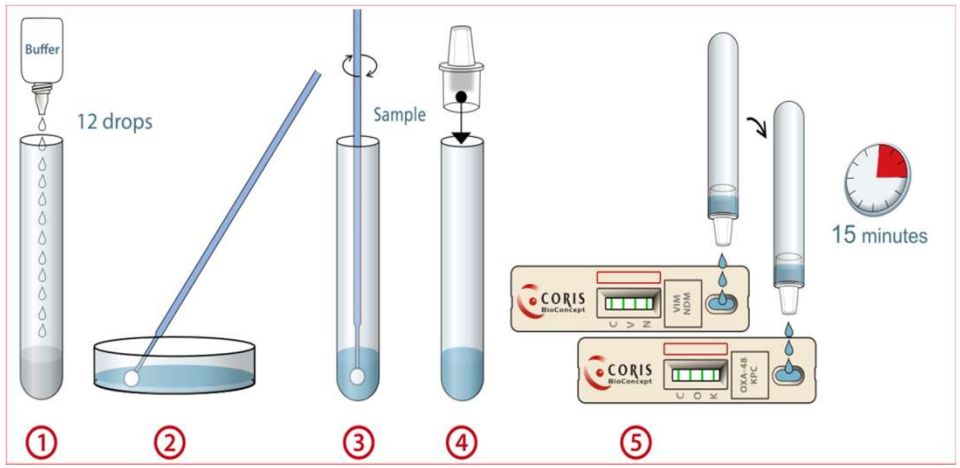
24 h – Identificazione (solo alcune specie) e informazioni su alcune resistenze

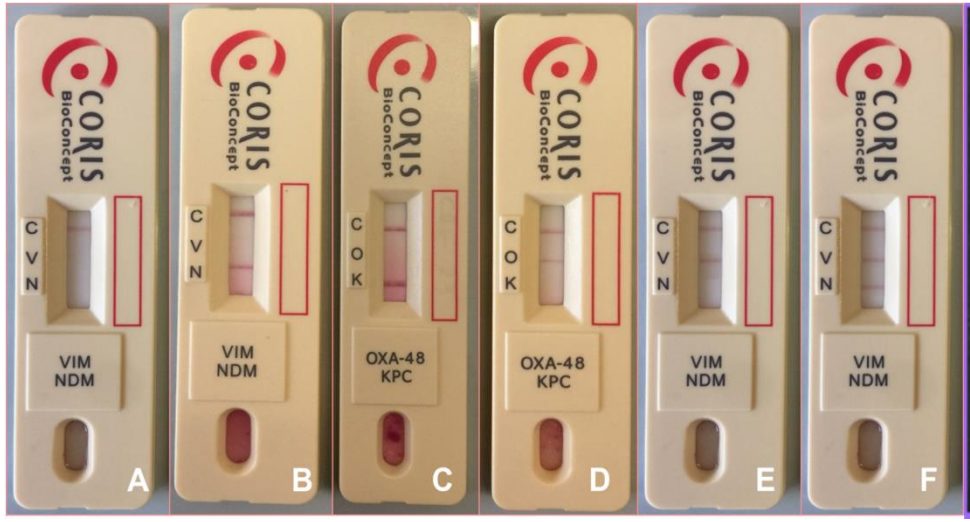
Qualche ora dal prelievo – Identificazione batterica e fungina (solo alcune specie)

24-30 h – Identificazione e antibiogramma definitivo con MIC (solo alcune specie e alcuni antibiotici)

Test rapidi per la rilevazione di resistenze

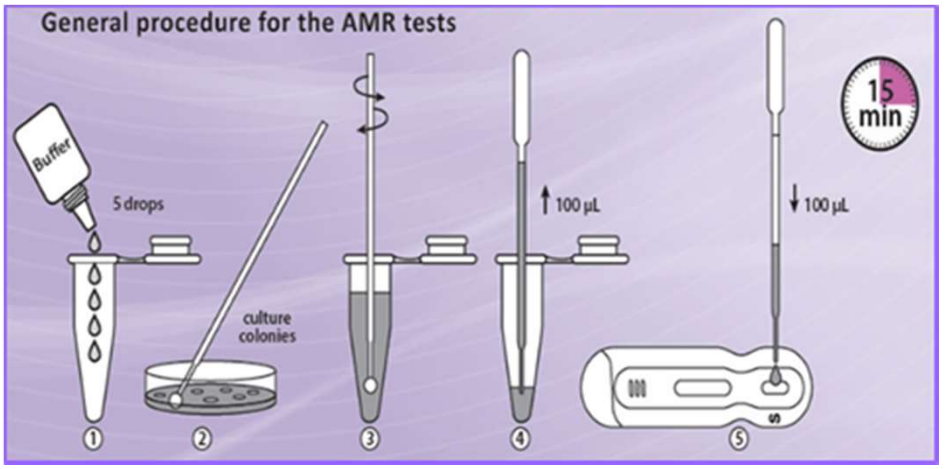
P122

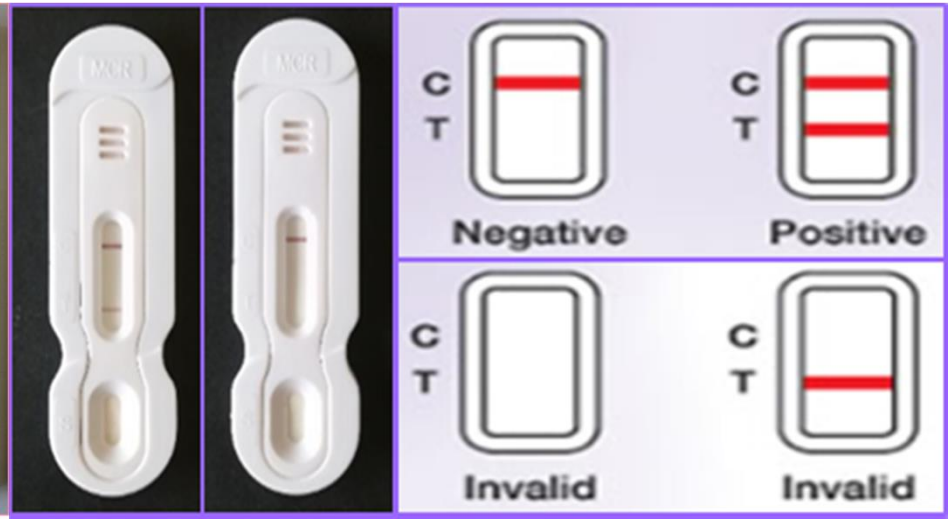




Carbapenemasi

P121





MCR-1

Trasmissione materno-infantile di *K. pneumoniae* produttore di KPC

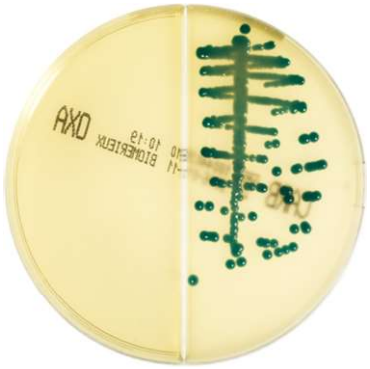
Klebsiella pneumoniae

Antibiotico	MIC mg/L(S/I/R)
Amoxi/Clav	>32 (R)
Pipera/Tazo	>64 (R)
Cefotaxime	>4 (R)
Ceftazidime	>16 (R)
Cefepime	>8 (R)
Ertapenem	>4 (R)
Imipenem	8 (I)
Meropenem	>8 (R)
Amikacina	<=1 (S)
Gentamicina	<=0.5 (S)
Ciprofloxacina	4 (R)
Trimet/Sulfam	<=10 (S)
Tigeciclina	0.5 (S)
Colistina	0.5 (S)

Mother-to-child transmission of KPC-producing *Klebsiella pneumoniae*: potential relevance of a low microbial urinary load for screening purposes

Journal of Hospital Infection
Available online 16 October 2017

L. Principe[a]
E. Meroni[a]
V. Conte[b]
C. Mauri[a]
V. Di Pilato[c]
T. Giani[b]
P. Bonfanti[d]
G.M. Rossolini[e,f]
F. Luzzaro[a,*]



Madre colonizzata da *K. pneumoniae* KPC e trasmissione ai **due gemelli** durante il parto.

L' **urina** delle madre era positiva a bassa carica (**10^3 CFU/ml**) per *K. pneumoniae* KPC.

Lo stesso ceppo è stato riscontrato a livello del **liquido amniotico** e dai **tamponi rettali** di screening dei gemelli. I ceppi **(ST 307)** presentavano lo **stesso profilo genetico** in seguito a sequenziamento completo del genoma.

Il **rapido riconoscimento** di *K. pneumoniae* KPC, **anche se a bassa carica da urine**, ha permesso una **pronta comunicazione** al reparto in modo da evitare la diffusione del microrganismo in **ostetricia e patologia neonatale**

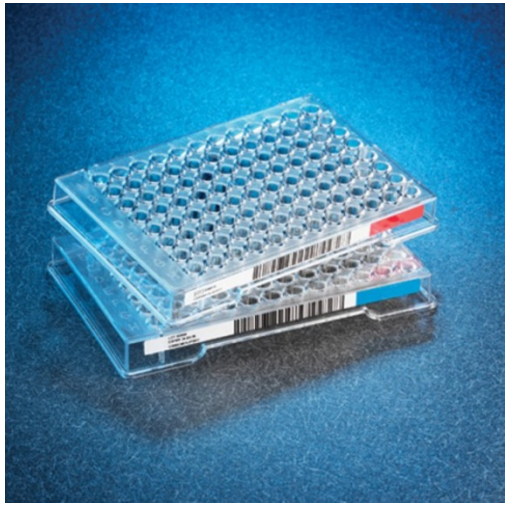
2-Antibiotici last-resource

Antibiotici «problematici» se saggiati con metodiche alternative a quella di riferimento:

- Colistina
- Piperacillina/Tazobactam
- Carbapenemi
- Tigeciclina
- Gentamicina
- Fosfomicina
- Vancomicina

Problematiche inerenti alla metodica utilizzata

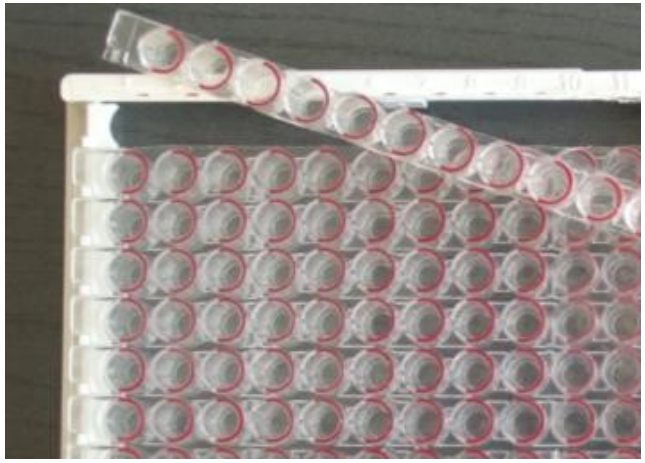
Microdiluizione in brodo



Pannello Gram-negativi MDR

	1	2	3	4	5	6	7	8	9	10
A	MERO	MERO	MERO	MERO	MERO	MERO	MERO	MERO	AMI	AM
	0.12	0.25	0.5	1	2	4	8	16	4	8
B	GEN	GEN	GEN	GEN	GEN	AZT	AZT	AZT	AZT	AZ
	0.5	1	2	4	8	0.5	1	2	4	8
C	CIP	CIP	CIP	CIP	CIP	CIP	P/T4	P/T4	P/T4	P/T
	0.06	0.12	0.25	0.5	1	2	1/4	2/4	4/4	8/
D	AUGC	AUGC	AUGC	AUGC	AUGC	C/T	C/T	C/T	C/T	C/T
	4/2	8/2	16/2	32/2	64/2	0.5/4	1/4	2/4	4/4	8/4
E	COL	COL	COL	COL	COL	COL	FOT	FOT	FOT	FO
	0.25	0.5	1	2	4	8	0.5	1	2	4
F	TGC	TGC	TGC	TGC	TGC	SXT	SXT	SXT	SXT	TO
	0.25	0.5	1	2	4	1/19	2/38	4/76	8/152	2
G	TAZ	TAZ	TAZ	TAZ	TAZ	TAZ	CZA	CZA	CZA	CZ

Sistemi di microdiluizione in brodo per singolo antibiotico



1	2	3	4	5	6	7	8	9	1
GC	COL	COL	COL	COL	COL	COL	COL	COL	C

Enterobacteriaceae (new taxonomy: Enterobacterales

EUCAST Clinical Breakpoint Tables v. 8.1, valid fror

Miscellaneous agents	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Chloramphenicol	8	8	30
Colistin[1]	2	2	
Daptomycin	-	-	
Fosfomycin iv	32[2]	32[2]	200[B]
Fosfomycin oral (uncomplicated UTI only)	32[2]	32[2]	200[B]
Fusidic acid	-	-	

1. La determinazione della MIC della colistina dovrebbe essere eseguita mediante microdiluizione in brodo.

A. Usa un metodo per la MIC (solo microdiluizione in brodo).

Original article

Antimicrobial susceptibility testing of colistin – evaluat commercial MIC products against standard broth microc *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aer* *Acinetobacter* spp.

Clinical Microbiology and Infection 24 (2018) 865–870

A B S T R A C T

Objective: Both EUCAST and CLSI recommend broth microdilution (BMD) for antimic testing of colistin, but BMD is rarely used in routine microbiology laboratories. The ob was to evaluate five commercially available BMD products and two brands of gradi MIC determination using BMD according to ISO standard 20776-1 as reference.

Methods: Colistin MIC determination was performed according to the manufacturer's commercially available BMD products (Sensititre, MICRONAUT-S, MICRONAUT MIC-UMIC) and two gradient tests (Etest and MIC Test Strip). Colistin reference MICs we frozen panels according to ISO standard 20776-1. An international collection of Gra (n=75) with varying levels of colistin susceptibility was tested.

Results: The colistin BMD products correlated well with reference tests, in particul the two MICRONAUT products (essential agreement ≥96%: 66/69 (96%, CI 88–99%) 99%) and 74/75 (99%, CI 92–100%)). The results were somewhat poorer for the BMI

Conclusioni: Non utilizzare test basati sul gradiente (Etest) per valutare la MIC a colistina, ma utilizzare sitemi commerciali basati su microdiluizione in brodo

susceptible results (9–18 of total 75 tests, compared with 1–3 for the BMD produc

Comparison of Etest, Vitek and aga dilution for susceptibility testing of

Table 1. Errors in comparison with agar dilution when testing susceptibility to colistin by Etest and the Vitek 2 system

		Etest		Vitek	
Organism tested	No. tested	Major error (% of total)	Very major error (% of total)	Major error (% of total)	Very major error (% of total)
Acinetobacter spp.	58	1 (2)	0	0	0
Enterobacteriaceae	58	0	2 (4)	0	15 (26)
Pseudomonas aeruginosa	47	14 (30)	5 (11)	0	14 (30)

Clin Microbiol Infect 2007; **13**: 541–544

Evaluation of two automated systems for colistin susceptibility testing of carbapenem-resistant *Acinetobacter baumannii* clinical isolates

Sophia Vourli[1], Konstantina Dafopoulou[2], Georgia Vrioni[2], Athanassios Tsakris[2] and Spyros Pournaras[1,2]*

Objectives: In the present study, two commonly used semi-automated systems were evaluated for colistin AST of contemporary CRAB clinical isolates.

Methods: A total of 117 single-patient CRAB isolates collected randomly during 2015 from distinct tertiary hospitals located throughout Greece were tested. Colistin MICs were determined using the semi-automated systems Phoenix100 and Vitek2 and also agar dilution (AD), compared with the reference BMD.

Results: Colistin resistance rates for Phoenix100/Vitek2/AD/BMD were 15.4%/16.2%/35.9%/24.8%. The essential/categorical agreement rates were as follows: Phoenix100, 91.5%/88.9%; Vitek2, 88.9%/89.7%; and AD,

Conclusioni. La resistenza alla colistina di *A. baumannii* è fortemente sottostimata con i sistemi Phoenix e Vitek, portando potenzialmente ad una inappropriata somministrazione. I risultati ottenuti per la colistina con strumenti automatizzati all'interno del range di sensibilità, particolarmente quelli con valori pari al breakpoint (2 mg/L) devono essere validati con un test di microdiluizione in brodo.

J Antimicrob Chemother 2017; **72**: 2528–2530

Evaluation of Sensititre Broth Microdilution Plate for determining the susceptibility of carbapenem-resistant *Klebsiella pneumoniae* to polymyxins☆

Sandra S. Richter [a,*], James Karichu [a], Joshua Otiso [a], Hillary Van Heule [a], George Keller [a], Eric Cober [a], Laura J. Rojas [b,e], Andrea M. Hujer [b,c], Kristine M. Hujer [b,d], Steve Marshall [b], Frederico Perez [b,c,d], Susan D. Rudin [b,d], T. Nicholas Domitrovic [b,d], Keith S. Kaye [i], Robert Salata [c], David van Duin [j], Robert A. Bonomo [b,c,d,e,f,g,h]

A B S T R A C T

Colistin and polymyxin B MICs were determined for 106 carbapenem-resistant *Klebsiella* isolates using Sensititre Research Use Only GNX2F plates (Thermo Fisher) and com macrodilution (BMD) as the reference method. For colistin, EUCAST breakpoints were appl

Valutazione del pannello Sensititre GNX2F (RUO) rispetto al metodo di riferimento (macrodiluizione in brodo) su isolati di *Klebsiella pneumoniae* resistenti ai carbapenemi

Essential agreement per colistina: 94.3%

Very major errors: 4 (dovuti alla variabilità della MIC nel range 2-4 mg/L)

Diagnostic Microbiology and Infectious Disease 91 (2018) 89–92

Enterobacteriaceae (new taxonomy: Enterobacterales

EUCAST Clinical Breakpoint Tables v. 8.1, valid fror

Miscellaneous agents	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Chloramphenicol	8	8	30
Colistin[1]	2	2	
Daptomycin	-	-	

2. L'agar-diluizione è il metodo di riferimento per la fosfomicina. La MIC deve essere valutata in presenza di glucoso-6-fosfato (25 mg/L). Per i sistemi commerciali vanno seguite le istruzioni del produttore.
B. I dischi di fosfomicina contengono 50 µg di glucoso-6-fosfato.
C. Gli aloni di inibizione si applicano solo ad *E. coli* (per gli altri enterobatteri va utilizzato un metodo per la MIC).
D. Le colonie isolate all'interno dell'alone di inibizione non vanno considerate.

Enterobacteriaceae (new taxonomy: Enterobacterales*)

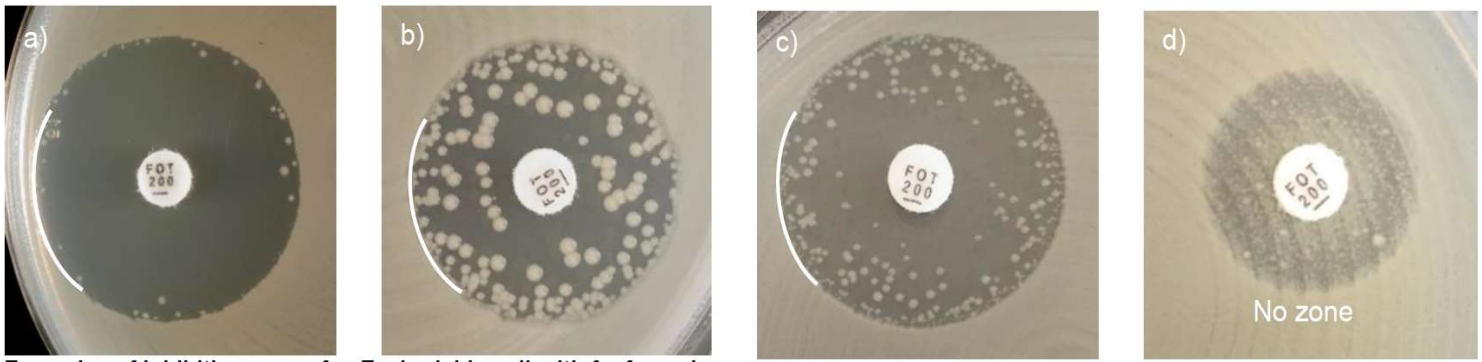
EUCAST Clinical Breakpoint Tables v. 8.1, valid from 2018-05-15

Notes

Numbered notes relate to general comments and/or MIC breakpoints.
Lettered notes relate to the disk diffusion method.

1. Quality control of colistin must be performed with both a susceptible QC strain (*E. coli* ATCC 25922 or *P. aeruginosa* ATCC 27853) and the colistin resistant *E. coli* NCTC 13846 (*mcr-1* positive).
2. Agar dilution is the reference method for fosfomycin. MICs must be determined in the presence of glucose-6-phosphate (25 mg/L in the medium). Follow the manufacturers' instructions for commercial systems.
3. Trimethoprim:sulfamethoxazole in the ratio 1:19. Breakpoints are expressed as the trimethoprim concentration.

A. Use an MIC method.
B. Fosfomycin 200 µg disks must contain 50 µg glucose-6-phosphate.
C. Zone diameter breakpoints apply to *E. coli* only. For other Enterobacteriaceae, use an MIC method.
D. Ignore isolated colonies within the inhibition zone (**see pictures below**).



Examples of inhibition zones for *Escherichia coli* with fosfomycin.
a-c) Ignore all colonies and read the outer zone edge.
d) Record as no inhibition zone.

Discrepancies in fosfomycin susceptibility testing of KPC-producing *Klebsiella pneumoniae* with various commercial methods

Giulio Camarlinghi [a], Eva Maria Parisio [a], Alberto Antonelli [b], Maria Nardone [a], Marco Coppi [b], Tommaso Giani [b], Romano Mattei [a], Gian Maria Rossolini [b,c,*]

Fosfomycin susceptibility testing with Sensititre, Vitek2, Etest, Mic Strip Test and disk dif was compared versus reference agar dilution method (AD) with 78 clinical isolates of KP *pneumoniae*. All methodologies showed a Categorical Agreement and Essential Agreeme

Tutte le metodologie testate (Sensititre, Vitek 2, Etest, MIC Strip Test, diffusione da disco) mostravano una bassa concordanza rispetto al metodo di riferimento (agar- diluizione).

In particolare, Sensititre ed Etest avevano alte percentuali di VME e presumibilmente tendono a sottostimare i valori.

Vitek 2, il MIC Strip Test e la diffusione da disco avevano alte percentuali di ME e quindi tendono a sovrastimare i valori di MIC.

Diagnostic Microbiology and Infectious Disease xxx (2018) xxx–xxx

Susceptibility of ESBL *Escherichia coli* and *Klebsiella pneumoniae* to fosfomycin in the Netherlands and comparison of several testing methods including Etest, MIC test strip, Vitek2, Phoenix and disc diffusion

Wouter van den Bijllaardt [1,2]*, Maarten J. Schijffelen[3], Ron W. Bosboom[4], James Cohen Stuart[5], Bram Diederen[6], Greetje Kampinga[7], Thuy-Nga Le[8], Ilse Overdevest[9], Frans Stals[10], Paul Voorn[11], Karola Waar[12], Johan W. Mouton[2] and Anouk E. Muller[2,13]

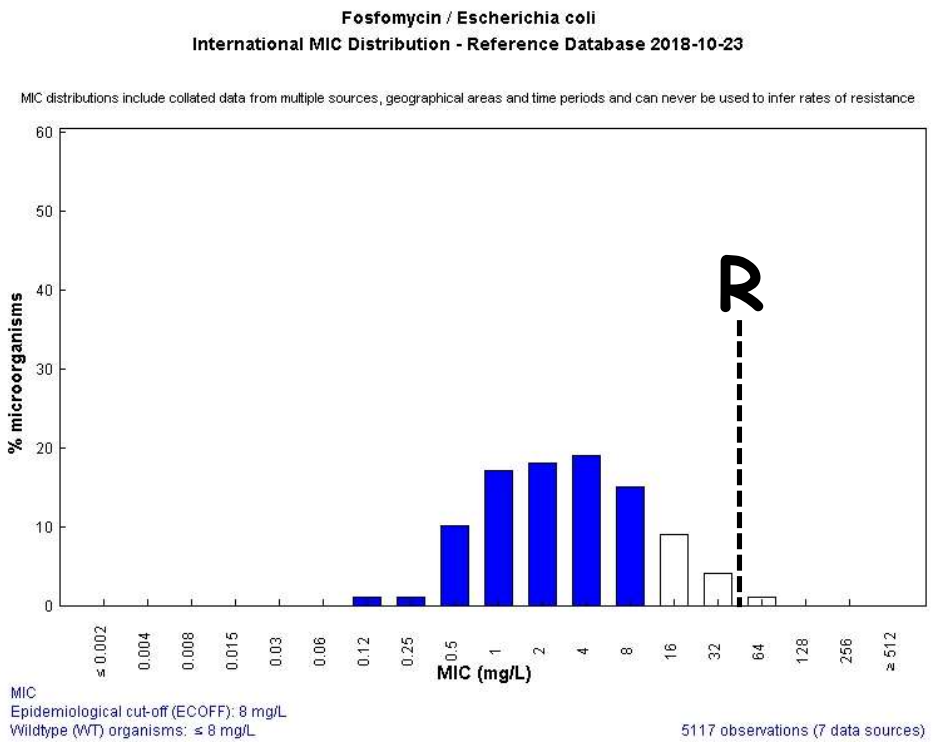
Results: In total, 775 *E. coli* and 201 *K. pneumoniae* isolates were tested by agar dilution. The ECOFF was 2 mg/L for *E. coli* and 64 mg/L for *K. pneumoniae*. Susceptibility rates based on the EUCAST breakpoint of ≤32 mg/L were 95.9% for *E. coli* and 87.6% for *K. pneumoniae*. Despite high categorical agreement rates for all methods, notably in *E. coli*, none of the alternative antimicrobial susceptibility testing methods performed satisfactorily. Due to poor detection of resistant isolates, very high error rates of 23.3% (Etest), 18.5% (MTS), 18.8% (Vitek2), 12.5% (Phoenix) and 12.9% (disc diffusion) for *E. coli* and 22.7% (Etest and MTS), 16.0% (Vitek2) and 12% (Phoenix) for *K. pneumoniae* were found. None of the methods adequately differentiated between WT and non-WT populations.

Nessuna delle metodologie testate (Vitek 2, Phoenix, Etest, MIC Strip Test, diffusione da disco) rappresenta una opzione utilizzabile come alternativa all'agar-diluizione per la determinazione della MIC della fosfomicina nella routine di laboratorio.

J Antimicrob Chemother 2018; **73**: 2380–2387

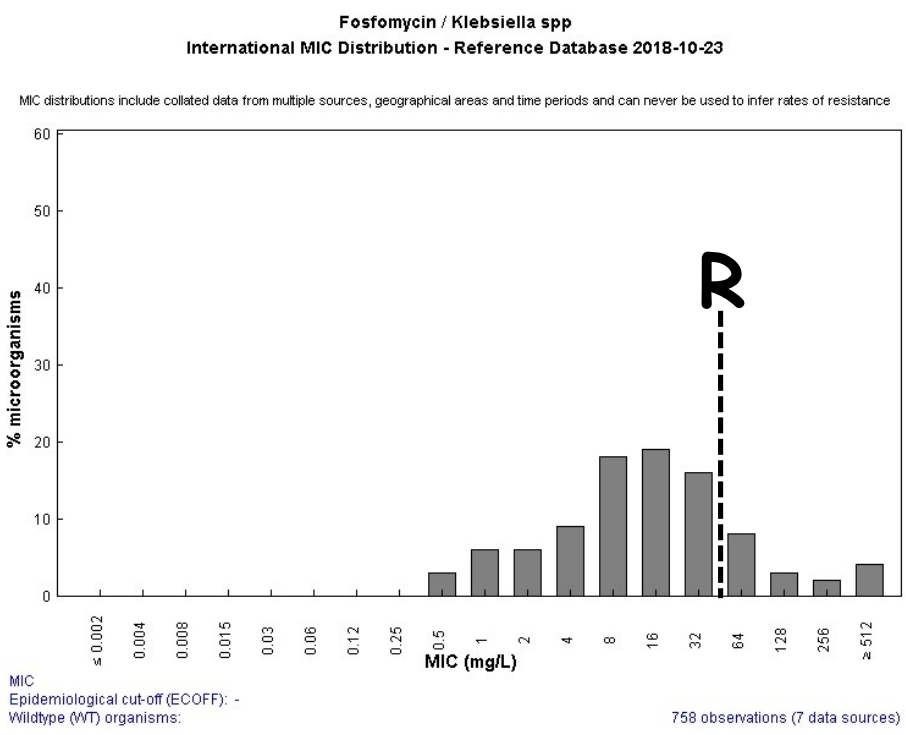
Sensibilità alla Fosfomicina

Escherichia coli



ECOFF= 8 mg/L

Klebsiella spp.



NO ECOFF

Enterobacteriaceae (new taxonomy: Enterobacterales

EUCAST Clinical Breakpoint Tables v. 8.1, valid fror

Tetracyclines	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Doxycycline	-	-	
Minocycline	-	-	
Tetracycline			

Notes
Numbered notes relate to general comments and/or MIC breakpoints.

2. Per determinare la MIC mediante microdiluizione in brodo, il terreno deve essere preparato fresco il giorno dell'uso.
A. I breakpoint per gli aloni di inibizione sono validati solo per *Escherichia coli*. Per gli altri enterobatteri, va usato un metodo con la MIC

Comparative Evaluation of Tigecycline Susceptibility Tes for Expanded-Spectrum Cephalosporin- and Carbapenen Gram-Negative Pathogens

Olympia Zarkotou,[a] Spyros Pournaras,[b] George Altouvas,[a] Vassiliki Pitiriga,[c] Maria Tziraki,[a] Vassiliki Mamali,[a] Katerina Themeli-Digalaki,[a] and Athanassios Tsakris[c]

We evaluated the Vitek2, Etest, and MIC Test Strip (MTS) methods of tigecycline susceptibility testing with 241 expanded-spectrum cephalosporin-resistant and/or carbapenem-resistant *Enterobacteriaceae* and *Acinetobacter baumannii* clinical isolates by using dry-form broth microdilution (BMD) as the reference method. The $MIC_{50/90}$s were as follows: BMD, 1/4 μg/ml; Vitek2, 4/≥8 μg/ml; Etest, 2/4 μg/ml; MTS, 0.5/2 μg/ml. Vitek2 produced 9.1/21.2% major errors, Etest produced 0.4/0.8% major errors, and MTS produced no major errors but 0.4/3.3% very major errors (FDA/EUCAST breakpoints). Vitek2 tigecycline results require confirmation by BMD or Etest for multidrug-resistant pathogens.

Per enterobatteri e *Acinetobacter baumannii*, il Vitek2 produceva 9.1/21.2% major errors mentre l'Etest produceva 0.4/0.8% major errors. Il test MTS non produceva major errors ma determinava 0.4/3.3% very major errors.

November 2012 Volume 50 Number 11

Journal of Clinical Microbiology p. 3747–3750

False non-susceptible results of tigecycline susceptibility testing against *Enterobacteriaceae* by an automated system: a multicentre study

Evgeny A. Idelevich,[1] Marina Büsing,[1] Alexander Mischnik,[2]† Martin Kaase,[3] Isabelle Bekeredjian-Ding[4]‡ and Karsten Becker[1]

Lo studio ha dimostrato una alta percentuale di risultati falsamente non-sensibili per la tigegiclina con il Vitek2. Gli isolati non-sensibili alla tigeciclina dovrebbero essere ritestati con una metodica di microdiluizione in brodo.

Our study has demonstrated a high rate of false non-susceptible Vitek 2 tigecycline categorization for *Enterobacteriaceae*, which is in line with other recent reports (Huang *et al.*, 2012; Zarkotou *et al.*, 2012; Marchaim *et al.*, 2014). Because of the false results, patients infected with multidrug-resistant *Enterobacteriaceae* might be deprived of one of few remaining therapeutic options. Clinical laboratories should be aware of this failure, and isolates reported as non-susceptible by Vitek 2 should be re-tested by other method in particular when tigecycline represents a treatment option. Verification of such Vitek 2 results is recommended with BMD. The use of freshly ($\leq$12 h) prepared broth is required for tigecycline

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Appendice 2.a. Resistenze per materiali

Emocolture 2016

I isolato 2016		paz. testati	paz. R	% R		paz. IR
Microrganismo	**Antibiotico**					
Klebsiella pneumoniae	amoxicillina-acido clavulanico	1.202	613	51,0	617	51,3
n. pazienti 1.204	piperacillina-tazobactam	1.182	482	40,8	597	50,5
	cefalosporine III generazione	1.203	576	47,9	600	49,9
	fluorochinoloni	1.204	560	46,5	598	49,7
	gentamicina	1.203	271	22,5	411	34,2
	amikacina	1.204	198	16,4	292	24,3
	imipenem/meropenem	1.066	250	23,5	255	23,9
	ertapenem	700	179	25,6	187	26,7
	colistina	845	49	5,8	49	5,8
	tigeciclina §	394	31	7,9	63	16,0

§ La percentuale di isolati resistenti o con sensibilità intermedia alla tigeciclina potrebbe essere sovrastimata a causa della metodica analitica utilizzata.

FDA Approved Drugs for Infections and Infectious Diseases

Infections and Infectious Diseases

Dalvance (dalbavancin); Durata Therapeutics; For the treatment of acute bacterial skin and skin structure infections, Approved May 2014

Sivextro (tedizolid phosphate) ; Cubist Pharmaceuticals; For the treatment of acute bacterial skin and skin structure infections, Approved June 2014

Orbactiv (oritavancin); The Medicines Company; For the treatment of acute bacterial skin and skin structure infections, Approved August 2014

Zerbaxa (ceftolozane + tazobactam) ; Cubist Pharmaceuticals; For the treatment of complicated intra-abdominal and urinary tract infections, Approved December 2014

Avycaz (ceftazidime-avibactam); Actavis; For the treatment of complicated intra-abdominal and urinary tract infections, Approved February 2015

Baxdela (delafloxacin) tablets and injection; Melinta Therapeutics; For the treatment of acute bacterial skin and skin structure infections, Approved June 2017

Vabomere (meropenem and vaborbactam); The Medicines Company; For the treatment of complicated urinary tract infections , Approved August 2017

Cephalosporins	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Cefaclor	-	-		-	-
Cefadroxil	-	-		-	-
Cefalexin	-	-		-	-
Cefazolin	-	-		-	-
Cefepime[1]	8	8	30	21	21
Cefixime	-	-		-	-
Cefotaxime	-	-		-	-
Cefoxitin	NA	NA		NA	NA
Cefpodoxime	-	-		-	-
Ceftaroline	-	-		-	-
Ceftazidime[2]	8	8	10	17	17
Ceftazidime-avibactam, *P. aeruginosa*	8[3]	8[3]	10-4	17	17
Ceftibuten	-	-		-	-
Ceftobiprole	IE	IE		IE	IE
Ceftolozane-tazobactam, *P. aeruginosa*	4[4]	4[4]	30-10	24	24
Ceftriaxone	-	-		-	-
Cefuroxime iv	-	-		-	-
Cefuroxime oral	-	-		-	-

Ministero della Salute

DIREZIONE GENERALE DELLA PREVENZIONE SANITARIA
UFFICIO 5 PREVENZIONE DELLE MALATTIE TRASMISSIBILI E PROFILASSI INTERNAZIONALE

OGGETTO: ***Rapid Risk Assessment dell'ECDC: Emergenza della resistenza a ceftazidime-avibactam nelle Enterobacteriaceae resistenti ai carbapenemi – 12 giugno 2018.***

Ceftazidime-avibactam disponibile in Italia da febbraio 2018 per utilizzo ospedaliero

Resistenza sporadica rilevata in **USA** (2015, 2017), **Germania** (2017) e **Italia** (2018)

Humphries et al AAC, 2015; Both et al JAC, 2017; Shields et al AAC, 2017; Gaibani et al JAC, 2018; Giddins et al AAC, 2018

The Continued Value of Disk Diffusion for Assessing Antimicrobial Susceptibility in Clinical Laboratories: Report from the Clinical and Laboratory Standards Institute Methods Development and Standardization Working Group

Romney M. Humphries,[a] Susan Kircher,[b] Andrea Ferrell,[b] Kevin M. Krause,[c] Rianna Malherbe,[d] Andre Hsiung,[d] Carey-Ann D. Burnham[e]

TABLE 1 Summary of antimicrobial drugs approved since 2010 and times to AST devices

Antimicrobial agent	Month/year approved by FDA	Time (mo)[a] to: First disk clearance[b]	First gradient diffusion strip clearance	Manual MIC test (Sensititre) clearance	Rapid automated AST device clearance
Delafloxacin	6/2017	2	2	2	NA
Meropenem-vaborbactam	8/2017	2	4	4	6
Ceftazidime-avibactam	2/2015	8	7	10	25
Ceftolozane-tazobactam	12/2014	11	19	8	36
Dalbavancin	5/2014	ND	25	14	NA
Oritavancin	8/2014	ND	NA	7	NA
Tedizolid	6/2014	NA	36	15	NA
Ceftaroline	5/2010	7	29	14	34

Journal of Clinical Microbiology

August 2018 Volume 56 Issue 8 e00437-18

Validation of Sensititre Dry-Form Broth Microdilution Panels for Susceptibility Testing of Ceftazidime-Avibactam, a Broad-Spectrum-β-Lactamase Inhibitor Combination

Ronald N. Jones,[a] Nicole M. Holliday,[b] Kevin M. Krause[c]

Ceftazidime-avibactam is a broad-spectrum-β-lactamase inhibitor combination in late-stage clinical de
ment of serious infections. In preparation for clinical microbiology laboratory use, a validation experim
uate a commercial broth microdilution product (Sensititre dried MIC susceptibility system) compared t
525 recent clinical isolates. Among 11 pathogen groups, all had Sensititre MIC/reference MIC ratios pre
to 97.5%), and automated and manual endpoint results did not differ. *Enterobacteriaceae* MIC comparis
skewing of Sensititre MIC results toward an elevated MIC (33.9%), but the essential agreement was 98.9
ducibility. In conclusion, Sensititre panels produced accurate ceftazidime-avibactam MIC results allow

I pannelli Sensititre producevano accurati risultati di MIC per il ceftazidime-avibactam: essential agreement per gli enterobatteri pari al 98.9% con il 100 % di riproducibilità.

August 2015 Volume 59 Number 8

Antimicrobial Agents and Chemotherapy

Performance of the Etest for Susceptibility Testing of *Enterobacterales* (*Enterobacteriaceae*) and *Pseudomonas aeruginosa* toward Ceftazidime-Avibactam

Michael Kresken,[a,b] Barbara Körber-Irrgang[a]

TABLE 3 Evaluation of agreement and errors between results of the Etest and BMD

Organism(s)	No. of strains tested	CA[a]		ME[b]		VME[c]		Overall EA[d]		EA of evaluable results[e]	
		No.[f]	%	No.	%	No.	%	No.	%	No.	%
Enterobacterales	140	140	100.0	0	0.0	0	0.0	139	99.3	130	100.0
P. aeruginosa	60	59	98.3	0	0.0	1	4.5	59	98.3	48	100.0
Total	200	199	99.5	0	0.0	1	0.5	198	99.0	178	100.0

Risultati anche migliori rispetto ai precedenti sono stati pubblicati del tutto recentemente per l'Etest, che appare una opzione utilizzabile per la determinazione della MIC per ceftazidime-avibactam.

Journal of Clinical Microbiology

September 2018 Volume 56 Issue 9 e00528-18

Verification of Ceftazidime-Avibactam and Ceftolozane-Tazobactam Susceptibility Testing Methods against Carbapenem-Resistant *Enterobacteriaceae* and *Pseudomonas aeruginosa*

Ryan K. Shields,[a,b] Cornelius J. Clancy,[a,b,c] A. William Pasculle,[a,d] Ellen G. Press,[a] Ghady Haidar,[a] Binghua Hao,[b] Liang Chen,[e] Barry N. Kreiswirth,[e] M. Hong Nguyen[a,b]

TABLE 2 Essential and categorical agreement between BMD and Etest or disk diffusion for testing susceptibility to ceftazidime-avibactam and ceftolozane-tazobactam[a]

Drug, pathogen (no. of isolates)	BMD			Etest			Disk diffusion	
	Median MIC (μg/ml)[b]	Range of MIC (μg/ml)[b]	No. (%) of resistant isolates	No. (%) of isolates with EA	No. (%) of isolates with CA	No. of errors	No. (%) of isolate with CA	No. of errors

La determinazione della sensibilità a ceftazidime-avibactam e ceftolozano-tazobactam eseguita con Etest correlava strettamente con i risultati ottenuti con la microdiluizione in brodo (overall essential agreement pari rispettivamente a 89% e 79%). La diffusione da disco tendeva a sovrastimare la resistenza a ceftazidime-avibactam.

Journal of Clinical Microbiology

February 2018 Volume 56 Issue 2 e01093-17

Performance of Ceftolozane-Tazobactam Etest, MIC Test Strips, and Disk Diffusion Compared to Reference Broth Microdilution for β-Lactam-Resistant *Pseudomonas aeruginosa* Isolates

Romney M. Humphries,[a]* Janet A. Hindler,[a] Paul Magnano,[a] Annie Wong-Beringer,[b] Robert Tibbetts,[c] Shelley A. Miller[a]

TABLE 1 Activity of beta-lactams for 308 *P. aeruginosa* evaluated in this study, as determined by rBMD

	No. (%) of isolates	
Beta-lactam[a]	Susceptible	Resistant
Ceftazidime	76 (24.6)	209 (67.6)
Cefepime	80 (25.9)	149 (48.2)
Imipenem	37 (12.0)	259 (83.8)
Meropenem	49 (15.9)	228 (73.8)
TZP	64 (20.7)	183 (59.2)
C-T	224 (72.5)	66 (21.4)

Journal of Clinical Microbi

March 2018 Volume 56 Issue 3 e(

Performance of Ceftolozane-Tazobactam Etest, MIC Test Strips, and Disk Diffusion Compared to Reference Broth Microdilution for β-Lactam-Resistant *Pseudomonas aeruginosa* Isolates

Romney M. Humphries,[a]* Janet A. Hindler,[a] Paul Magnano,[a] Annie Wong-Beringer,[b] Robert Tibbetts,[c] Shelley A. Miller[a]

TABLE 2 Performance of disk diffusion, Etest, and MTS compared to rBM *aeruginosa* isolates[a]

Assay	EA (%)	CA (%)	No. (%) of isolates w VME	ME
Hardy disk	NA	92.9	0 (0)	0 (0)
Etest	96.8	96.8	0 (0)	0 (0)

Journal of Clinical Microbi

March 2018 Volume 56 Issue 3 e(

Multicenter Evaluation of the Etest Gradient Diffusion Method for Ceftolozane-Tazobactam Susceptibility Testing of *Enterobacteriaceae* and *Pseudomonas aeruginosa*

Adam L. Bailey,[a] Tom Armstrong,[b] Hari-Prakash Dwivedi,[b] Gerald A. Denys,[c] Janet Hindler,[d] Shelley Campeau,[d*] Maria Traczewski,[e] Romney Humphries,[d*] Carey-Ann D. Burnham[a]

TABLE 2 Challenge study of C/T Etest[a]

Organism(s)	Site	No. of isolates	No. with indicated result by BMD			Performance, no. (%)				
			S	I	R	EA	CA	VMEs	MEs	mEs
Enterobacteriaceae	A	51	27	1	23	47 (92.2)	51 (100)	0 (0)	0 (0)	0 (0)
	B	51	27	1	23	49 (96.1)	49 (96.1)	0 (0)	1 (3.7)	1 (2.0)
	C	51	27	1	23	48 (94.1)	49 (96.1)	1 (4.3)	0 (0)	1 (2.0)
P. aeruginosa	A	39	21	0	18	39 (100)	39 (100)	0 (0)	0 (0)	0 (0)
	B	39	21	0	18	39 (100)	39 (100)	0 (0)	0 (0)	0 (0)
	C	39	21	0	18	39 (100)	39 (100)	0 (0)	0 (0)	0 (0)

Nel caso di ceftolozano-tazobactam (challenge study), l'Etest mostrava una buona correlazione con la microdiluizione in brodo, specie nel caso di *Pseudomonas aeruginosa* (essential agreement: 100%).

Journal of Clinical Microbiology

September 2018 Volume 56 Issue 9 e00717-18

Retraction for Flynt et al., "Comparison of Etest to Broth Microdilution for Testing of Susceptibility of *Pseudomonas aeruginosa* to Ceftolozane-Tazobactam"

Lauren K. Flynt,[a] Michael P. Veve,[a,b] Linoj P. Samuel,[a] Robert J. Tibbetts[a]

Volume 55, no. 1, p. 334–335, 2017, https://doi.org/10.1128/JCM.01920-16. We hereby retract this article. In our paper we described discrepant results between ceftolozane-tazobactam Etests and broth microdilution. However, when repeat testing on the same isolates was done for a second, larger study recently published by R. M. Humphries, J. A. Hindler, P. Magnano, A. Wong Beringer, R. Tibbetts, and S. A. Miller (J Clin Microbiol 56:e01633-17, 2018, https://doi.org/10.1128/JCM.01633-17) we could not replicate the initial results. Upon review of the procedure used for broth microdilution it was determined that the tazobactam concentrations were not prepared according to CLSI guidelines (Clinical Laboratory Standards Institute, *Performance Standards for Antimicrobial Susceptibility Testing*, 26th ed, CLSI supplement M100S, 2016). We hypothesized that this may have contributed to the high MICs and very major errors. In order to test this hypothesis, we repeated the broth microdilution in the original laboratory using the same procedure as initially performed; however, we could not replicate the errors. Based on this outcome, a second hypothesis was that perhaps the bacteria possessed a resistance mechanism at the time of initial testing but that upon repeated subculture the mechanism was lost; however, we are unable to test this hypothesis.

Journal of Clinical Microbi

June 2018 Volume 56 Issue 6 e00541-18

Multicenter Evaluation of the Etest Gradient Diffusion Method for Ceftolozane-Tazobactam Susceptibility Testing of *Enterobacteriaceae* and *Pseudomonas aeruginosa*

TABLE 3 Clinical performance of C/T Etest

Organism(s)	No. of isolates	No. (%) matching CLSI breakpoint criteria							
		Result by BMD			Performance				
		S	I	R	EA	CA	VMEs	MEs	mEs
Enterobacteriaceae (total)	793	728 (91.8)	9 (1.1)	56 (7.1)	768 (96.8)	781 (98.5)	0 (0)	2 (0.3)	10 (1.3)
Citrobacter koseri	48	48 (100)	0 (0)	0 (0)	48 (100)	48 (100)	0 (ND[a])	0 (0)	0 (0)
Enterobacter cloacae	53	44 (83.0)	1 (1.9)	8 (15.1)	51 (96.2)	51 (96.2)	0 (0)	0 (0)	2 (3.8)
Escherichia coli	159	146 (91.8)	1 (0.6)	12 (7.5)	153 (96.2)	159 (100)	0 (0)	0 (0)	2 (1.3)
Klebsiella oxytoca	58	52 (89.7)	1 (1.7)	7 (12.1)	56 (96.6)	58 (100)	0 (0)	0 (0)	0 (0)

Dati altrettanto buoni sono stati ottenuti nello studio eseguito su un numero elevato di isolati clinici. L'Etest mostrava una buona correlazione con la microdiluizione in brodo, sia per gli enterobatteri che per *Pseudomonas aeruginosa* (essential agreement pari rispettivamente al 96.8% ed al 98.8%, categorical agreement pari rispettivamente al 98.5% ed al 99.4%).

Journal of Clinical Microbiology

September 2018 Volume 56 Issue 9 e00717-18

Journal of Antimicrobial Chemotherapy Advance Access published Oct

J Antimicrob Chemother
doi:10.1093/jac/dkw442

Etest® versus broth microdilution for ceftaroline MIC d with *Staphylococcus aureus*: results from PREMIUM, multicentre study

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Received 21 May 2016; returned 9 June 2016; revised 17 September 2016; accepted 20 Sep

Objectives: To compare the concordance of ceftaroline MIC values by reference broth microd Etest (bioMérieux, France) for MSSA and MRSA isolates obtained from PREMIUM (D372SL0001) ticentre study.

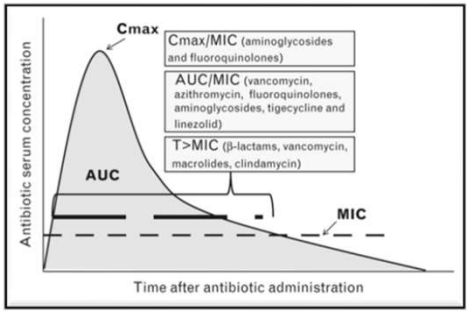
Methods: Ceftaroline MICs were determined by reference BMD and by Etest for 1242 MSSA a collected between February and May 2012 from adult patients with community-acquired pneu cated skin and soft tissue infections; tests were performed across six European laboratories. with ceftaroline resistance in broth (MIC >1 mg/L) were retested in three central laborator behaviour.

Results: Overall concordance between BMD and Etest was good, with >97% essential agree categorical agreement. Nevertheless, 12 of the 26 MRSA isolates found resistant by BMD scor

3-Valori precisi di MIC

Valori precisi di MIC sono necessari per il monitoraggio terapeutico del farmaco:

- Ottimizzazione dei dosaggi
- Caratteristiche del paziente
- Prevenire le resistenze



VRSA

Worldwide Epidemiology and Antibiotic Resistance of *Staphylococcus aureus*

Monica Monaco, Fernanda Pimentel de Araujo, Melania Cruciani, Eliana M. Coccia and Annalisa Pantosti

Table 1 VRSA isolated from 2002 to 2013 reported in indexed journals

Country or state or city	Date	Source	Vancomycin MIC (μg/ml)	SCC*mec*	*spa* type	MLST	CC	References
USA/MI	2002	Plantar ulcers	1024	II	t062	ST371	CC5	Weigel et al. 2003, Limbago et al. 2014
USA/PA	2002	Plantar ulcers	32	II	t002	ST5	CC5	Tenover et al. 2004, Sievert et al. 2008
USA/NY	2004	Urine	64	IV	t002	ST5	CC5	Sievert et al. 2008
USA/MI	2005	Toe wound	256	II	t002	ST5	CC5	Zhu et al. 2008; Sievert et al. 2008
USA/MI	2005	Surgical site wound	512	II	t002	ST231	CC5	Zhu et al. 2008; Sievert et al. 2008
USA/MI	2005	Plantar ulcers	1024	NT	t002	ST85	CC5	Zhu et al. 2008; Sievert et al. 2008
USA/MI	2006	Triceps wound	512	II	t062	ST231	CC5	Zhu et al. 2008; Sievert et al. 2008
USA/MI	2007	Toe wound	1024	ND	t002	ST5	CC5	Finks et al. 2009
USA/MI	2007	Surgical wound	1024	ND	t002	ST5	CC5	Finks et al. 2009
India/West Bengal	2007	Pus	64	ND	-	-	-	Saha et al. 2008
USA/MI	2009	Plantar wound	NR	ND	t002	ST5	CC5	Limbago et al. 2014
USA/DE	2010	Wound drainage	NR	ND	t002	ST5	CC5	Limbago et al. 2014
USA/DE	2010	Vaginal swab	NR	ND	t045	ST5	CC5	Limbago et al. 2014
USA/DE	2012	Foot wound	256	ND	t019	-	CC30	Limbago et al. 2014
Iran/Mashhad	2011	Bronchial aspirate	512	III	t037	ST239[a]	CC8	Azimian et al. 2012
Brazil/Sao Paolo	2012	Blood culture	32	IV	t292	ST85	CC8	Rossi et al. 2014
Portugal/Lisbon	2013	Toe wound	1024	II	t002	ST105	CC5	Friaes et al. 2015

hGISA: Heterogeneous glycopeptide intermediate *S. aureus*.

S. aureus isolates susceptible to vancomycin (MICs ≤2mg/L) but with minority populations (1 in 10^6 cells) with vancomycin MIC >2 mg/L, as judged by population analysis profile investigation.

BORDERLINE

Valori di MIC tra 1 e 2 mg/L

REVIEW

The management of multidrug-resistant *Enterobacteriaceae*

Bassetti M., et al. Curr Opin Infect Dis 2016

- In KPC-Kp with meropenem MIC 8–16 mg/l or less, the combination of a carbapenem-containing regimen (administered with high-dosed, prolonged infusion) with colistin or high-dose tigecycline or aminoglycoside can be administered with TDM.
- In KPC-Kp with meropenem MIC higher than 8–16 mg/l, the use of carbapenem should be avoided and various combination therapies based on the in-vitro susceptibility of antimicrobials (e.g., colistin, high-dose tigecycline, fosfomycin, and aminoglycosides) should be selected.

MIC MEROPENEM 8-16 mg/L

Redefining susceptibility testing categories **S**, **I** and **R**.

Gunnar Kahlmeter and the EUCAST Steering Committee

EUCAST definitions of clinical breakpoints (2018)

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

- **Clinically Susceptible (S)**

  a micro-organism is defined as susceptible by a **level of antimicrobial activity** associated with a high likelihood of **therapeutic success**

- **Clinically Intermediate (I)**

  a micro-organism is defined as intermediate by a **level of antimicrobial agent** activity associated with **uncertain therapeutic effect**. It implies that an infection due to the isolate may be appropriately treated in body sites where the drugs are physically concentrated or when a high dosage of drug can be used; it also indicates a buffer zone that should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations.

- **Clinically Resistant (R)**

  a micro-organism is defined as resistant by a **level of antimicrobial activity** associated with a high likelihood of **therapeutic failure**.

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EUCAST definitions of clinical breakpoints (2019)

- **S - Susceptible, standard dosing regimen**

  a microorganism is categorised as ***Susceptible, standard dosing regimen***, when there is a high likelihood of **therapeutic success** using a standard dosing regimen of the agent.

- **I – Susceptible, increased exposure**

  a microorganism is categorised as ***Susceptible, Increased exposure**** when there is a **high likelihood of therapeutic success** because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.

- **R - Resistant**

  a microorganism is categorised as *Resistant* when there is a high likelihood of **therapeutic failure** even when there is **increased exposure**.

*Exposure is a function of how the mode of administration, dose, dosing interval, infusion time, as well as distribution and excretion of the antimicrobial agent will influence the infecting organism at the site of infection.

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Dosages

EUCAST Clinical Breakpoint Tables v. 8.1, valid from 2018-05-15

EUCAST breakpoints are based on the following dosages (see section 8 in Rationale Documents).

Penicillins	Standard dose	High dose	Special situations
Benzylpenicillin	0.6 g x 4 iv	1.2 g x 4-6 iv	**Meningitis:** For a dose of 2.4 g x 6 iv, isolates with MIC≤0.06 mg/L are susceptible. **Pneumonia caused by *S. pneumoniae:* breakpoints are related to dosage:** For a dose of 1.2 g x 4 iv, isolates with MIC ≤0.5 mg/L are susceptible. For a dose of 2.4 g x 4 iv or 1.2 g x 6 iv, isolates with MIC ≤1 mg/L are susceptible. For a dose of 2.4 g x 6 iv, isolates with MIC ≤2 mg/L are susceptible.
Ampicillin	1 g x 3-4 iv depending on species and/or infection type	2 g x 3-4 iv depending on species and/or infection type	**Meningitis:** 2 g x 6 iv
Ampicillin-sulbactam	3 g x 3 iv	3 g x 4 iv	
Amoxicillin	0.5 g x 3 iv Oral dosage under discussion	2 g x 6 iv Oral dosage under discussion	**Meningitis:** 2 g x 6 iv
Amoxicillin-clavulanic acid	(1 g amoxicillin + 0.2 g clavulanic acid) x 3 iv Oral dosage under discussion	(2 g amoxicillin + 0.2 g clavulanic acid) x 3 iv Oral dosage under discussion	
Piperacillin	4 g x 3 iv	4 g x 4 iv	***Pseudomonas* spp.:** High dose only
Piperacillin-tazobactam	(4 g piperacillin + 0.5 g tazobactam) x 3 iv	(4 g piperacillin + 0.5 g tazobactam) x 4 iv	***Pseudomonas* spp.:** High dose only
Ticarcillin	3 g x 4 iv	3 g x 6 iv	***Pseudomonas* spp.:** High dose only
Ticarcillin-clavulanic acid	(3 g ticarcillin + 0.1 g clavulanic acid) x 4 iv	(3 g ticarcillin + 0.1 g clavulanic acid) x 6 iv	***Pseudomonas* spp.:** High dose only
Phenoxymethylpenicillin	0.5-2 g x 3-4 oral depending on species and/or infection type	None	
Oxacillin	Clinical breakpoints not available	Clinical breakpoints not available	
Cloxacillin	0.5 g x 4 oral or 1 g x 4 iv	1 g x 4 oral or 2 g x 6 iv	
Dicloxacillin	0.5-1 g x 4 oral or 1 g x 4 iv	2 g x 4 oral or 2 g x 6 iv	
Flucloxacillin	1 g x 3 oral or 2 g x 4 iv	1 g x 4 oral or 2 g x 6 iv	

I breakpoints sono costruiti in base ai dosaggi (standard e alti)
I dosaggi sono basati sulle concentrazioni di antibiotico raggiungibili nei tessuti, sulla tollerabilità dell'antibiotico, sul tipo e modo di somministrazione, sul tipo di patologia e sul tipo di microrganismo

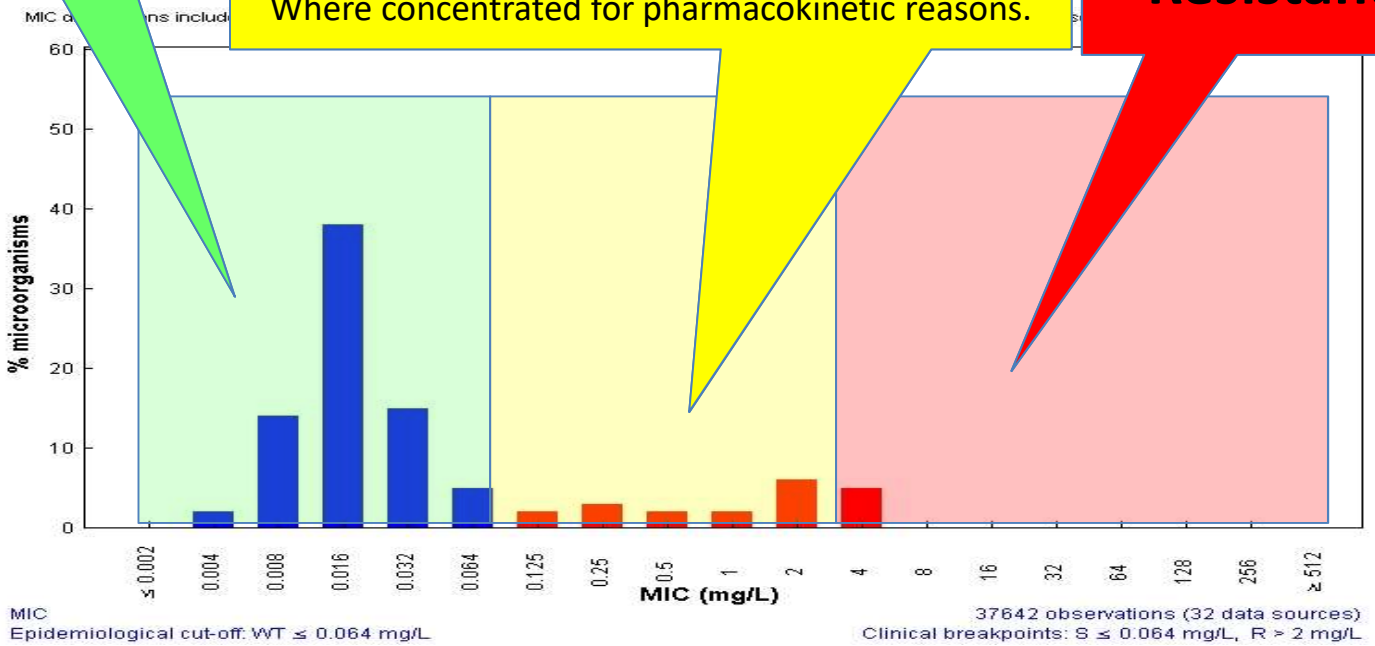
DEFINIZIONI EUCAST 2018

Susceptible

Intermediate

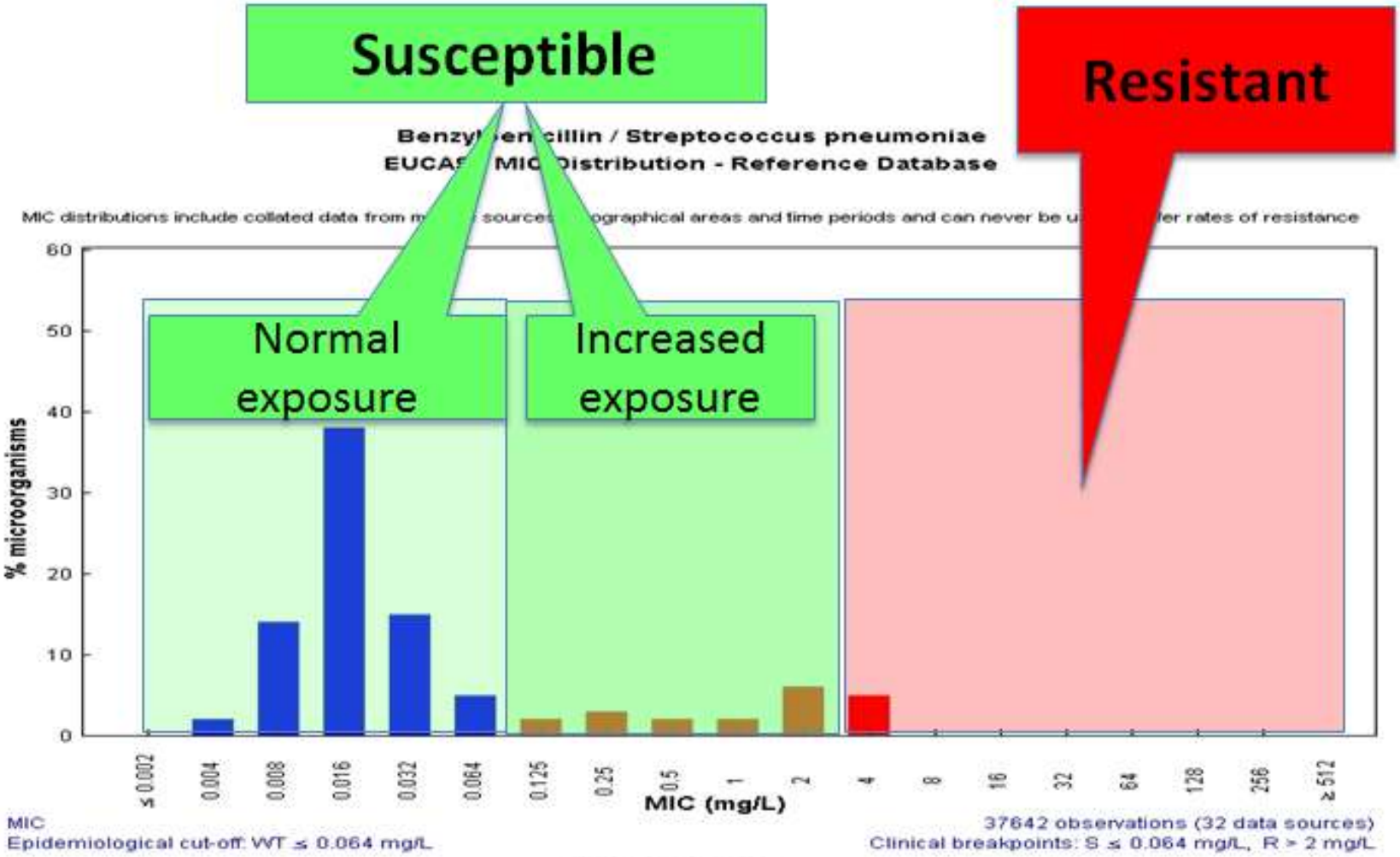
Uncertain effect.
Buffer zone for technical variation.
For a high dose.
Where concentrated for pharmacokinetic reasons.

Resistant



www.eucast.org

DEFINIZIONI EUCAST 2019



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New definitions of S, I and R

- The changes in the definitions of **S** and **R** categories are minor. They mostly emphasise the relationship between the susceptibility category and the level of exposure.

I cambiamenti nella categoria **«I»** avranno **un maggiore impatto clinico e tecnico e influenzeranno i dati di sorveglianza per la resistenza agli antibiotici**. Saranno inoltre necessari cambiamenti in alcuni breakpoint

Le nuove definizioni riflettono la necessità di una **corretta esposizione all'antibiotico**, e, **per i laboratori, la responsabilità di risolvere incertezze di risultato,** dovute a motivi tecnici, prima di finalizzare il risultato

Il simbolo per la categoria a sensibilità intermedia rimarrà «I»

La categoria "I" richiede un aumento dell'esposizione all'antibiotico che, secondo le raccomandazioni riportate da EUCAST, è in funzione di:

- ✓ **modalità di somministrazione**
- ✓ **dose più elevata**
- ✓ **diminuzione degli intervalli di somministrazione**
- ✓ **tempo di infusione**
- ✓ **distribuzione ed escrezione del farmaco** (che influenzano la concentrazione del farmaco nel sito di infezione e, quindi, l'attività sul microrganismo)

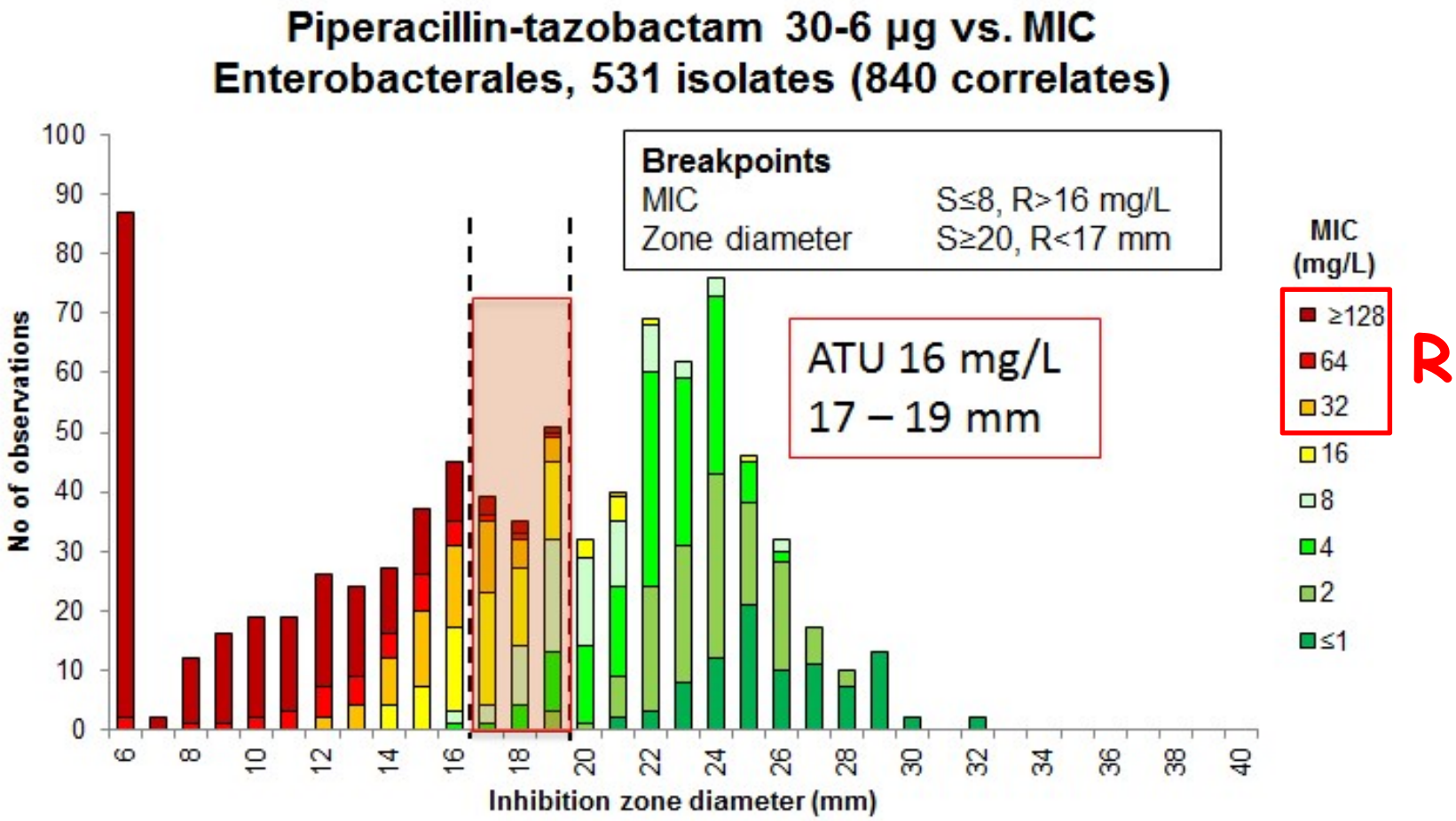
Area of Technical Uncertainty (ATU)

- EUCAST´s ability to detect areas where the technical uncertainty is such that it seriously affect the predictive value of antimicrobial susceptibility testing (AST) has improved.

Nel 2019 verrà introdotto il termine «**ATU**» nei test di sensibilità in cui è richiesto un «**warning**» per allertare il laboratorio dell'incertezza relativa al risultato del test

Il warning **interessa solo il laboratorio, non il clinico,** e il laboratorio necessita di una strategia per **1) assicurare la correttezza o 2) riportare l'incertezza del risultato**

Piperacillin-tazobactam vs. Enterobacterales



Redefining S, I and R 2019 - www.eucast.org

Preliminary ATUs in *Enterobacterales*, *Pseudomonas* and *Staphylococcus*

Species	Agent	MIC (mg/L, ATU)	Zone diameter (mm, ATU)
Enterobacterales	Amoxicillin-clavulanic acid	-	19-20
	Piperacillin-tazobactam	16	17-19
	Ceftaroline	-	22-23
	Ciprofloxacin	0.5	22-24
Ps. aeruginosa	Piperacillin-tazobactam	-	18-19
	Ceftazidime-avibactam	-	16-17
	Colistin	4	-
St. aureus	Ceftaroline	1	19-20
	Ceftobiprole	2	16-17
	Amikacin	16	15-19
St. epidermidis	Cefoxitin	-	25-27

Preliminary ATUs

Preliminary ATUs in *H. influenzae*

Species	Agent	MIC (mg/L, ATU)	Zone diameter (mm, ATU)
H. influenzae	Ampicillin		16-19
	Amoxicillin-clavulanic acid		14-16
	Piperacillin-tazobactam	0.5	24-27
	Cefotaxime		25-27
	Ceftriaxone		31-33
	Cefuroxime (iv and oral)	2	25-27
	Cefepime, Cefpodoxime and Imipenem		See flow chart

Preliminary ATUs

EUCAST breakpoint table v.9.0 (2019) with columns for ATU warnings for MIC and/or disk diffusion testing

Penicillins[1]	MIC breakpoint (mg/L)			Disk content (µg)	Zone diameter breakpoint (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Benzylpenicillin	-	-			-	-		**1/A.** Wild type Enterobacterales are categorised as susceptible to aminopenicillins. Some countries prefer to categorise wild type isolates of *E. coli* and *P. mirabilis* as "Susceptible, increased exposure". When this is the case, use the MIC breakpoint S ≤ 0.5 mg/L and the corresponding zone diameter breakpoint S ≥ 50 mm.
Ampicillin	8[1]	8		10	14[A,B]	14[B]		
Ampicillin-sulbactam	8[1,2]	8[2]		10-10	14[A,B]	14[B]		
Amoxicillin	8[1]	8		-	Note[C]	Note[C]		
Amoxicillin-clavulanic acid	8[1,3]	8[3]		20-10	19[A,B]	19[B]	19-20	
Amoxicillin-clavulanic acid (uncomplicated UTI only)	32[1,3]	32[3]		20-10	16[A,B]	16[B]		
Piperacillin	8	16		30	20	17		
Piperacillin-tazobactam	8[4]	16[4]	16	30-6	20	17	17-19	
Ticarcillin	8	16		75	23	20		**B.** Ignore growth that may appear as a thin inner zone on some batches of Mueller-Hinton agars.
Ticarcillin-clavulanic acid	8[3]	16[3]		75-10	23	20		**C.** Susceptibility inferred from ampicillin.
Temocillin	Note[5]	Note[5]			Note[5]	Note[5]		**D.** Ignore isolated colonies within the inhibition zone for *E. coli*.
Phenoxymethylpenicillin	-	-			-	-		
Oxacillin	-	-			-	-		
Cloxacillin	-	-			-	-		
Dicloxacillin	-	-			-	-		
Flucloxacillin	-	-			-	-		
Mecillinam (uncomplicated UTI only) *E. coli*, *Klebsiella* spp. (except *K. aerogenes*), *Raoultella* spp. and *P. mirabilis*	8[6]	8[6]		10	15[D]	15[D]		

ATU – alternative actions for the laboratory

Ripetere il test con la stessa metodica – quando si sospetta un errore tecnico

Ripetere il test con un'altra metodica – mediante rilevazione della MIC o tramite PCR per rilevare il meccanismo di resistenza (rilevazione di *vanA* o *vanB* negli enterococchi)

Riportare il risultato come «incerto» – inserimento di note, asterischi e commenti nei quali si spiega il motivo dell'incertezza del risultato

Riportare il risultato come «R» - se nell'antibiogramma ci sono altre buone alternative terapeutiche

Valutare l'opportunità di **discutere il risultato col clinico**

Criticità per il laboratorio:
Dovremo controllare tutti gli intermedi?

ccesso ai servizi per | monza per bambini | Instant Virtual Extran | Surveillance Atlas of | GenoType NTM-DR | Gallery of ba

Home Con

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AST of bacteria

- Organization
- EUCAST News
- Clinical breakpoints
- Expert rules and intrinsic resistance
- Resistance mechanisms

EUCAS
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The EUC
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against standard broth microdilution for *Escherichia coli*, *Klebsiella Pseudomonas aeruginosa*, and *Acinetobacter spp*.

4. Warning against the use of vancomycin Etest™ MTS™ (Liofilchem) for vancomycin MIC determina in *Enterococcus faecalis and E. faecium with low- resistance.*

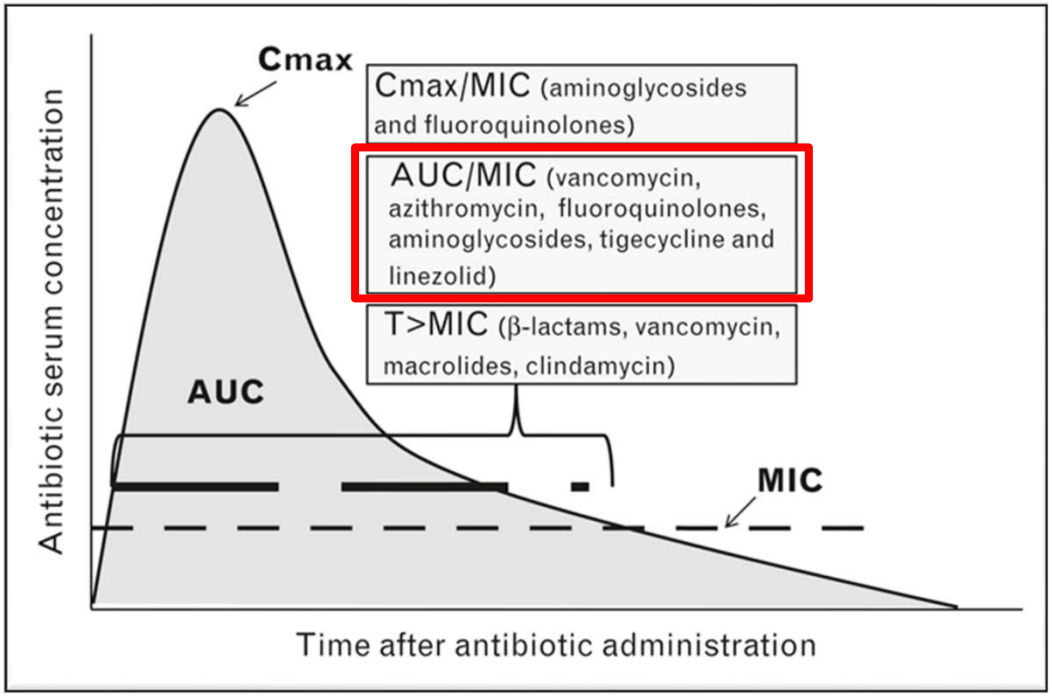
Warning issued 10 July, 2018.

A study performed by the Norwegian reference laboratory in T found that currently available gradient tests from bioMerieux a Liofilchem underestimate vancomycin MIC in low level vancomycin and E. faecium positive for vanA/vanB and with broth microdilution that this causes false susceptibility in these strains. The finding has EUCAST Development Laboratory. Liofilchem and bioMerieux are problem. The M.I.C.E from Oxoid/Thermofisher was not part of the now been evaluated using the same strain collection and the same problem has been identified for M.I.C.E.

Until this has been resolved, EUCAST warns against the use o tests to confirm low level vanB mediated resistance in *E. faec* This is until further notice best confirmed by the use of PCR o MIC using broth microdilution.

Monitoraggio terapeutico (TDM)

VANCOMICINA



Vancomicina: dosaggio ottimale
AUC/MIC > 400

MIC=1? MIC=2?

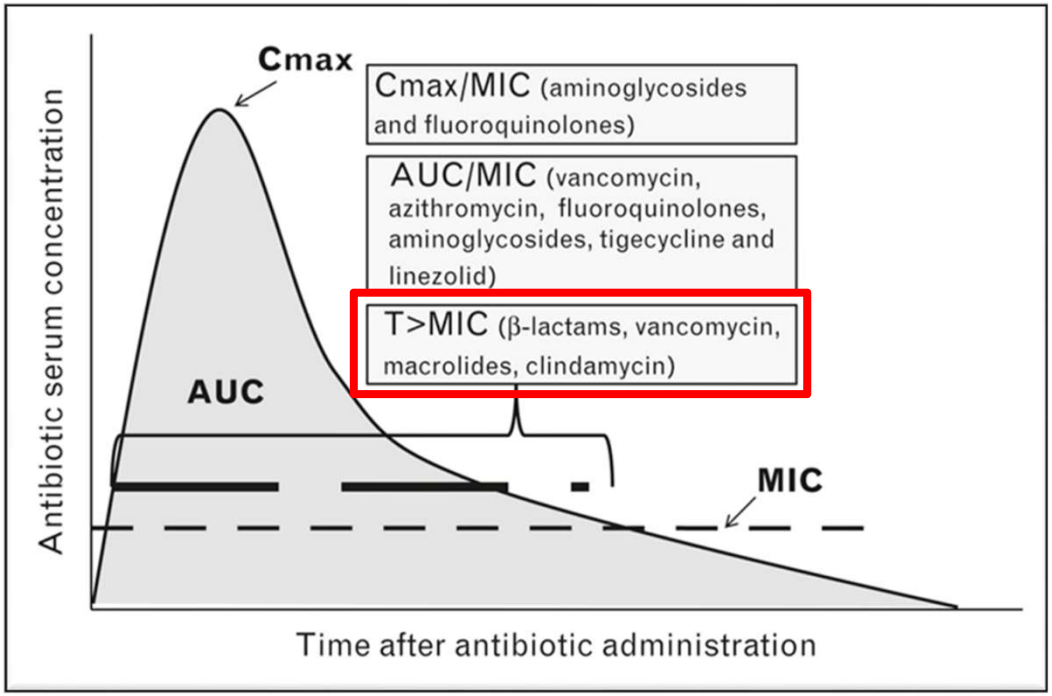
Microdiluizione in brodo come sistema di riferimento

Valori precisi di MIC sono necessari per prevedere l'effetto terapeutico:

- Ottimizzazione dei dosaggi
- Caratteristiche del paziente
- Prevenire le resistenze

Monitoraggio terapeutico (TDM)

MEROPENEM



VIRULENCE
2017, VOL. 8, NO. 4, 470–484
https://doi.org/10.1080/21505594.2017.1292196

Taylor & Francis
Taylor & Francis Group

REVIEW

Check for updates

Therapeutic options for carbapenem-resistant Enterobacteriaceae infections

Enrico Maria Trecarichi and Mario Tumbarello

Institute of Infectious Diseases, Catholic University of Sacred Heart, Rome, Italy

survival benefit. The use of carbapenems in association with other active drugs is likely ineffective for CRE isolates with carbapenem Minimum Inhibitory Concentrations (MICs) >8 mg/l. The

REVIEW

The management of multidrug-resistant *Enterobacteriaceae*

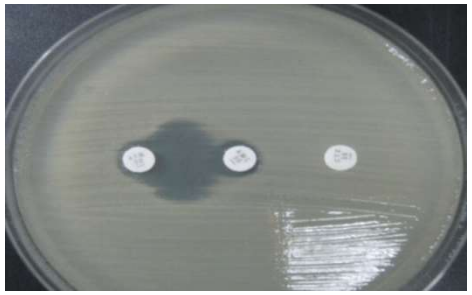
Bassetti M., et al. Curr Opin Infect Dis 2016

- In KPC-Kp with meropenem MIC 8–16 mg/l or less, the combination of a carbapenem-containing regimen (administered with high-dosed, prolonged infusion) with colistin or high-dose tigecycline or aminoglycoside can be administered with TDM.
- In KPC-Kp with meropenem MIC higher than 8–16 mg/l, the use of carbapenem should be avoided and various combination therapies based on the in-vitro susceptibility of antimicrobials (e.g., colistin, high-dose tigecycline, fosfomycin, and aminoglycosides) should be selected.

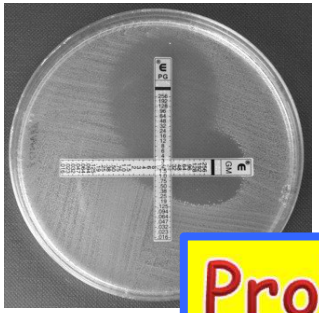
Automated — ***Escherichia coli-KPC*** — **BMD**

Antibiotic	MIC mg/L(S/I/R)	Antibiotic	MIC mg/L(S/I/R)
Pip/Tazo	>64 (R)	Pip/Tazo	>32 (R)
Cefotaxime	>32 (R)	Cefotaxime	>8 (R)
Ceftazidime	>32 (R)	Ceftazidime	>16 (R)
Cefepime	>32 (R)	Aztreonam	>32 (R)
Ertapenem	>4 (R)	Ertapenem	>2 (R)
Imipenem	>8 (R)	Imipenem	8 (I)
Meropenem	>8 (R)	Meropenem	4 (I)
Amikacin	≤2 (S)	Amikacin	≤4 (S)
Gentamicin	≤1(S)	Gentamicin	1(S)
Ciprofloxacin	>2 (R)	Ciprofloxacin	>2 (R)
Tigecycline	≤0.5 (S)	Tigecycline	≤0.25 (S)
Colistin	≤0.5 (S)	Colistin	≤0.25 (S)

4-Interazioni sinergiche

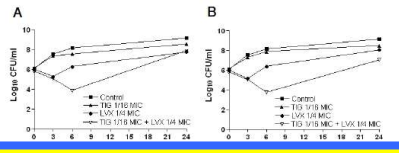


Disco approssimazione
Solo qualitativo, no dati sulle concentrazioni sinergiche,
Sistema statico
Sinergia: distorsione degli aloni



E-test
Comodo, quantitativo,
poco riproducibile
Sistema statico

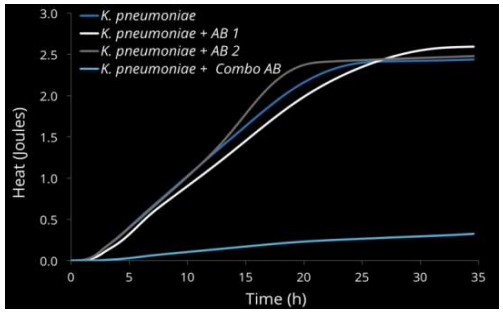
Petersen et al JAC, 2006; Entenza & Moreiilon IJAM, 2009; Jian et al MDR, 2017;Lashram et al Indian JMM, 2017; Jiang et al IDR, 2018



Problematiche inerenti alla metodica!!

Sistemi standardizzati per valutare l'attività di antibiotici in combinazione

Piastre Checkerboard preformate



Calorimetria

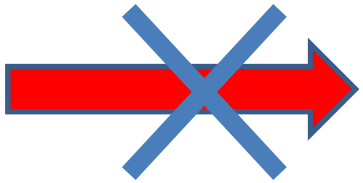
Interazioni tra antibiotici per:
- Valutare antagonismi
- Valutare sinergie (trattamento, abbassamento dei dosaggi, prevenire resistenze)

Problematiche interpretative:
Interazioni sinergiche non correlabili alla specie
Interazioni sinergiche non correlabili al clone
Interazioni sinergiche sono ceppo-specifiche
(vanno saggiate ceppo per ceppo)

Concentrazioni sinergiche raggiungibili nel sito di infezione?

Terapia empirica ragionata
(sulla base della sinergia comunicata dal laboratorio)

Antibiotio A+
Antibiotico B
Sinergia



Outcome clinico favorevole

Probabilità elevata di successo terapeutico

Solo dato in vitro, pochi lavori in letteratura che correlano la sinergia in vitro con l'outcome clinico

Nessun ente certifica che l'interazione in vitro sia efficace in vivo:

(NO dati organizzati: studi in vitro, studio PK/PD, studi su modelli animali/umani, simulazioni)

Antibiotico A
+
Antibiotico B

SINERGIA

Antibiotico A	R
Antibiotico B	R

Antibiotico A	S
Antibiotico B	R

Antibiotico A	S
Antibiotico B	S

Terapia empirica ragionata

(sulla base della sinergia comunicata dal laboratorio)

5-Resistenze rare e inconsuete

Salmonella enterica ser. Napoli	
Antibiotico	**MIC mg/L(S/I/R)**
Amoxi/Clav	4 (S)
Pipera/Tazo	4 (S)
Cefotaxime	>64 (R)
Ceftazidime	4 (I)
Cefepime	4 (I)
Ertapenem	<=0.5 (S)
Imipenem	<=0.25 (S)
Meropenem	<=0.25 (S)
Ciprofloxacina	0.016 (S)
Trimet/Sulfam	<=20 (S)
Tigeciclina	1 (S)

WGS: conferma presenza $bla_{CTX-M-1}$

Journal of Global Antimicrobial Resistance 15 (2018) 101–102

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: www.elsevier.com/locate/jgar

Emergence of CTX-M-1-producing *Salmonella enterica* serovar Napoli: A novel 'enzyme–pathogen association' in the Italian extended-spectrum β-lactamase (ESBL) endemic context

Isolato da coprocoltura
Pz: bambina di 1 anno con sintomi gastroenterici

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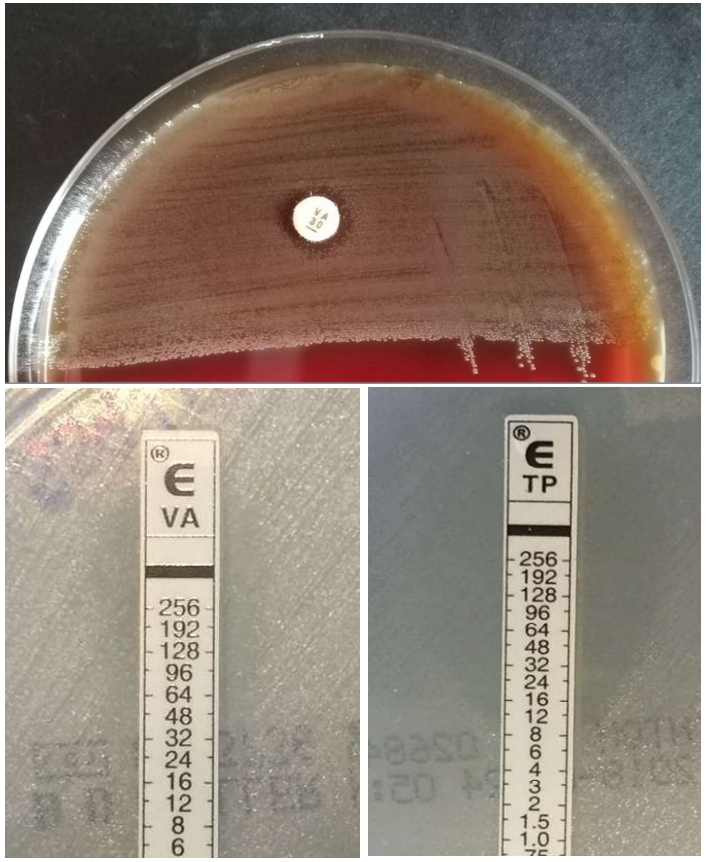
5-Resistenze rare e inconsuete

Enterococcus avium	
Antibiotico	**MIC mg/L(S/I/R)**
Ampicillina	≤2 (S)
Ampicillina/Sulbactam	≤2 (S)
Cefuroxime	>32 (R)
Imipenem	≤1 (S)
Gentamicina HL	SYN-S
Streptomicina HL	SYN-R
Levofloxacina	0.25 (S)
Linezolid	2 (S)
Tigeciclina	<=0.12 (S)
Teicoplanina	16 (R)
Vancomicina	>16 (R)

WGS: conferma presenza *vanA*

Paziente ricoverato in Rianimazione colonizzato a livello rettale

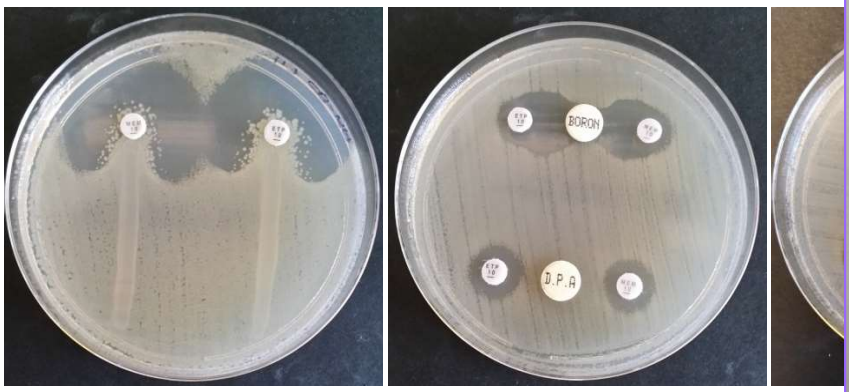
Filmarray:
positivo per *Enterococcus* spp. *vanA/vanB*

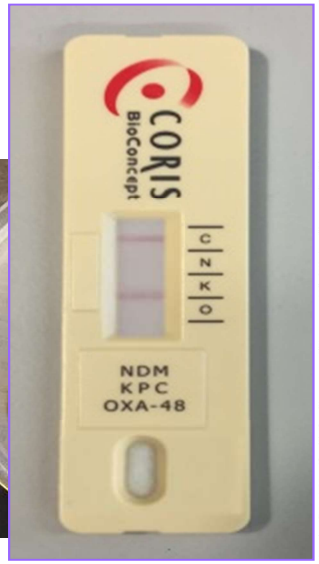


Paziente ricoverato in Terapia intensiva, nessun ricovero precedente (proveniente dal domicilio), tamponi da ulcera e rettali positivi per *C. braakii* (prima) e *K. pneumoniae* (dopo)

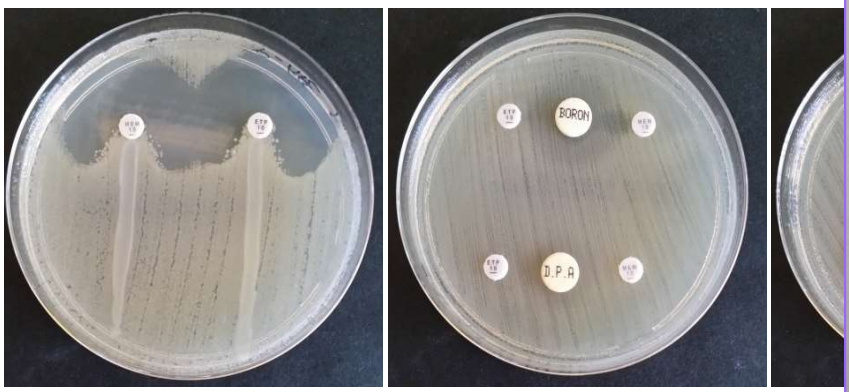
PRIMO ISOLAMENTO DI *CITROBACTER BRAAKII* PRODUTTORE DI KPC

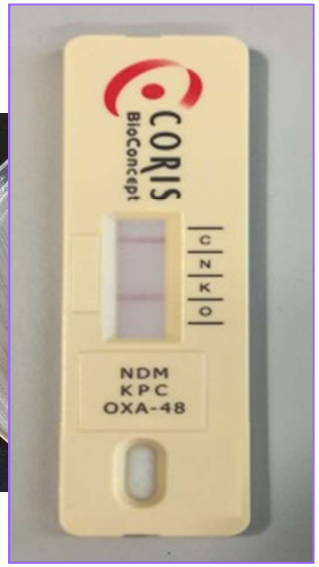
C. braakii





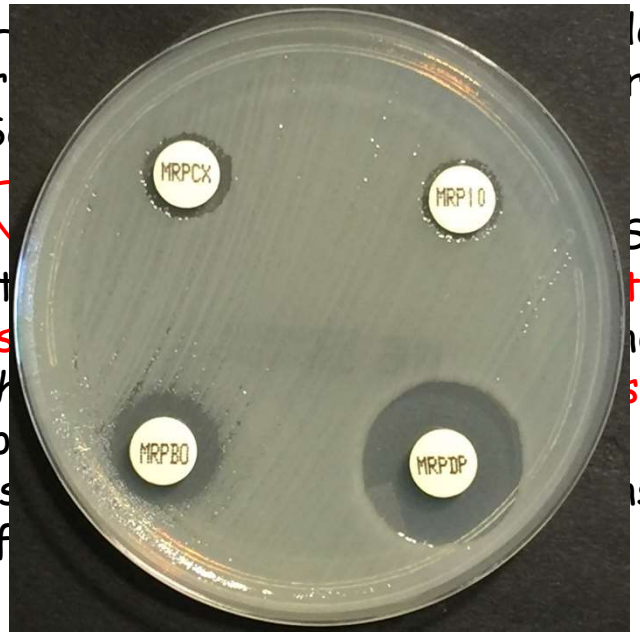
K. pneumoniae





Antibiotici	MICs mg/L (S, I, R)
	C. braakii
Amoxicillina/acido clavulanico	>64/2 (R)
Piperacillina/tazobactam	>32/4 (R)
Cefotaxime	8 (R)
Ceftazidime	16 (R)
Ertapenem	>2 (R)
Imipenem	8 (I)
Meropenem	4 (I)
Amikacina	16 (I)
Gentamicina	2 (S)
Tobramicina	>8 (R)
Ciprofloxacina	>2 (R)
Tigeciclina	1 (S)
Cotrimossazolo	4/76 (I)
Colistina	<0.25 (S)
Aztreonam	>32 (R)
Ceftolozano/tazobactam	16/4 (R)
Ceftazidime/avibactam	<0.5/4 (S)

NDM in our experience



Two indipe frican

Case #1 - origin,invo hospitalize . In Italy, N ST15) wasisolate age fluid linked to c He was dis er 25 days of ho

Case #2 - leveloped an acute r ruise in the Red S the Red Sea H In Italy, N ST11) Was isolat tory secretions d *S. maltoph* s caused by NDM-p He was dis s after 61 days of

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Short Communication

First report of NDM-1-producing *Klebsiella pneumoniae* imported from Africa to Italy: Evidence of the need for continuous surveillance

Luigi Principe[a], Carola Mauri[a], Viola Conte[b], Beatrice Pini[a], Tommaso Giani[b], Gian Maria Rossolini[b,c,d,e], Francesco Luzzaro[a,*]

Klebsiella pneumoniae-NDM-1

Antibiotico	MIC mg/L(S/I/R)
Pip/Tazo	>128 (R)
Ceftriaxone	>64 (R)
Ceftazidime	>64 (R)
Cefepime	>64 (R)
Ertapenem	>8 (R)
Imipenem	>16 (R)
Meropenem	>16 (R)
Amikacina	>64 (R)
Gentamicina	>16 (R)
Ciprofloxacina	>4 (R)
Tigeciclina	≤0.5 (S)
Colistina	≤0.5 (S)

R-3GC *Haemophilus parainfluenzae*

P130

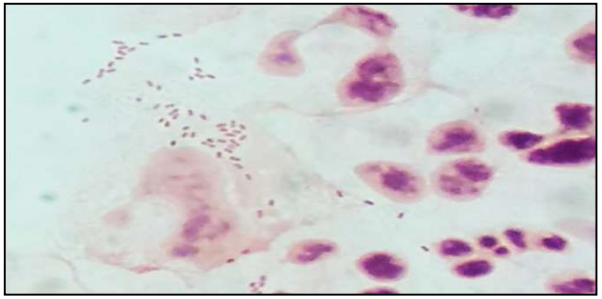
Paziente maschio, italiano (45 anni), con **sintomi di uretrite** (secrezioni mucopurulente)
Rapporti a rischio, partner di origini balcaniche (Serbia)

Prima del tampone uretrale, **terapia empirica con ceftibuten** (Isocef) per 7 giorni
➡ persistenza dei sintomi

Dopo antibiogramma **terapia mirata con ciprofloxacina** per 10 giorni
➡ scomparsa dei sintomi, risoluzione dell'infezione

Haemophilus parainfluenzae

Antibiotico	MIC mg/L(S/I/R)
Penicillina	R
Ampicillina	R
Amoxi/Clav	R (MIC=24 mg/L)
Ceftriaxone	R (MIC=2 mg/L)
Ciprofloxacina	S
Ertapenem	R (MIC >2 mg/L)
Meropenem	S
Trimet/Sulfam	S
β-lattamasi	Neg

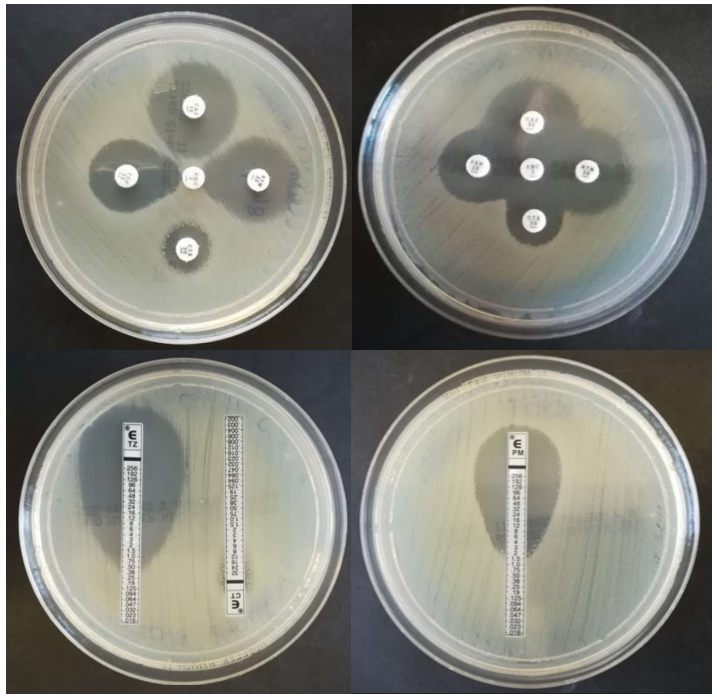


R-3GC *Shigella sonnei*

Ragazza di origini albanesi con dissenteria sanguinolenta. Nei giorni precedenti aveva partecipato ad una festa in Albania insieme ai genitori. Il giorno dopo si mettono in viaggio in auto per tornare in Italia. La ragazza sviluppa i sintomi durante il viaggio. La famiglia si ferma in un ospedale in Croazia, no antibiotici ma idratazione. Ricovero in Italia a Merate, no antibiotico. Meropenem in seguito a comunicazione del laboratorio

Shigella sonnei

Antibiotico	MIC mg/L(S/I/R)
Amoxi/Clav	16 (R)
Pipera/Tazo	4 (S)
Cefotaxime	8 (R)
Ceftazidime	2 (I)
Cefepime	2 (I)
Ertapenem	≤0.5 (S)
Imipenem	≤0.25 (S)
Meropenem	≤0.25 (S)
Ciprofloxacina	≤0.06 (S)
Trimet/Sulfam	160 (R)
Gentamicina	≤1 (S)



WGS: conferma la presenza di CTX-M-37

6-MDR non trattabili coi nuovi antibiotici

Antibiotico	MIC mg/L(S/I/R)
Pip/Tazo	>64 (R)
Cefotaxime	>32 (R)
Ceftazidime	>32 (R)
Cefepime	>32 (R)
Ertapenem	>4 (R)
Imipenem	>8 (R)
Meropenem	>8 (R)
Amikacina	>64 (R)
Gentamicina	>16 (R)
Ciprofloxacina	>2 (R)
Tigeciclina	≤0.5 (S)
Colistina	≤0.5 (S)

K. pneumoniae NDM

Ceftazidime/Avibactam NO
Ceftolozano/Tazobactam NO

Soluzioni future

Cefiderocol
Aztreonam/Avibactam

Antibiotico	MIC mg/L(S/I/R)
Pip/Tazo	>64 (R)
Cefotaxime	>32 (R)
Ceftazidime	>32 (R)
Cefepime	>32 (R)
Ertapenem	>4 (R)
Imipenem	>8 (R)
Meropenem	>8 (R)
Amikacina	>32 (R)
Gentamicina	>8 (R)
Ciprofloxacina	>2 (R)
Tigeciclina	≤0.5
Colistina	≤0.5 (S)

A. baumannii CARBA-R

Ceftazidime/Avibactam NO
Ceftolozano/Tazobactam NO

Soluzioni future

Cefiderocol
Everacyclina

Antibiotico	MIC mg/L(S/I/R)
Ampicillina	>32 (R)
Ampicillina/Sulbactam	>32 (R)
Chinupristina/ Dalfopristina	0,5 (S)
Imipenem	>16 (R)
Gentamicina HL	SYN-R
Streptomicina HL	SYN-R
Levofloxacina	>4 (R)
Linezolid	>8 (R)
Tigeciclina	<=0.12 (S)
Teicoplanina	>16 (R)
Vancomicina	>16 (R)

E. faecium VRE LIN-R

Ceftarolina NO
Ceftobiprolo NO
Dalbavancina NO
Tedizolid NO
Oritavancina SI

Soluzioni future

Everacyclina

…ed ai microbiologi cosa serve?

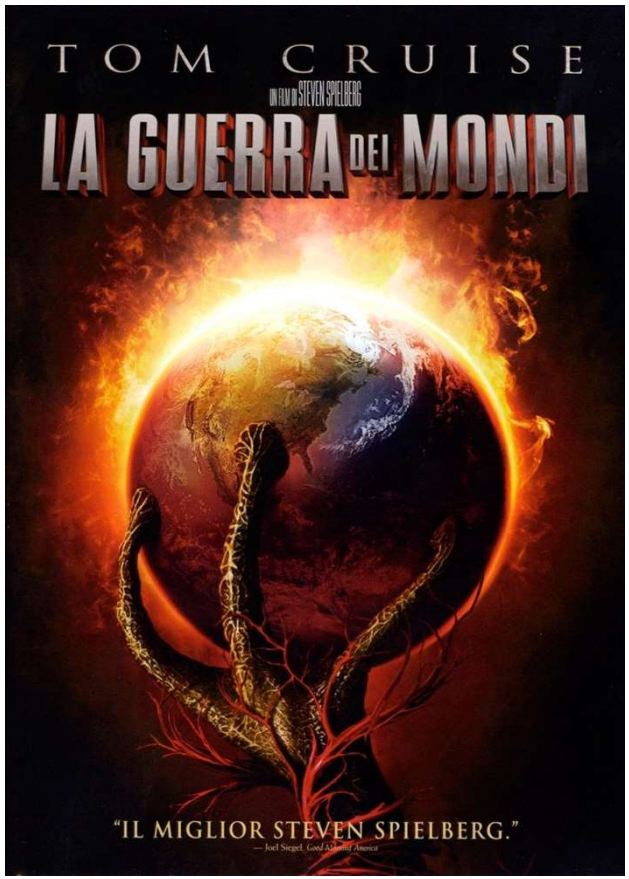
Informazioni!!!

Senza informazioni cliniche non si possono dare risultati microbiologici

+ informazioni = qualità migliore dei risultati

Consulenze microbiologiche in reparto
(storia microbiologica del paziente, esami microbiologici da eseguire, modalità di prelievo, trasporto e conservazione del campione)

Scambio culturale con i clinici,
Tirocini formativi in reparto durante i percorsi di studio



«Quando tutti i mezzi escogitati dagli uomini erano falliti, i marziani vennero distrutti dagli esseri più microscopici che Dio, nella sua infinita saggezza, aveva messo su questa Terra»

Grazie per l'attenzione