IL PAZIENTE CRITICO CON INFEZIONE DA GERMI GRAM NEGATIVI MULTIRESISTENTI - 19 giugno 2025

GESTIONE DELLE INFEZIONI DIFFICILI

Strategie diagnostiche per l'identificazione

Valeria Ghisetti

S.C. Microbiologia e Virologia

Ospedale Amedeo di Savoia - ASL Città di Torino

Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050

GBD 2021 Antimicrobial Resistance Collaborators*

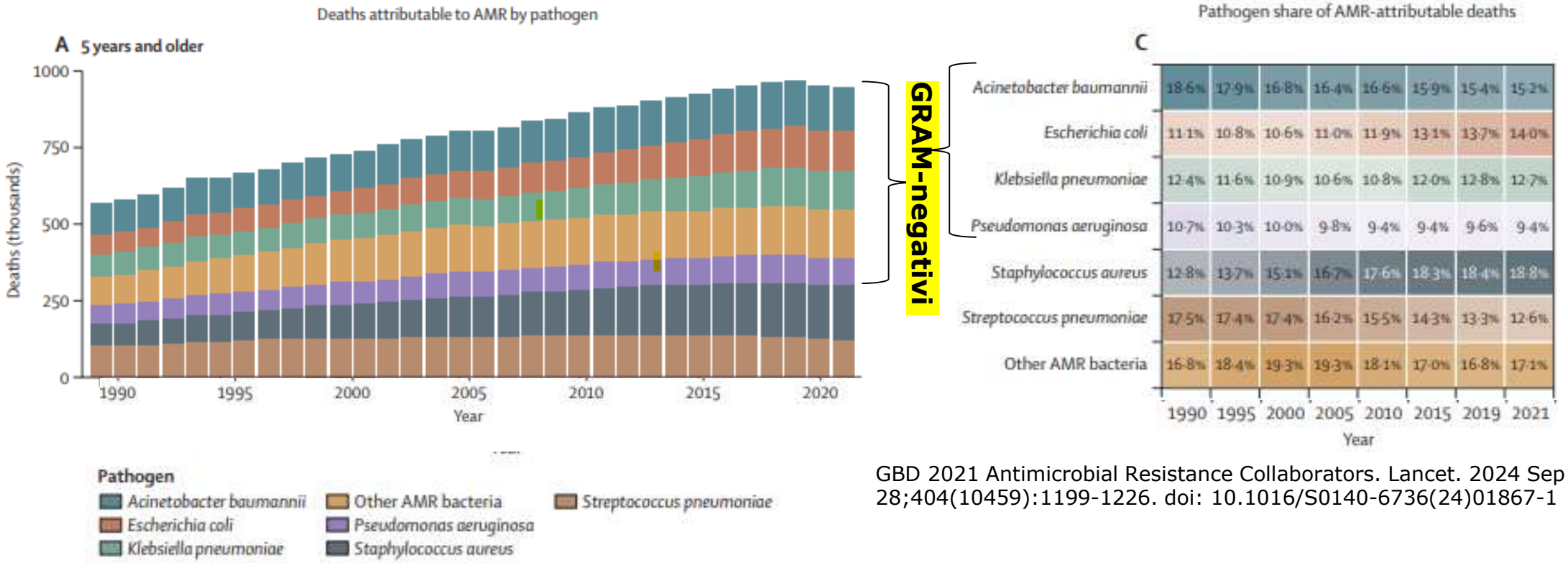
The Lancet: More than 39 million deaths from antibiotic-resistant infections estimated between now and 2050, suggests first global analysis

Published September 16, 2024

Summary

Background Antimicrobial resistance (AMR) poses an important global health challenge in the 21st century. A previous study has quantified the global and regional burden of AMR for 2019, followed with additional publications that provided more detailed estimates for several WHO regions by country. To date, there have been no studies that produce comprehensive estimates of AMR burden across locations that encompass historical trends and future forecasts.

Lancet 2024; 404: 1199–226
Published Online
September 16, 2024
https://doi.org/10.1016/
S0140-6736(24)01867-1

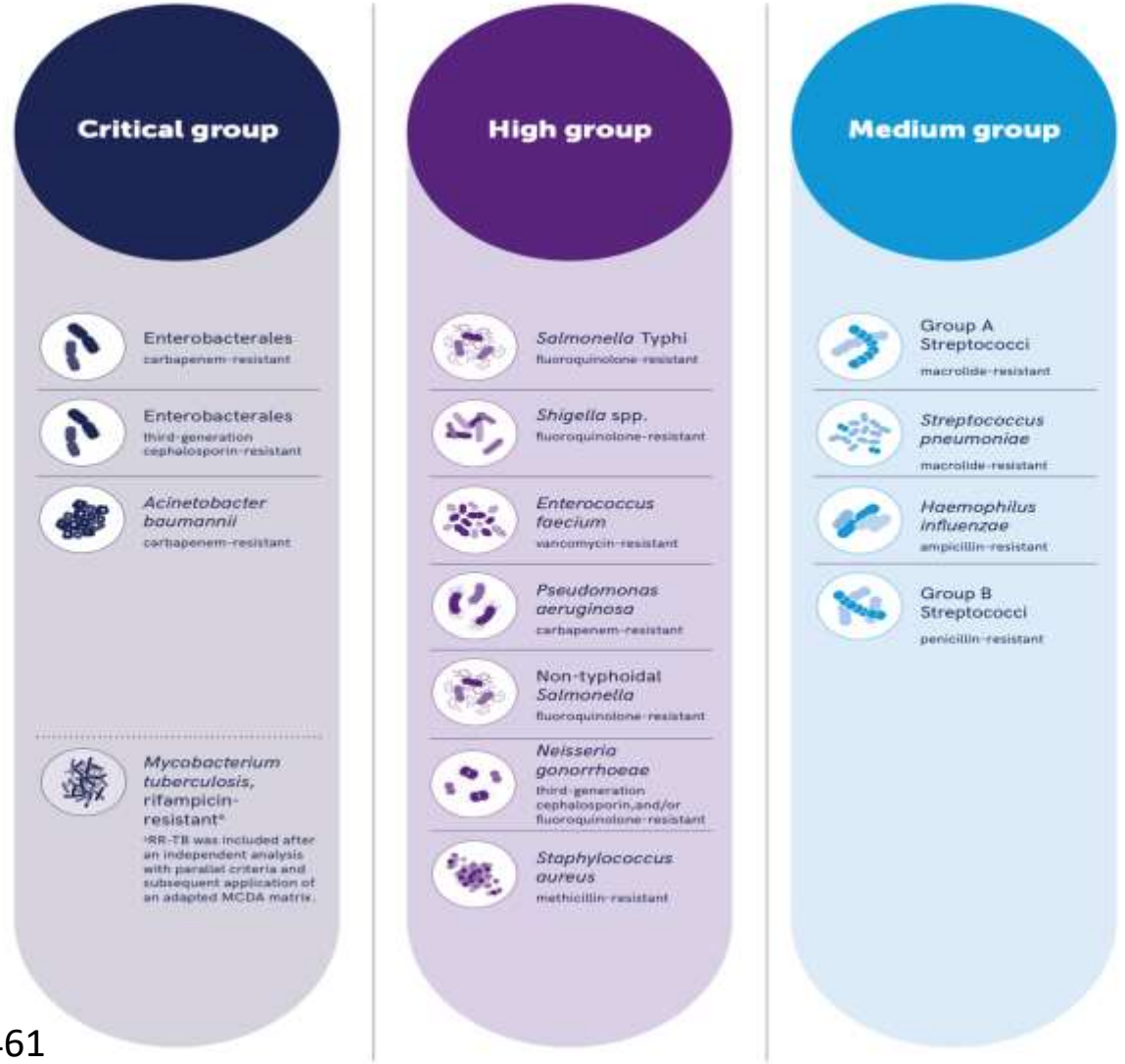


GBD 2021 Antimicrobial Resistance Collaborators. Lancet. 2024 Sep 28;404(10459):1199-1226. doi: 10.1016/S0140-6736(24)01867-1

Batteri Gram-negative Multiresistenti (MDRO)

Lista di priorità del WHO, 2024 perstrategie di contenimento dell'antibioticoresistenza e indirizzare la ricerca scientifica

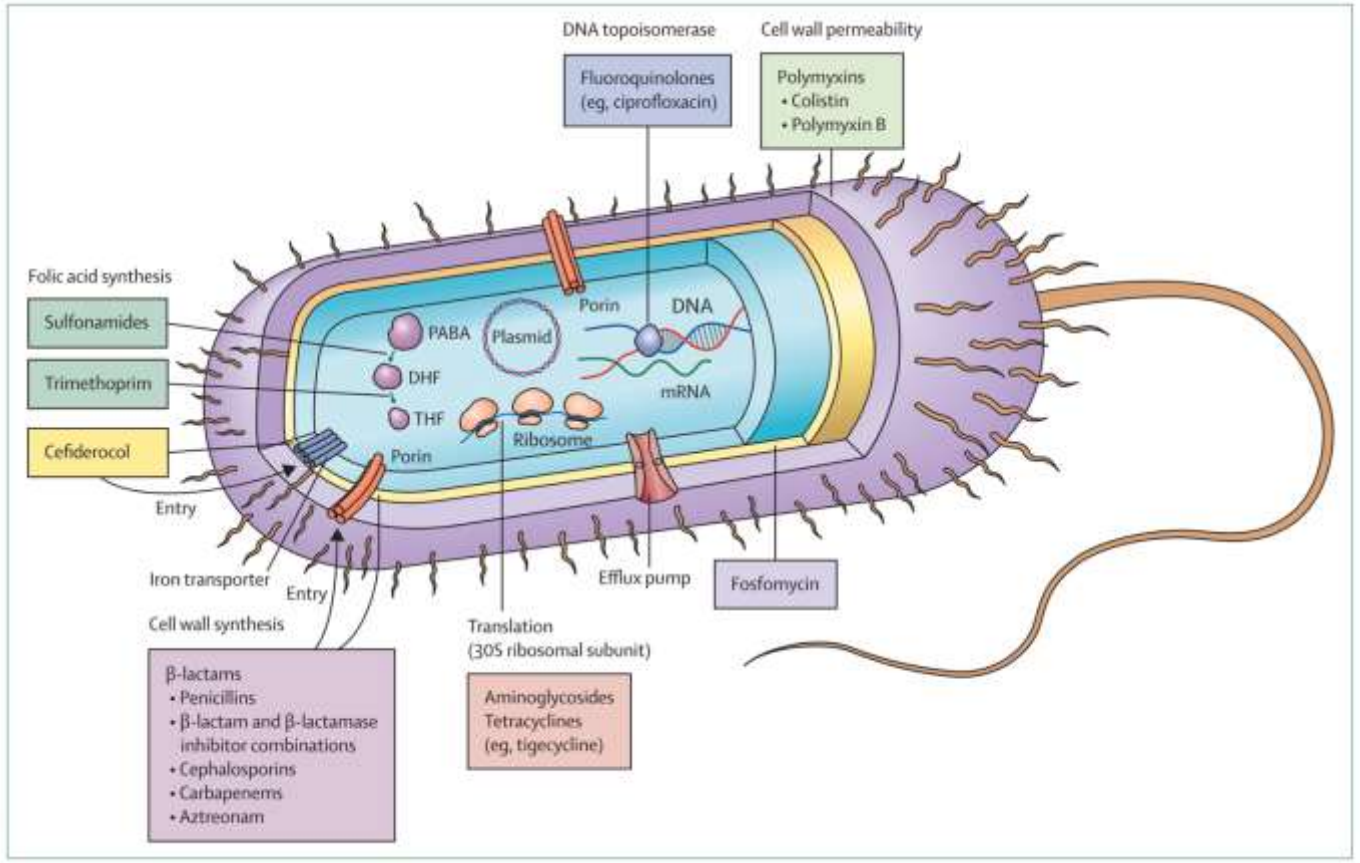
PNCAR 2022-2025



WHO 2024. https://www.who.int/publications/i/item/9789240093461

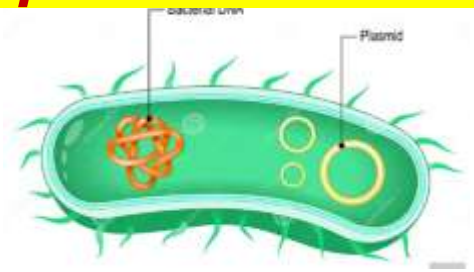
Meccanismi di antibiotico-resistenza dei batteri Gram-negativi MDR

	Categories	Examples
β-lactams[19,20] (eg, piperacillin–tazobactam, cefepime, meropenem, and ceftazidime–avibactam)		
Antibiotic modification	β-lactamase enzymes	Extended-spectrum β-lactamases (SHV, TEM, and CTX-M); carbapenemases (KPC, OXA-48, NDM, IMP, and VIM)
Decreased entry	Porin mutations	*Escherichia coli* (OmpC and OmpF); *Klebsiella pneumoniae* (OmpK35 and OmpK36); *Pseudomonas aeruginosa* (OprD); *Acinetobacter baumannii* (CarO)
Increased efflux	Efflux pumps	*E coli* (AcrAB-TolC); *P aeruginosa* (MexAB-OprM); *A baumannii* (AdeABC and AdeIJK)



Meccanismi di antibiotico-resistenza dei batteri Gram-negativi MDR

- **Di tipo plasmidico**
  - E’ il più importante e il più diffuso meccanismo di trasferimento orizzontale di geni perchè si diffonde con rapidità tra batteri delle stessa specie e di specie diversa
  - ***Interessa prevalentemente gli Enterobacterales***



Super MDR-bugs

- **Di tipo cromosomico**
  - Mediato da mutazioni/eventi ricombinati che presiedono alla permeabilità di membrana (porine) e alle pompe di efflusso, <u>può sovrapporsi al precedente</u>
  - ***Interessa prevalentemente Pseudomonas e Acinetobacter***

β-LATTAMASI: CLASSIFICAZIONE

β-lattamasi

4 classi distinte

Sito attivo

serina-enzimi

zinco-enzimi: MBL

A

C

AmpC

D

B

ESBL+

TEM-SHV
CTX-M
2006

KPC
1996

OXA-48 like
2004

Horizontal gene transfer by plasmid

NDM
IMP
VIM
2009

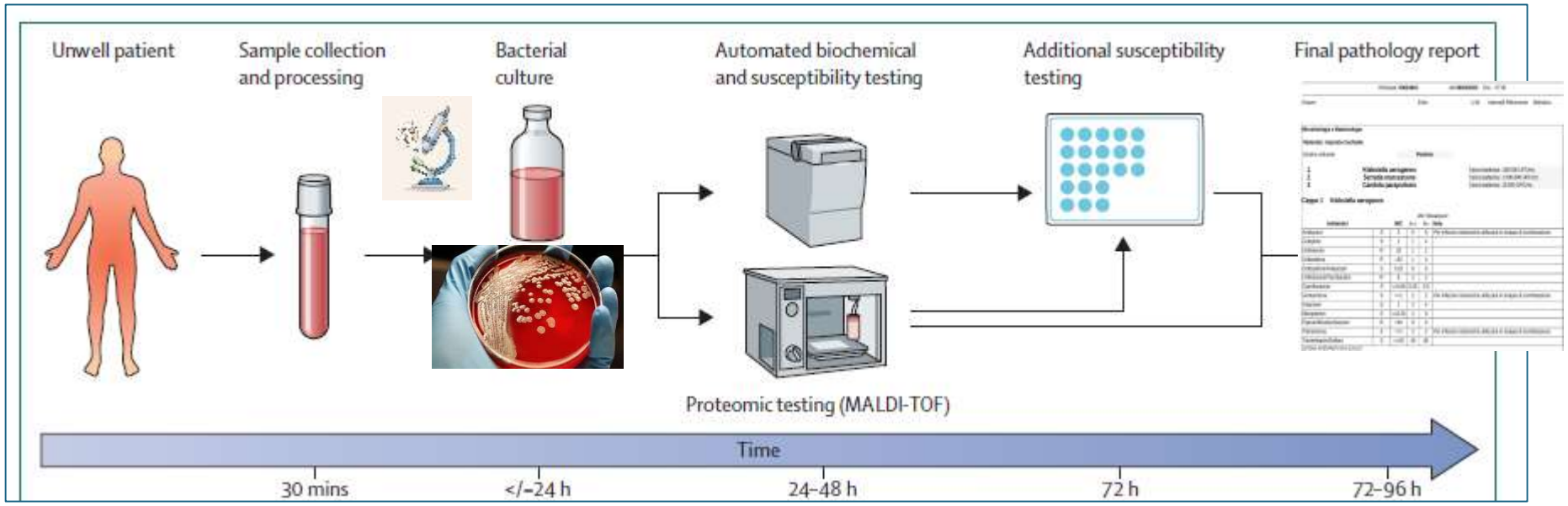
Carbapenemasi

La diagnostica microbiologica è essenziale per contrastare la resistenza agli antibiotici

Laboratorio di Microbiologia

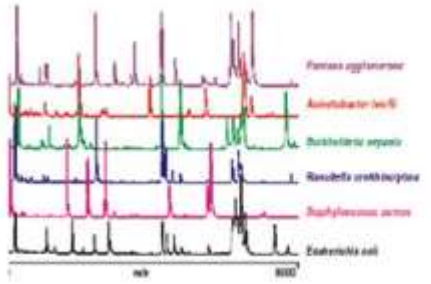
Fase pre-analitica | **Fase analitica** | **Fase post-analitica**

Automazione



Dal 2000.....

Identificazione mediante spettrometria di massa MALDI-TOF
TAT in minuti
Massima accuratezza di typing e subtyping

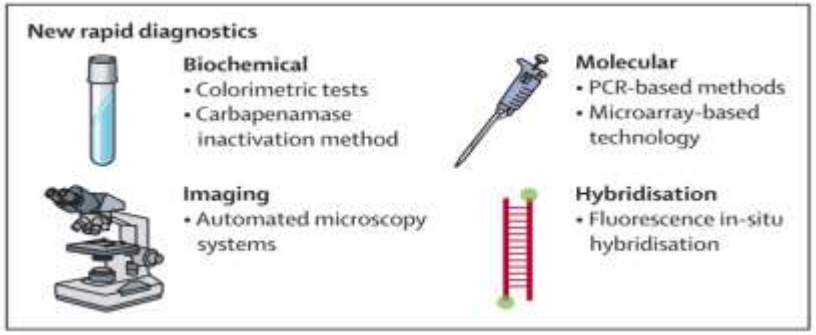


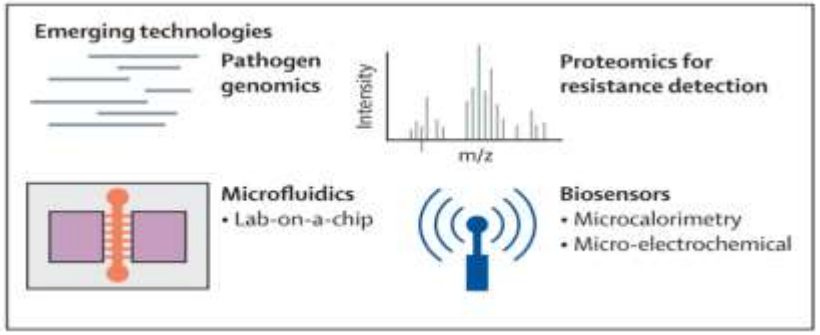
Spettro di massa delle proteine microbiche

«Fast Microbiology»

Modello organizzativo (H24 e 7/7) integrato
più flessibile alle esigenze cliniche e di sorveglianza AMR,
riduzione del TAT e maggiore accuratezza nella caratterizzazione
degli isolati batterici e dei meccanismi di antibioticoresistenza

Test GENOTIPICI e Antibiogramma MOLECOLARE
Test AST/FENOTIPICI «rapidi»





www.thelancet.com Vol 405 January 18, 2025

Test GENOTIPICI

Su materiale diretto (oltre che da coltura) e su brodi di emocolture+

TAT Rapido ~1h

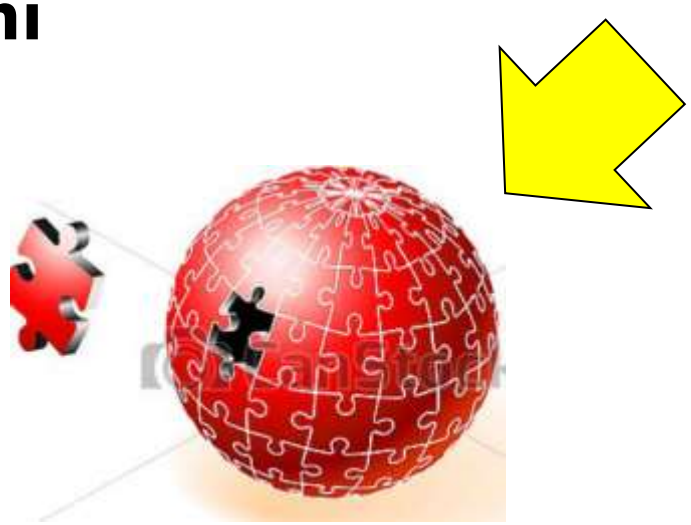
Caratterizzazione principali meccanismi di resistenza

Ottimali per sorveglianza MDRO

ATB Molecolare: Proxy per il fenotipo

Discrepanza tra genotipo e fenotipo

Costi da moderati a elevati



Xpert® Carba-R Identificazione

ALL KPCs

IMP-1 subgroup

ALL VIMS

All NDMS

OXA-48

OXA-162

OXA-163

OXA-204

IMP 1

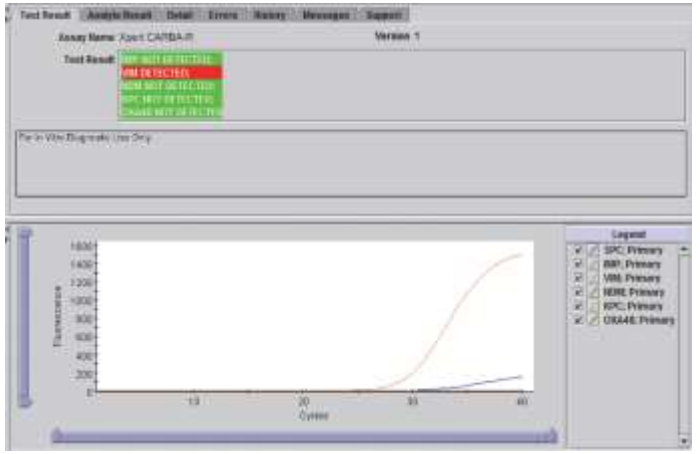
IMP 6

IMP 3

IMP 25

IMP 10

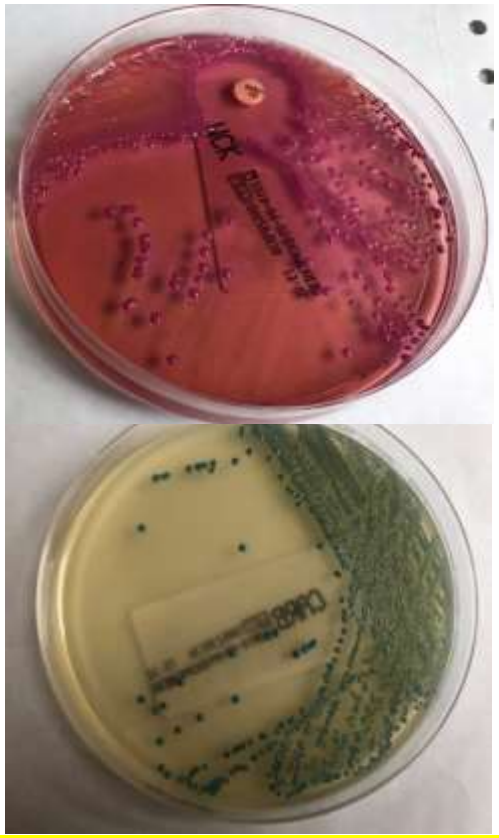
IMP 30



© Cepheid

Enterobacterales e resistenza ai Carbapenemi: sorveglianza MDRO

Tampone rettale



Kp-pneumoniae-NDM+

TAT <24 H

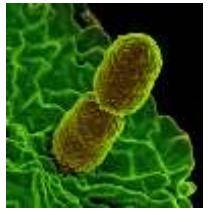
NO ATB

Isolamento e precauzioni da contatto

Test per Carbapenemasi Anni 2015-22	
KPC	POSITIVO
OXA-48	NEGATIVO
VIM	NEGATIVO
IMP-1	NEGATIVO
NDM	NEGATIVO

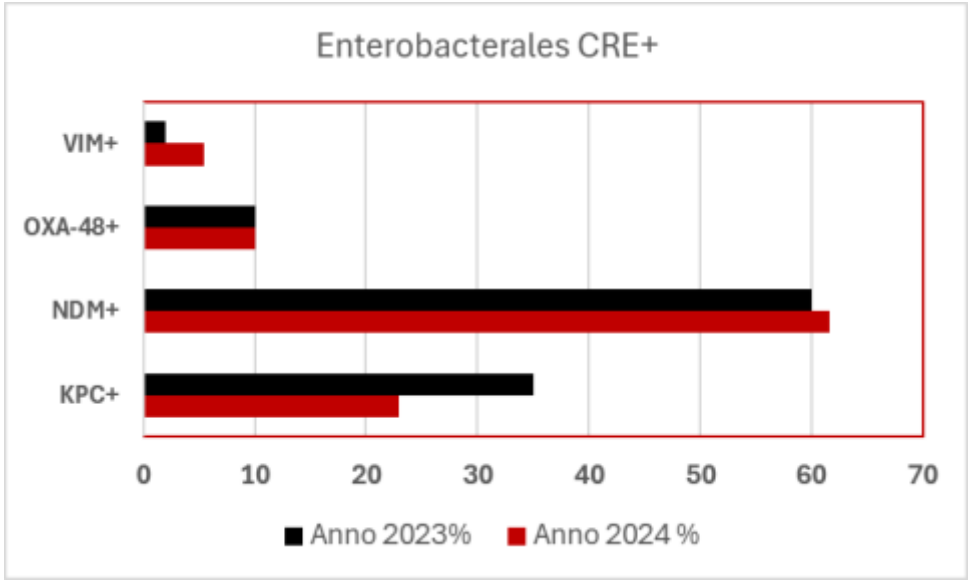
Test per Carbapenemasi Anni 2023-24	
KPC	NEGATIVO
OXA-48	NEGATIVO
VIM	NEGATIVO
IMP-1	NEGATIVO
NDM+	POSITIVO

Enterobacterales e resistenza ai Carbapenemi: sorveglianza MDRO



OAS-SGB-OMV Numero Pazienti/anno (Kp, E.coli, ENC) positivi per CRE

Anno	Pazienti testati	CRE+ (N.pazienti)	CRE+%
2021	1980	159	8.0
2022	2369	419	17.7
2023	3734	1056	28.3
2024	4559	347	7.6



Enterobacterales e resistenza ai Carbapenemi: sepsi/batteriemie da CRE

Anno 2024	N.	%
Numero pazienti (numero set)	5164 (17038 set)	-
Numero Pazienti positivi	1575	30.5
ENTEROBACTERALES	566	35.9
Klebsiella pneumoniae (KP)	156	27.6
KP-CRE+	44	28.2
Altri Enterobacterales CRE+	2	-
Totale CRE+	46	29.5
Acinetobacter Baumanni	1	-
AcB-MDRO	1	100
Pseudomonas aeruginosa	53	-
PA-MDRO	4	7.5

Enterobacterales e resistenza ai Carbapenemi: sepsi/batteriemie da CRE+

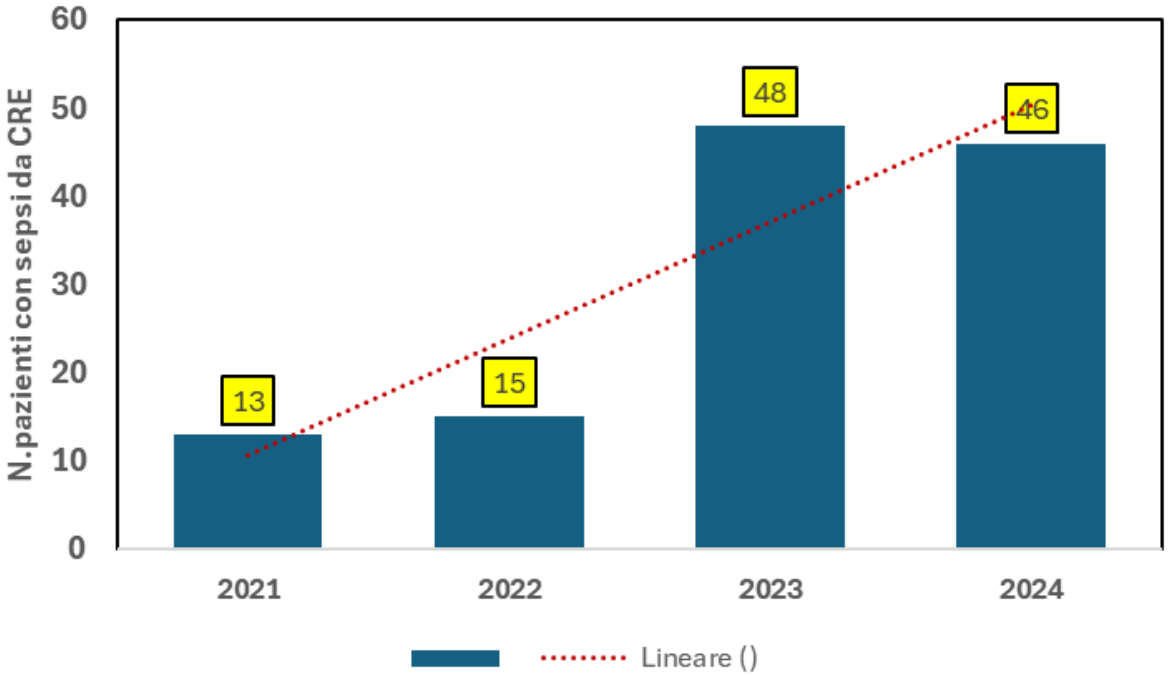
Antibiogramma molecolare <1H dalla positività

Modello di gestione emocolture
ASL Città di Torino
N.4 ospedali

media 22-48 h
95% Emo+

95%

ASL CdT (900 posti letto, sede di DEA II° livello)
Andamento pazienti con sepsi da Enterobacterales CRE+



2024 Pipeline dei test molecolari multiplex e rapidi per sepsi/batteriemie

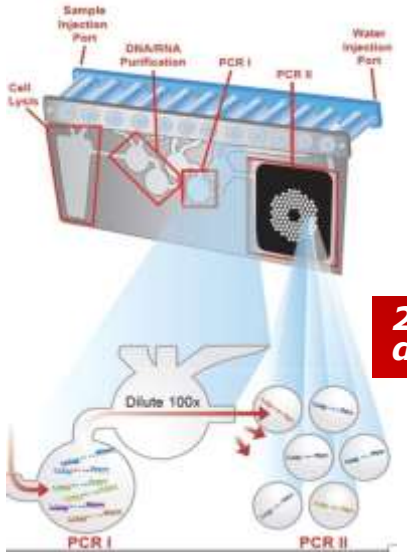
BC-based

Table 1. Selected rapid diagnostic tests for pathogen identification in sepsis.

System (Company)	Technology	Regulatory Status (for Bacteria)	Sample	Gram Stain Dependent	ID Targets	TAT	Type of AMR Testing	Resistance Markers or Antibiotics Tested
Accelete Pheno™ (Accelerate Diagnostics, Tucson, AZ, USA)	PNA-FISH and morphokinetic cellular analysis	CE marked/FDA cleared	BC	No	6 g-positive 8 g-negative 2 yeasts	1-7 H	Phenotypic	gram-pos: ampicilin, ceftaroline, daptomycin, linezolid, vancomycin, and cefoxitin gram-neg: ampicilin-sulbactam, ciprofloxacin, gentamicin, tobramycin piperacillin-tazobactam, aztreonam cefepime, ceftazidime, ceftriaxone ertapenem, meropenem, and amikacin
Verigene® (Nanosphere, Northbrook, IL, USA)	PCR + microarray *NanoGrid*	CE marked/FDA cleared	BC	Yes	13 g-positive 9 g-negative	2,5 H	Genotypic	*mecA*, *vanA/B*, CTX-M, KPC, NDM, VIM, IMP, and OXA
cobas® eplex (Roche Diagnostics, Rotkreuz, Switzerland)	PCR + microarray	CE marked/FDA cleared	BC	Yes	20 g-positive 21 g-negative 16 fungal	1,5 H	Genotypic	*mecA*, *mecC*, *vanA*, *vanB* *CTX-M*, *IMP*, *KPC* *NDM*, *VIM* *OXA* (*OXA-23* and *OXA-48*)
BioFire® FilmArray® (bioMérieux, Marcy-l'Étoile, France)	PCR + microarray	CE marked/FDA cleared	BC	No	8 g-positive 11 g-negative 5 Candida species	1 H	Genotypic	IMP, KPC, OXA-48-like NDM, VIM, *mcr-1*, ESBL CTX-M, *mecA*/C *mecA*/C and MREJ (MRSA), *vanA*/B
Rapid MBT Sepsityper® (Bruker Daltonik, Bremen, Germany)	MALDI-TOF MS	CE marked/FDA cleared	BC	No	>425 organism (including bacteria and yeasts)	30 min	Phenotypic	-
T2Bacteria Panel (T2Dx®, T2 Biosystems, Lexington, MA, USA)	Miniaturized magnetic resonance	CE marked/FDA cleared	WB	No	*E. faecium* *S. aureus* *K. pneumoniae* *A. baumannii* *P. aeruginosa* *E. coli*	4 H	-	-

Microorganisms 2024, 12, 1824

FilmArray e batteriemie: 43 target e determinanti di resistenza



200 ul di brodo da emocolture +

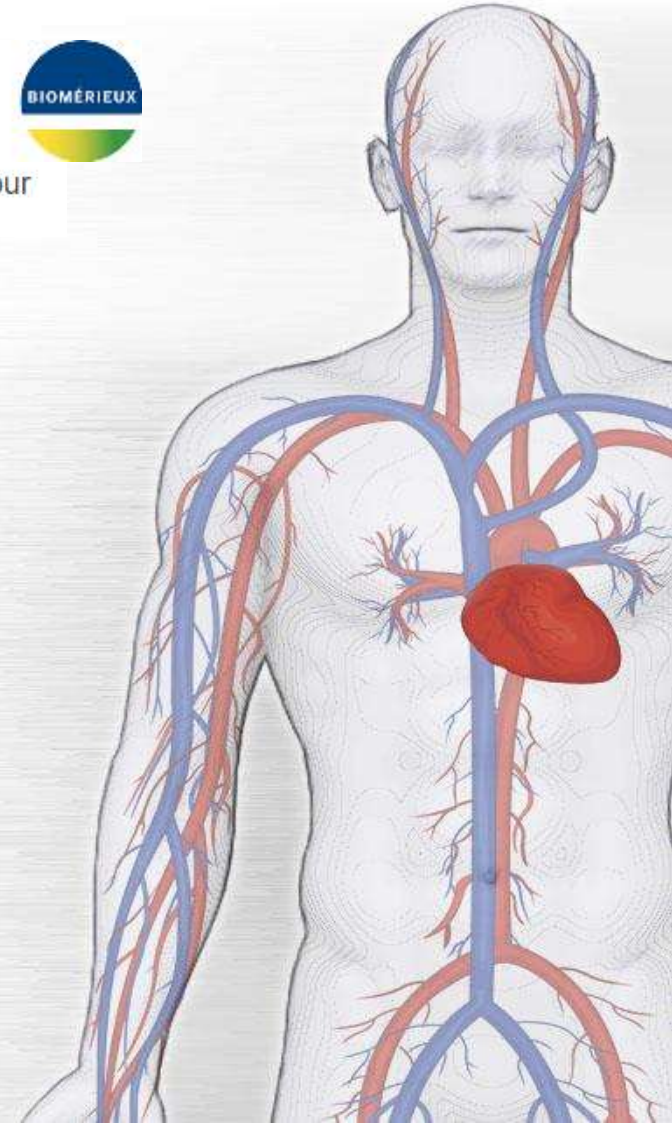
FAST BIOFIRE BIOMÉRIEUX

Turnaround time of about one hour

Gram Positive Bacteria	Gram Negative Bacteria	

• *Enterococcus faecalis*
• *Enterococcus faecium*
• *Listeria monocytogenes*
• *Staphylococcus* spp.
  ○ *Staphylococcus aureus*
  ○ *Staphylococcus epidermidis*
  ○ *Staphylococcus lugdunensis*
• *Streptococcus* spp.
  ○ *Streptococcus agalactiae* (Group B)
  ○ *Streptococcus pneumoniae*
  ○ *Streptococcus pyogenes (Group A)*
	• *Acinetobacter calcoaceticus-baumannii* complex
	• *Bacteroides fragilis*
	• *Haemophilus influenzae*
	• *Neisseria meningitidis* (encapsulated)
	• *Pseudomonas aeruginosa*
	• *Stenotrophomonas maltophilia*
		• *Enterobacterales*
		• *Enterobacter cloacae* complex
		• *Escherichia coli*
		• *Klebsiella aerogenes*
		• *Klebsiella oxytoca*
		• *Klebsiella pneumoniae* group
		• *Proteus* spp.
		• *Salmonella* spp.
		• *Serratia marcescen*

Yeast	**Antimicrobial Resistance Genes**	
• *Candida albicans* • *Candida auris* • *Candida glabrata* • *Candida krusei* • *Candida parapsilosis* • *Candida tropicalis* • *C. neoformans/C. gattii*	• CTX-M • IMP • KPC • *mcr-1* • *mecA/C*	• *mecA/C* and MREJ (MRSA) • NDM • OXA-48-like • *vanA/B* • VIM



SEPSI da Klebsiella pneumoniae CRE+

Antibiogramma molecolare <1H

Data Nascita: 01/03/1937 Età: 87 Anni Sesso F

Richiesta: 03853200 del 22/08/2024

Esame	*Esito*
Materiale: Sangue da emocoltura	
Test molecolare per sepsi	
Esito	**Positivo**
Enterobacterales	**Positivo**
Klebsiella pneumoniae group	**Positivo**
	Metodo: FilmArray
Test molecolare per geni di resistenza	
Esito	**Positivo**
ESBL: CTX-M	**Positivo**
Carbapenemasi: NDM	**Positivo**
Carbapenemasi: OXA-48-like	**Positivo**
Materiale: Sangue da p.venoso periferico	
EMOCOLTURA I° set	
Esame batterioscopico (GRAM) I° set	**Positivo**
	Bacilli Gram negativi
EMOCOLTURA II° Set	
Esame batterioscopico (GRAM) II° set	**Positivo**
	Bacilli Gram negativi

	***Bla*CTX-M**	**Carbapenemasi**
Sensibilità	94.7 (84.8 to 98.3)	94.6 (82.1 to 98.5)
Specificità	99.3 (97.6 to 99.8)	99.7 (98.8 to 99.9)

Laboratorio di Microbiologia e Virologia – ospedale Amedeo di Savoia

Lunedì-Venerdi ore 8-20, sabato e festivi

Gram

MALDI-Tof

Prelievo

Incubazione

Identificazione (ID)

Antibiogramma (AB)

media 22-48 h

95% Emo+

AB

<48-72 h

1 Klebsiella pneumoniae

Microrganismo "alert": applicare idonee misure di isolamento

Ceppo 1 Klebsiella pneumoniae

Antibiotici		MIC	MIC Breakpoint S<=	MIC Breakpoint R>	Note
Amoxicillina/A.CLAV.	R	>32	8	8	
Ciprofloxacina	R	>2	0.25	0.5	
Gentamicina	S	<=1	2	2	
Imipenem/Relebactam	R	>8	2	2	
Meropenem	R	>8	2	8	
Meropenem/Vaborbactam	R	>32	8	8	
Piperacillina/tazobactam	R	>64	8	8	
Amikacina	R	16	8	8	
Cefepime	R	>16	1	4	
Ceftazidima	R	>32	1	4	
Ceftazidime/Avibactam	R	>8	8	8	
Ceftolozzane/Tazobactam	R	>16	2	2	

SISTEMA INTERPRETATIVO EUCAST

C = In Corso S = Ceppo Sensibile R = Ceppo Resistente I = Ceppo Intermedio ID= Insufficiente Evidenza

I-R* = Categoria interpretativa presuntiva non supportata da Evidenze Cliniche

I-R-R = Non è possibile sinergia con antibiotici Beta-Lattamici S-I-R-S = E' possibile sinergia con antibiotici Beta-Lattamici

MIC = Minima Concentrazione Inibente in mcg/ml ESBL = Ceppo produttore di Beta-Lattamasi a Spettro Esteso

emocolture +

Antibiogramma molecolare <1H

ANTIBIOTICO STEWARDSHIP

Terapia empirica

Aggiustamento terapia empirica

Terapia mirata

<48- 72 h

Polmoniti da GRAM-negativi MDR (HAP/VAP)

BAL
BR
AT

BACTERIA (Semi-Quantitative)

Acinetobacter calcoaceticus-baumannii complex
Enterobacter cloacae complex
Escherichia coli
Haemophilus influenzae
Klebsiella aerogenes
Klebsiella oxytoca
Klebsiella pneumoniae group
Moraxella catarrhalis
Proteus spp.
Pseudomonas aeruginosa
Serratia marcescens
Staphylococcus aureus
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

ATYPICAL BACTERIA (Qualitative)

Chlamydia pneumoniae
Legionella pneumophila
Mycoplasma pneumoniae

VIRUSES

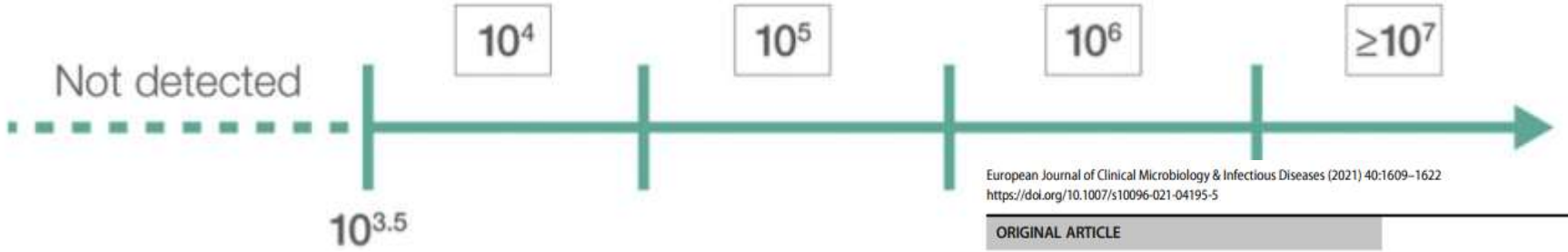
Adenovirus
Coronavirus
Human metapneumovirus
Human rhinovirus/enterovirus
Influenza A virus
Influenza B virus
Middle East respiratory syndrome coronavirus (MERS-CoV)
Parainfluenza virus
Respiratory syncytial virus

ANTIMICROBIAL RESISTANCE GENES

Carbapenemases
IMP
KPC
NDM
OXA-48-like
VIM

ESBL
CTX-M

Methicillin Resistance
mecA/C and MREJ (MRSA)



BIOFIRE BY BIOMÉRIEUX

European Journal of Clinical Microbiology & Infectious Diseases (2021) 40:1609–1622
https://doi.org/10.1007/s10096-021-04195-5

ORIGINAL ARTICLE

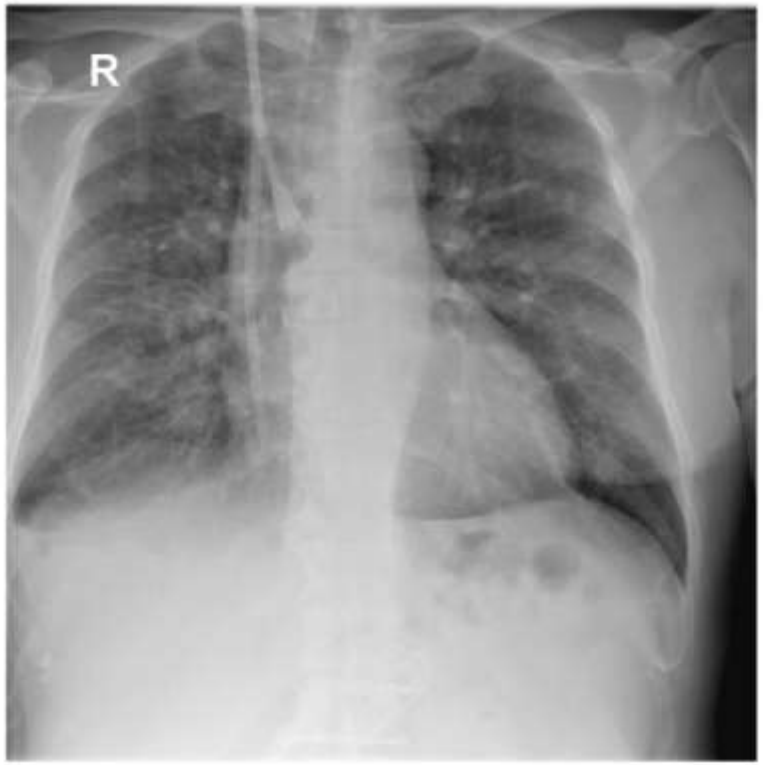
Multinational evaluation of the BioFire® FilmArray® Pneumonia *plus* Panel as compared to standard of care testing

Christine C. Ginocchio[1,2] · Carolina Garcia-Mondragon[3] · Barbara Mauerhofer[3] · Cory Rindlisbacher[1] · and the EME Evaluation Program Collaborative

BAL-like: 96.2% sensitivity and 98.4% specificity

Sputum-like: 96.3% sensitivity and 97.3% specificity

PAZ. M 64 anni SGB semintensiva
BAL del 16/03/2024
VAP da Kp-KPC+/VIM+/CTX-M+



Materiale: Broncolavaggio

Ceppo 1 Klebsiella pneumoniae

Antibiotici		*MIC*	*S<=*	*R>*	*Note*
				MIC Breakpoin	
Amikacina	R	32	8	8	
Cefepime	R	>16	1	4	
Ceftazidima	R	>32	1	4	
Ceftazidime/Avibactam	R	>8	8	8	
Ceftolozane/Tazobactam	R	>16	2	2	
Ciprofloxacina	R	>2	0.25	0.5	
Gentamicina	S	<=1	2	2	
Imipenem/Relebactam	R	>8	2	2	
Meropenem	R	>8	2	8	
Meropenem/Vaborbactam	R	32	8	8	
Piperacillina/tazobactam	R	>64	8	8	
Amoxi/Ac.Clav. (iv)	R	>32	8	8	
Amoxi/Ac.Clav (os) UTI	R	>32	32	32	
Amoxi/Ac.Clav (os) altre infezioni	R	>32	0.001	8	

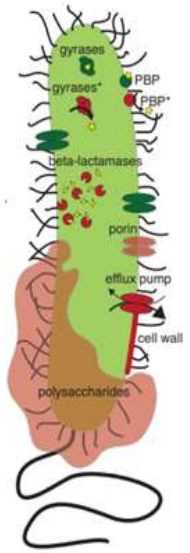
SISTEMA INTERPRETATIVO EUCAST

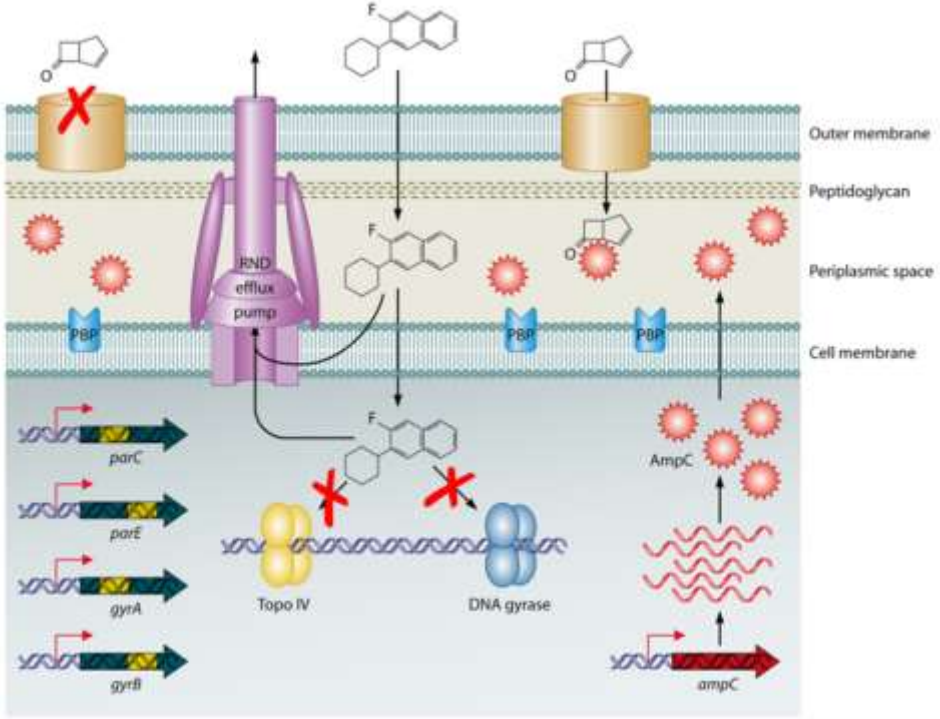
Test molecolare per geni di resistenza

Esito	**Positivo**
Carbapenemasi: IMP	**Negativo**
Carbapenemasi: KPC	**Positivo**
Carbapenemasi: NDM	**Negativo**
Carbapenemasi: OXA-48-like	**Negativo**
Carbapenemasi: VIM	**Positivo**
ESBL: CTX-M	**Positivo**

Metodo: FilmArray

Pseudomonas aeruginosa - MDR





Test molecolare per geni di resistenza	
Esito	Negativo
Carbapenemasi: IMP	Negativo
Carbapenemasi: KPC	Negativo
Carbapenemasi: NDM	Negativo
Carbapenemasi: VIM	Negativo
ESBL: CTX-M	Negativo
	Metodo: FilmArray

Emocolture +

FilmArray
BAL/BR/AT

Materiale: Frammento di tessuto

Esame colturale — Positiv

1 **Pseudomonas aeruginosa**

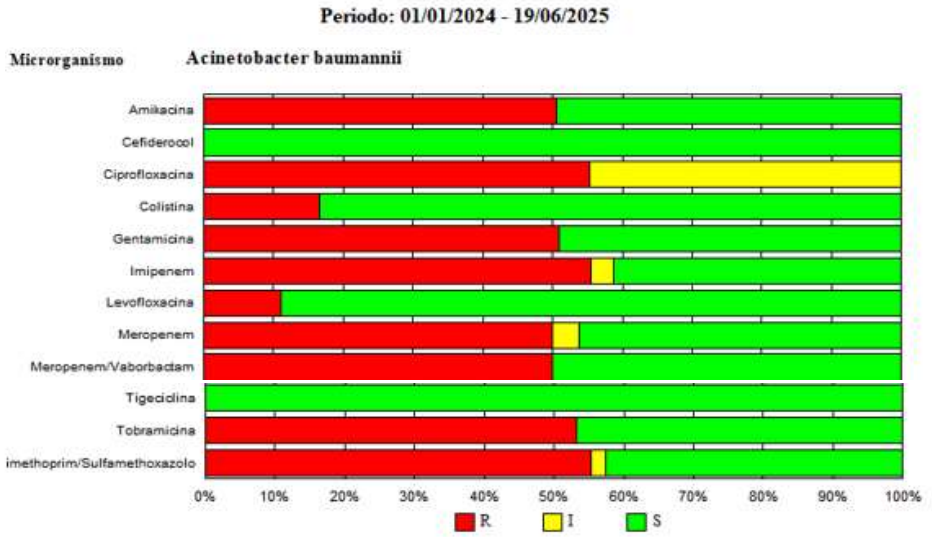
Ceppo 1 Pseudomonas aeruginosa

Antibiotici		*MIC*	*S<=*	*R>*
Amikacina	S	4	16	16
Aztreonam	I	4	0.001	16
Cefepime	I	2	0.001	8
Ceftazidima	I	2	0.001	8
Ciprofloxacina	I	<=0.06	0.001	0.5
Imipenem	I	2	0.001	4
Imipenem/Relebactam	S	0.5	2	2
Meropenem	S	<=0.25	2	8
Piperacillina/tazobactam	I	8	0.001	16
Tobramicina	S	<=1	2	2
Ceftazidime/Avibactam	S	2	8	8
Ceftolozane/Tazobactam	S	0.5	4	4

Anno	N.isolati	Ceftazidime-R	%	Cefepime-R	%	MDRO (Meropenem=R)	% MDRO
2021	1078	139	**12.9**	159	**14.7**	108	**10.0**
2022	1085	229	**21.1**	198	**18.2**	134	**12.4**
2023	1064	199	**18.7**	191	**18.0**	94	**8.8**
2024	1130	191	**16.9**	178	**15.8**	97	**8.6**

Dati di Laboratorio. Numero di isolati univoci e AMR

Acinetobacter baumanni - MDR



Anno	N.isolati	MDRO (Meropenem=R)	% MDRO
2021	77	60	77.9
2022	108	86	79.6
2023	85	44	51.8
2024	90	53	58.9

Dati di Laboratorio. Numero di isolati univoci e MDR

≈40% degli isolati ACB sono colonizzazioni rettali di cui 90% è MDRO)

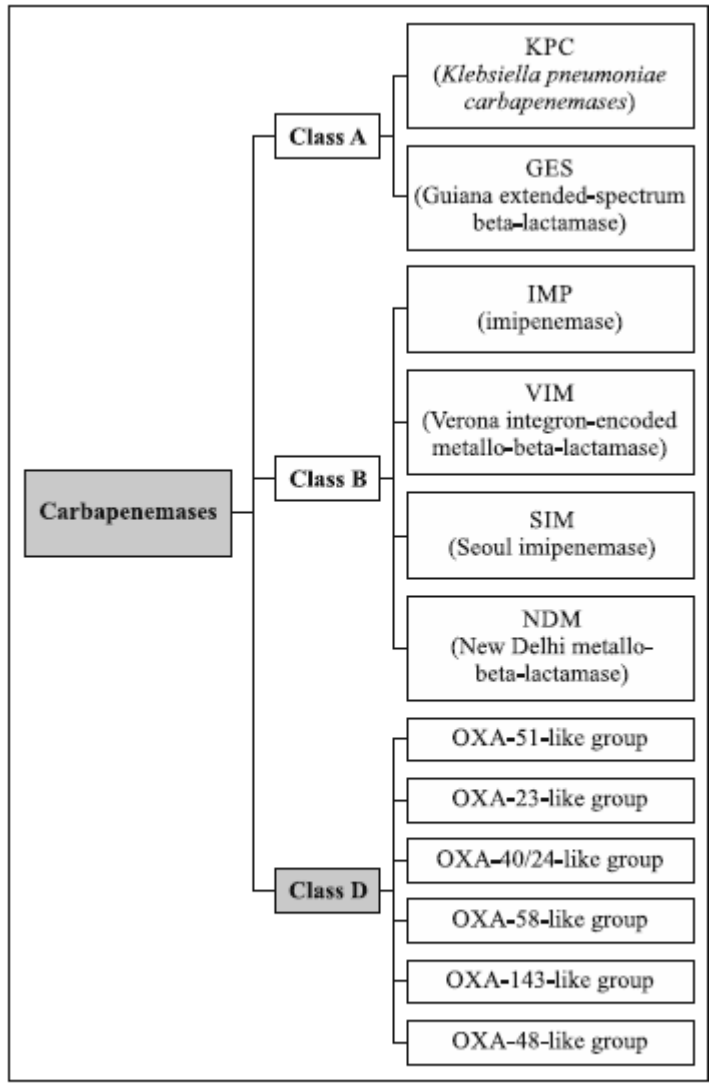
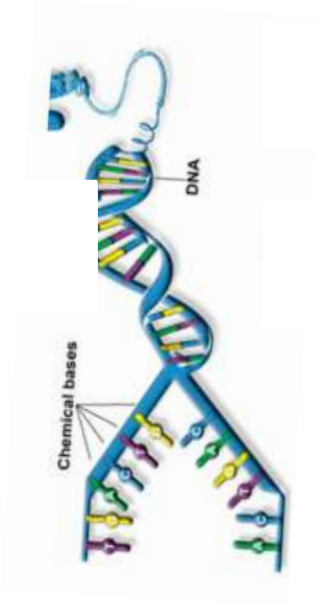


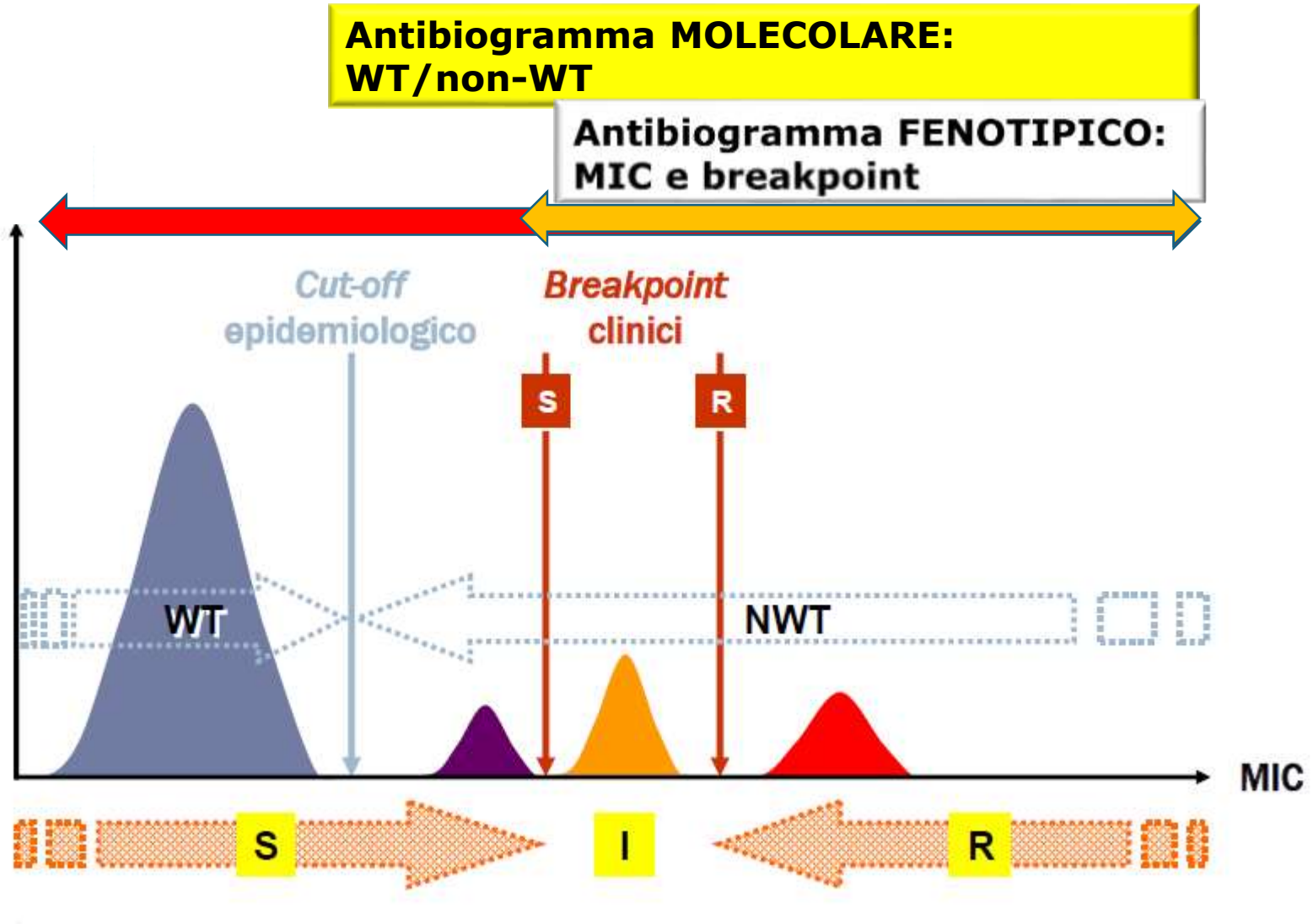
Figure 2. Clinically relevant carbapenemases occurring among *Acinetobacter baumannii*.

Emocolture +

FilmArray BAL/BR/AT

Cut-off epidemiologici e *breakpoint* clinici, sensibilità e resistenza





www.eucast.org

Next Generation Phenotipic test: TAT<8H
Test fenotipici in assetto «rapido» per sepsi

Risultati disponibili entro 8 h lavorative da BC+ (CDC, 2016)

Emocolture + GRAM-negativi

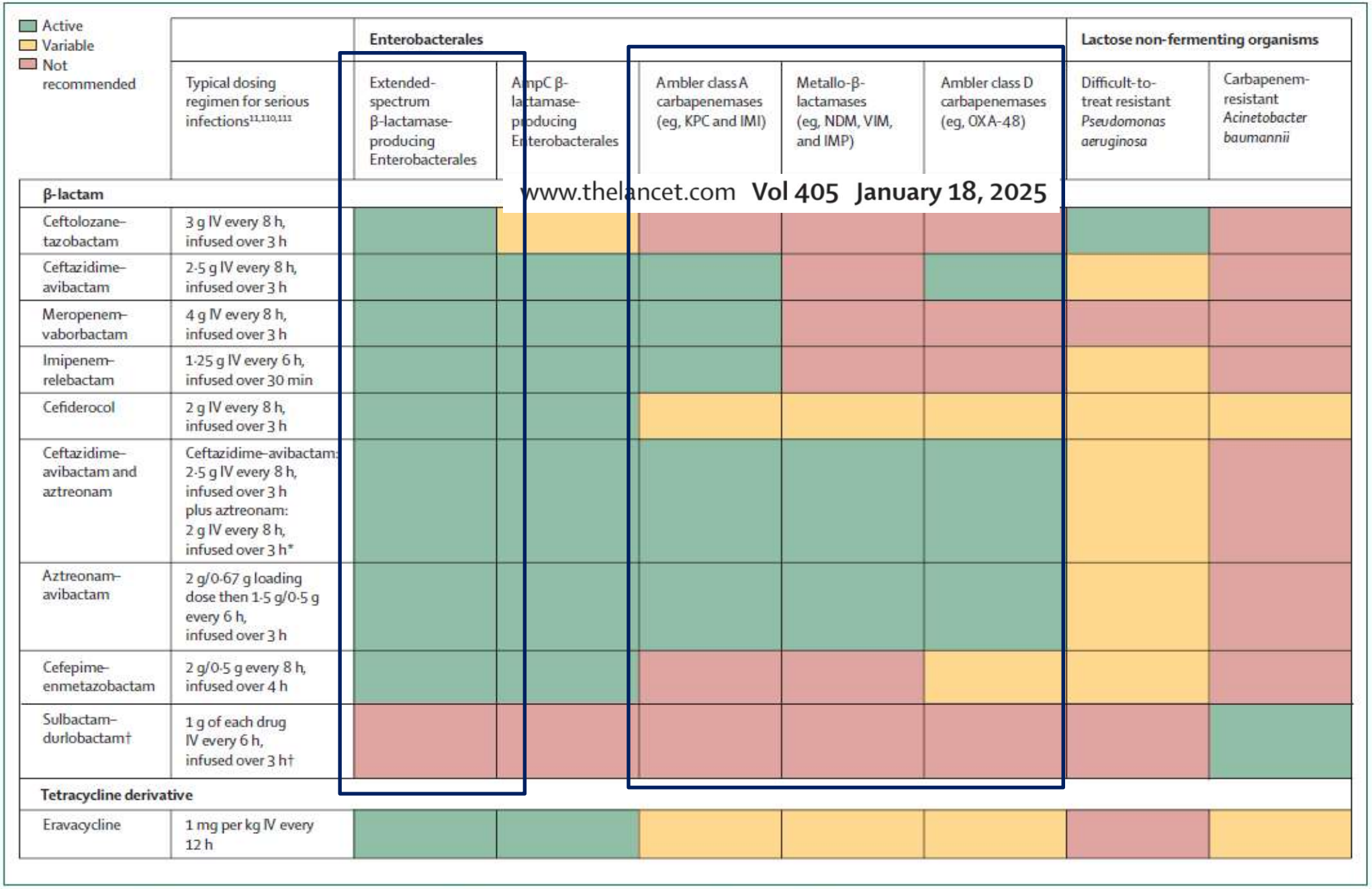
ANTIMICROBIAL DRUG	MIC CALLING RANGE (µg/ml)	A. baumannii	C. freundii	C. koseri	E. cloacae	E. coli	K. aerogenes	K. oxytoca	K. pneumoniae	P. mirabilis	P. aeruginosa	
Amikacin	4 - 16	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Amoxicillin / Clavulanate	4/2 - 16/2			✓		✓		✓	✓	✓		5
Ampicillin	4 - 8					✓				✓		2
Aztreonam	1 - 16		✓	✓	✓	✓	✓	✓	✓		✓	8
Cefepime	0.125 - 64		✓	✓	✓	✓		✓	✓	✓	✓	8
Cefotaxime	0.125 - 4		✓	✓	✓	✓	✓	✓	✓	✓		8
Cefoxitin	8 - 16			✓		✓		✓	✓	✓		5
Ceftazidime	0.125 - 64		✓	✓	✓	✓	✓	✓	✓	✓	✓	9
Ceftazidime / Avibactam	0.25/4, 1/4 - 16/4		✓	✓	✓	✓	✓	✓	✓	✓	✓	9
Ceftazidime / Clavulanate	0.25/4 - 8/4					✓		✓	✓			3
Ceftolozane / Tazobactam	1/4 - 4/4				✓	✓	✓	✓		✓	✓	6
Ciprofloxacin	0.06, 0.25 - 1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Ertapenem	0.125 - 1		✓	✓	✓	✓	✓	✓	✓	✓		8
Gentamicin	2 - 4	✓	✓	✓	✓	✓	✓	✓	✓			9
Imipenem	1 - 8	✓	✓	✓	✓	✓	✓	✓		✓	✓	9
Levofloxacin	0.25 - 1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Meropenem	0.125 - 8	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Meropenem / Vaborbactam	2/8 - 8/8		✓	✓	✓	✓	✓	✓	✓	✓	✓	9
Piperacillin	8 - 16		✓		✓	✓	✓	✓	✓	✓	✓	8
Piperacillin / Tazobactam	4/4 - 16/4		✓	✓	✓	✓	✓	✓	✓	✓	✓	9
Tigecycline	0.5 - 1			✓		✓						2
Tobramycin	2 - 4	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Trimethoprim / Sulfamethoxazole	2/38 - 4/76	✓	✓	✓	✓	✓	✓	✓	✓			9

VITEK REVEAL

- **Growth-dependent**
  - **Alfred 60/AST** 4-6 hrs AST (No MIC)
  - **VITEK REVEAL** 6 hrs (MIC)
  - **QuickMIC**: 2-4 hrs (MIC)
  - **dRAST** 4-6 hrs (MIC)
  - **ASTar** 6 hrs (MIC)

- **Growth-independent**
  - ***Resistell Phenotech technology***
    Nanomotion: detection of bacterial motion by mechanical sensors and machine learning(<2 hrs)
  - ***LifeScale Phenotipic technology***
    microfluidic sensors & masses originated by antibiotics (BC, population profile in 4.5 hrs)
  - ***SeLux NGP***
    detection of metabolic activity with fluorescence markers (MIC, BC, 6 hrs)
  - ***FASTInov***
    flow cytometry (2 hrs)

Impegno dei Laboratori nella nuova pipeline di antibiotici



Active
Variable
Not recommended

		Enterobacterales					Lactose non-fermenting organisms	
	Typical dosing regimen for serious infections[11,110,111]	Extended-spectrum β-lactamase-producing Enterobacterales	AmpC β-lactamase-producing Enterobacterales	Ambler class A carbapenemases (eg, KPC and IMI)	Metallo-β-lactamases (eg, NDM, VIM, and IMP)	Ambler class D carbapenemases (eg, OXA-48)	Difficult-to-treat resistant *Pseudomonas aeruginosa*	Carbapenem-resistant *Acinetobacter baumannii*
β-lactam								
Ceftolozane–tazobactam	3 g IV every 8 h, infused over 3 h							
Ceftazidime–avibactam	2·5 g IV every 8 h, infused over 3 h							
Meropenem–vaborbactam	4 g IV every 8 h, infused over 3 h							
Imipenem–relebactam	1·25 g IV every 6 h, infused over 30 min							
Cefiderocol	2 g IV every 8 h, infused over 3 h							
Ceftazidime–avibactam and aztreonam	Ceftazidime–avibactam: 2·5 g IV every 8 h, infused over 3 h plus aztreonam: 2 g IV every 8 h, infused over 3 h*							
Aztreonam–avibactam	2 g/0·67 g loading dose then 1·5 g/0·5 g every 6 h, infused over 3 h							
Cefepime–enmetazobactam	2 g/0·5 g every 8 h, infused over 4 h							
Sulbactam–durlobactam†	1 g of each drug IV every 6 h, infused over 3 h†							
Tetracycline derivative								
Eravacycline	1 mg per kg IV every 12 h							

www.thelancet.com Vol 405 January 18, 2025

Impegno dei Laboratori nella sorveglianza dei GRAM-negativi MDR

REGIONE PIEMONTE

MICRO BIO

UO PRI

REPORT

REPARTI

Real-time Alert

ISTITVTO SVPERIORE DI SANITA

Conclusioni

Crescente ruolo della genomica nella diagnostica microbiologica con impatto sui flussi organizzativi e sugli algoritmi diagnostici

Il trattamento terapeutico delle infezioni batteriche da GRAM-negativi MDR è sempre più "challenging":

- Aumento dei pazienti fragili e immunodepressi
- Plasticità dei batteri: vantaggio selettivo e adattamento all'ospite

Necessaria sinergia tra diverse figure professionali

IL PAZIENTE CRITICO CON INFEZIONE DA GERMI GRAM NEGATIVI MULTIRESISTENTI - 19 giugno 2025

GRAZIE DELL'ATTENZIONE!!!!