

# 11

**WORKSHOP  
NAZIONALE CISAI**

**TORINO 2023**

20 • 21 APRILE



## **Tollerabilità dei farmaci antinfettivi e co-morbilità associate all'infezione da HIV**

**Presidenti del Convegno**

Paolo Bonfanti, Antonio Di Biagio, Giancarlo Orofino

FONDAZIONE  ASIA

CISAI  

# Corretto posizionamento delle nuove molecole attive su Gram-negativi MDR

**Francesco Cristini**  
Forlì-Cesena

## Potenziale conflitto di interessi da dichiarare

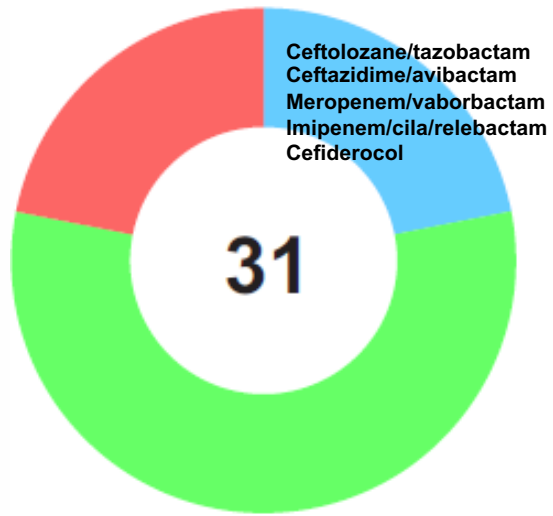
Tipo di affiliazione o supporto finanziario	Sponsor

Corretto posizionamento delle **nuove molecole attive (CHE ABBIAMO GIA' O IMMINENTI)** su Gram-negativi MDR

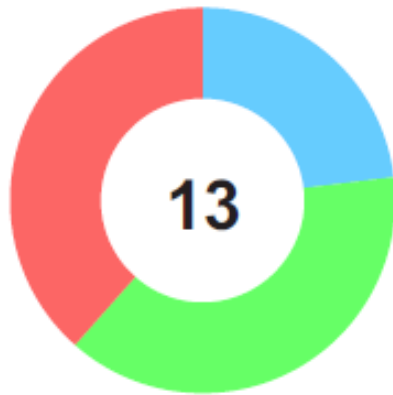
## Clinically Validated Targets

### Beta-lactams

Approved In Clinical Trials Discontinued



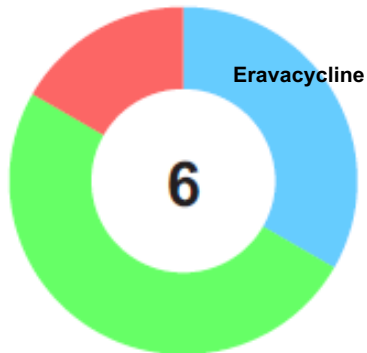
### Topoisomerase Inhibitors



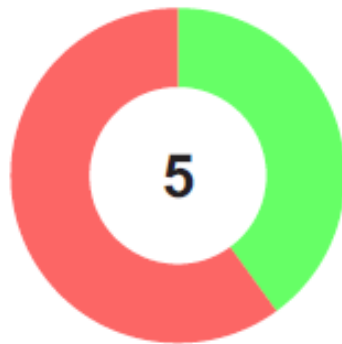
### Aminoglycosides



### Tetracyclines



### Polymyxins



### MurA Inhibitors



## Leaks in the Pipeline: a Failure Analysis of Gram-Negative Antibiotic Development from 2010 to 2020

Neha K. Prasad et al – Antimicrob Agents Chemother 2022 May 17;66(5):e0005422

## Clinically Unprecedented Targets

### LpxC Inhibitors



### tRNA synthetase Inhibitors



### LptD Inhibitors



### RNA polymerase inhibitors

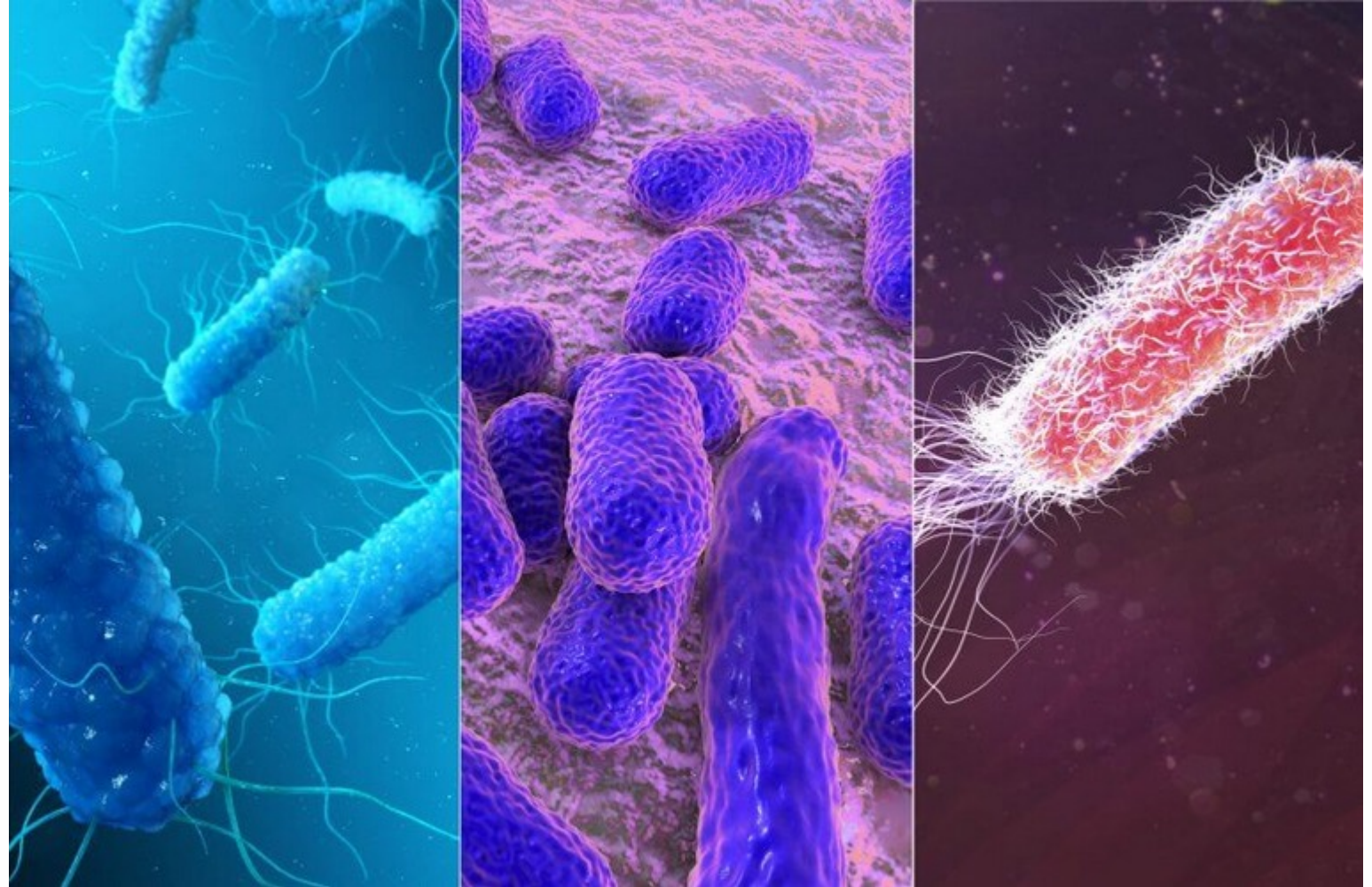


### Bioenergetic inhibitors



## ... gram negativi MDR

WHO “priority pathogens” list:  
Priority 1: **CRITICAL**



*Enterobacteriales*

3rd gen ceph-R  
carba-R

*A. baumannii*

carba-R

*P. aeruginosa*

carba-R  
DTR

## INDICAZIONI ATTUALI ceftolozane/tazobactam

### 4.1 Indicazioni terapeutiche

è indicato per il trattamento delle seguenti infezioni negli adulti (vedere paragrafo 5.1):

- Infezioni intra-addominali complicate (vedere paragrafo 4.4);
- Pielonefrite acuta;
- Infezioni complicate del tratto urinario (vedere paragrafo 4.4);
- Polmonite acquisita in ospedale (HAP), inclusa polmonite associata a ventilazione meccanica (VAP).

**Tabella 1: Dose per via endovenosa di [ ] per tipo di infezione in pazienti con clearance della creatinina >50 mL/min**

Tipo di infezione	Dose	Frequenza	Tempo di infusione	Durata del trattamento
Infezione intra-addominale complicata*	1 g ceftolozano / 0,5 g tazobactam	Ogni 8 ore	1 ora	4-14 giorni
Infezione complicata del tratto urinario Pielonefrite acuta	1 g ceftolozano / 0,5 g tazobactam	Ogni 8 ore	1 ora	7 giorni
Polmonite acquisita in ospedale, inclusa polmonite associata a ventilazione meccanica**	2 g ceftolozano / 1 g tazobactam	Ogni 8 ore	1 ora	8-14 giorni

\*Da usare in associazione con metronidazolo se si sospetta la presenza di patogeni anaerobi.

\*\*Da usare in associazione con un agente attivo antibatterico nei confronti di patogeni Gram-positivi, quando questi sono noti o sospetti nel contribuire al processo infettivo.

Scheda cartacea per la prescrizione della specialità medicinale [REDACTED] (ceftolozano-tazobactam)

Diagnosi	
Infezione intra-addominale complicata (cIAI) con eziologia <u>documentata/sospetta*</u> da batteri Gram-negativi, resistente ai trattamenti di prima linea (se si sospetta la presenza di patogeni anaerobi [REDACTED] dovrà essere associato a metronidazolo)	<input type="checkbox"/>
Infezione complicata del tratto urinario (cUTI), inclusa la pielonefrite acuta, con eziologia <u>documentata</u> da batteri Gram-negativi resistenti ai trattamenti di prima linea ( <u>Allegare antibiogramma</u> )	<input type="checkbox"/>
Polmonite acquisita in ospedale (HAP), inclusa la polmonite associata a ventilazione meccanica (VAP), con eziologia <u>documentata/sospetta*</u> da batteri Gram-negativi resistenti ai trattamenti di prima linea (da usare in associazione con un agente attivo antibatterico nei confronti di patogeni Gram-positivi, quando questi sono noti o sospetti nel contribuire al processo infettivo)	<input type="checkbox"/>
*L'infezione "sospetta" può essere considerata in pazienti selezionati sulla base di criteri epidemiologici, clinici e microbiologici (ad es. colonizzazione intestinale) in accordo a raccomandazioni terapeutiche definite dal programma di stewardship antibiotica del singolo ospedale.	

\* La prescrivibilità è riservata allo specialista infettivologo o, in sua assenza, ad altro specialista con competenza infettivologica ad hoc identificato dal Comitato Infezioni Ospedaliere (CIO) istituito per legge presso tutti i presidi ospedalieri (Circolare Ministero della Sanità n. 52/1985).



# INDICAZIONI ATTUALI ceftazidime/avibactam

## 4.1 Indicazioni terapeutiche

è indicato per il trattamento delle seguenti infezioni negli adulti (vedere paragrafi 4.4 e 5.1):

- infezione intra-addominale complicata (cIAI)
- infezione complicata del tratto urinario (cUTI), inclusa pielonefrite
- polmonite acquisita in ospedale (HAP), inclusa polmonite associata a ventilazione meccanica (VAP)

è inoltre indicato per il trattamento di infezioni causate da microrganismi Gram-negativi aerobi in pazienti adulti nei quali vi siano opzioni terapeutiche limitate (vedere paragrafi 4.2, 4.4 e 5.1).

Si devono considerare le linee-guida ufficiali sull'uso appropriato degli agenti antibatterici.

### Condizioni cliniche e criteri di rimborsabilità

Infezione complicata del tratto urinario (cUTI), incluse le pielonefriti, con eziologia <u>documentata</u> da batteri Gram-negativi resistenti ai trattamenti di prima linea ( <u>Allegare antibiogramma</u> ), compresa la batteriemia (solo negli adulti)	<input type="checkbox"/>
Infezione intra-addominale complicata (cIAI) con eziologia <u>documentata/sospetta*</u> da batteri Gram-negativi resistenti ai trattamenti di prima linea), compresa la batteriemia (solo negli adulti)	<input type="checkbox"/>
Polmonite acquisita in ospedale (HAP), inclusa polmonite associata a ventilazione meccanica (VAP), con eziologia <u>documentata/sospetta*</u> da batteri Gram-negativi resistenti ai trattamenti di prima linea, compresa la batteriemia (solo negli adulti)	<input type="checkbox"/>
Infezioni causate da microrganismi Gram-negativi aerobi in pazienti nei quali vi siano opzioni terapeutiche limitate, con eziologia <u>documentata/sospetta*</u> da batteri Gram-negativi, resistente ai trattamenti di prima linea	<input type="checkbox"/>

*\*L'infezione "sospetta" può essere considerata in pazienti selezionati sulla base di criteri epidemiologici, clinici e microbiologici (ad es. colonizzazione intestinale) in accordo a raccomandazioni terapeutiche definite dal programma di stewardship antibiotica del singolo ospedale.*

## MEROPENEM/VABORBACTAM

g 2/2 ogni 8 ore x cl creat  $\geq$  40 ml/min **infusione 3 ore**



### Indicazioni terapeutiche negli adulti :

- infezione del tratto urinario complicata (cUTI), compresa pielonefrite
- infezione intra-addominale complicata (cIAI)
- polmonite nosocomiale (HAP), inclusa polmonite associata a ventilazione (VAP)

**Trattamento di pazienti con batteriemia che si verifica in associazione o in sospetta associazione con una qualsiasi delle infezioni sopra elencate**

**E' inoltre indicato per il trattamento di infezioni dovute a organismi Gram-negativi aerobi in adulti che dispongono di opzioni terapeutiche limitate**



# IMIPENEM/CILASTATINA/RELEBACTAM

mg 500/500/250 ogni 6 ore x cl creat 90-150 ml/min infusione 1/2 ora

## Indicazioni terapeutiche negli adulti :

- Trattamento della polmonite acquisita in ospedale (HAP), compresa polmonite associata a ventilazione meccanica (VAP)**
- Trattamento della batteriemia che si manifesta in associazione o che si sospetta sia associata a HAP o VAP**
- Trattamento delle infezioni causate da organismi aerobi Gram-negativi con opzioni di trattamento limitate** ←

## CEFIDEROCOL

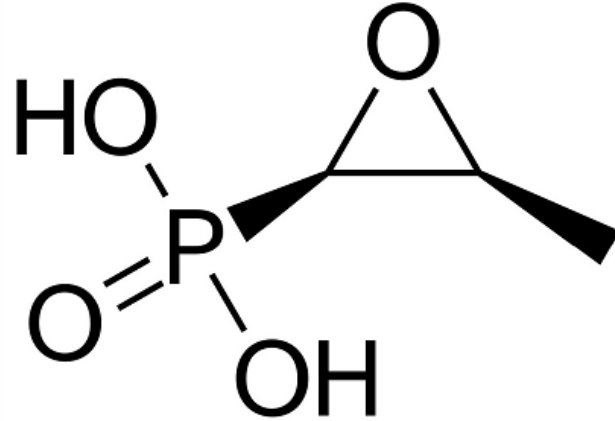
Funzionalità renale nella norma (cl creat 90-120 ml/min) 2g ogni 8 ore

Clearance renale aumentata (cl creat >120 ml/min) 2g ogni 6 ore ←

Infusione 3 ore ←

E' indicato per il trattamento delle infezioni dovute a organismi aerobi gram-negativi negli adulti con opzioni terapeutiche limitate ←

FOSFOMICINA infusiva



- infezioni ossee e articolari
- infezioni complicate del tratto urinario
- polmonite contratta in ospedale, compresa la polmonite associata a ventilazione
- meningite batterica
- **endocardite infettiva**
- **infezioni complicate della cute e dei tessuti molli**
- **infezioni complicate intra-addominali**
- batteriemia che si verifica in associazione con, o si sospetta sia associata a, qualsiasi delle infezioni sopra elencate

## ERAVACICLINA

1 mg/kg ogni 12 ore per una durata da 4 a 14 giorni

1.5 mg/kg ogni 12 ore in caso di **cosomministrazione di potenti induttori del CYP3A4**



E' indicato per il trattamento di infezioni intra-addominali complicate (cIAI) negli adulti

*Compromissione renale o epatica: NO aggiustamenti posologici*

# New betaLactam-betaLactamase Inhibitor Combinations

*Dafna Yahav et al - Clinical Microbiology Reviews January 2021 Volume 34 Issue 1*

Enzyme	Inhibited by:			
	Avibactam	Tazobactam	Vaborbactam	Relebactam
Class A				
KPC	Yes	No	Yes	Yes
SHV	Yes	Yes	Yes	Yes
TEM	Yes	Yes	Yes	Yes
CTX-M	Yes	Yes	Yes	Yes
Class B				
MBL	No	No	No	No
Class C				
AmpC	Yes	No	Yes	Yes
Class D				
OXA	VD <sup>a</sup>	No	No	VD

<sup>a</sup>VD, variable data.



## BL/BLI e altri farmaci ANTI GRAM NEGATIVI

	ESBL	CRE	DTR <i>P.aeruginosa</i>	MDR <i>Acinetobacter</i>
Ceftolozane/tazobactam	YES	NO	YES	NO
Ceftazidime/avibactam	YES	KPC & OXA48	YES	NO
Meropenem/vaborbactam	YES	KPCs	=mero	NO
Imipenem cil/relebactam	YES	KPC & some OXA48	YES	NO
<b>Cefiderocol</b>	YES	KPC & <b>NDM-1</b>	YES	<b>YES</b>
<b>Eravacyclin</b>	YES	KPC & <b>MBL</b>	NO	<b>YES</b>

## GUIDELINES and GUIDANCES

European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine)

Infectious Diseases Society of America Guidance on the Treatment of AmpC  $\beta$ -Lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections

Infectious Diseases Society of America 2022 Guidance on the Treatment of Extended-Spectrum  $\beta$ -lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and *Pseudomonas aeruginosa* with Difficult-to-Treat Resistance (DTR-*P. aeruginosa*)

Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)

RACCOMANDAZIONI AIFA PER USO OTTIMALE ANTIBIOTICI  
Terapia mirata delle infezioni causate da batteri Gram negativi resistenti a multipli antibiotici  
PAZIENTI OSPEDALIZZATI

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

## ***CARBAPENEM-RESISTANT ENTEROBACTERALES (CRE)***

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

**QUESTION #5: *What is the treatment of choice for carbapenem-resistant Enterobacterales (CRE) infections?***

### **Recommendation 5.1:**

*In patients with infections caused by carbapenem-resistant Enterobacterales (CRE), **rapid testing** should be used to identify **specific carbapenemase families** (e.g. KPC, NDM, VIM, OXA-48-like). Clinicians should adopt different treatment strategies based on the type of causative carbapenemase-producing Enterobacterales (CPE).*

Strength of recommendation: **STRONG** Certainty of evidence: **MODERATE**

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

**Recommendation 5.2:**

2.a In patients with infections caused by **KPC**-producing carbapenem-resistant Enterobacterales (CRE), novel  $\beta$ -lactam agents such as **ceftazidime/avibactam** and **meropenem/vaborbactam** should be the first-line treatment options.

2.b Imipenem/relebactam and cefiderocol may also be considered.

2.a Strength of recommendation: **STRONG** Certainty of evidence: **MODERATE**

2.b Strength of recommendation: **CONDITIONAL** Certainty of evidence: **LOW**

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

**Recommendation 5.3:**

In patients with infections caused by **OXA-48-like** producing carbapenem-resistant Enterobacterales (CRE), **ceftazidime/avibactam** should be the first-line treatment option.

Strength of recommendation: **CONDITIONAL** Certainty of evidence: **VERY LOW**

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

**Recommendation 5.4:**

4.a In patients with infections caused by metallo- $\beta$ -lactamase (MBL)-producing carbapenem-resistant Enterobacterales (CRE), ceftazidime/avibactam plus aztreonam should be preferred.

4.b Cefiderocol may also be considered.

4.a Strength of recommendation: **STRONG** Certainty of evidence: **MODERATE**

4.b Strength of recommendation: **CONDITIONAL** Certainty of evidence: **LOW**

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

## TARGETED COMBINATION TREATMENT

### Recommendation 5.5:

There are **insufficient data** supporting or against the use of ceftazidime/avibactam as combination therapy or monotherapy.



**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

## ***PSEUDOMONAS AERUGINOSA WITH DIFFICULT-TO-TREAT RESISTANCE (DTR-PA)***

... **defined** as *P. aeruginosa* exhibiting non-susceptibility to all of the following:

piperacillin-tazobactam

ceftazidime

cefepime

aztreonam

meropenem

imipenem-cilastatin

ciprofloxacin, and levofloxacin



FONDAZIONE ASIA

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

**QUESTION #6: *What is the therapy of choice for infections caused by *Pseudomonas aeruginosa* with difficult-to-treat resistance (DTR-PA)?***

**Recommendation 6.1 :** *In patients with invasive infections caused by *Pseudomonas aeruginosa* with difficult-to-treat resistance (DTR-PA), based on pre-clinical and clinical data, novel  $\beta$ -lactam agents such as **ceftolozane/tazobactam** and **ceftazidime/avibactam** are currently the first-line options for targeted treatment. **Imipenem/cilastatin–relebactam** and **cefiderocol** might be potential alternatives, as well as **colistin-based** therapy.*

Strength of recommendation: **STRONG** Certainty of evidence: **MODERATE**

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

## TARGETED COMBINATION TREATMENT

**Recommendation 6.2** : *In patients with invasive infections caused by *Pseudomonas aeruginosa* with difficult-to-treat resistance (DTR-PA), combination therapy should not be the routine choice but may be considered on a case-by- case basis, especially upon consultation with infectious diseases specialists. In particular, combination regimens including fosfomycin as companion agent could be considered.*

Strength of recommendation: **CONDITIONAL** Certainty of evidence: **LOW**

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

## ***CARBAPENEM-RESISTANT ACINETOBACTER BAUMANNII (CRAB)***

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

**QUESTION #7: *What is the treatment of choice for carbapenem-resistant Acinetobacter baumannii (CRAB) infections?***

**Recommendation 7.1 :** *There are **no convincing data** about the optimal antibiotic therapy against carbapenem-resistant Acinetobacter baumannii (CRAB) infections. Consultation by **infectious diseases specialists is needed** in patients with CRAB infections.*

Strength of recommendation: **STRONG** Certainty of evidence: **MODERATE**

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

**Recommendation 7.2** : *In patients who received **colistin-containing** regimens, **kidney function** should be strictly monitored because of the high risk of nephrotoxicity.*

Strength of recommendation: **STRONG** Certainty of evidence: **MODERATE**

**Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)**

*Tiseo G et al - Int J Antimicrob Agents 2022 Aug;60(2):106611*

**Recommendation 7.3** : *Cefiderocol* represents a promising antibiotic option for patients with carbapenem-resistant *Acinetobacter baumannii* (CRAB) infections. Further studies are needed to consolidate this recommendation and to evaluate the use of cefiderocol as monotherapy or in combination with other antibiotics.

Strength of recommendation: **STRONG** Certainty of evidence: **LOW**

**European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine).**

*Paul M et al - Clinical Microbiology and Infection 28 (2022) 521e547*

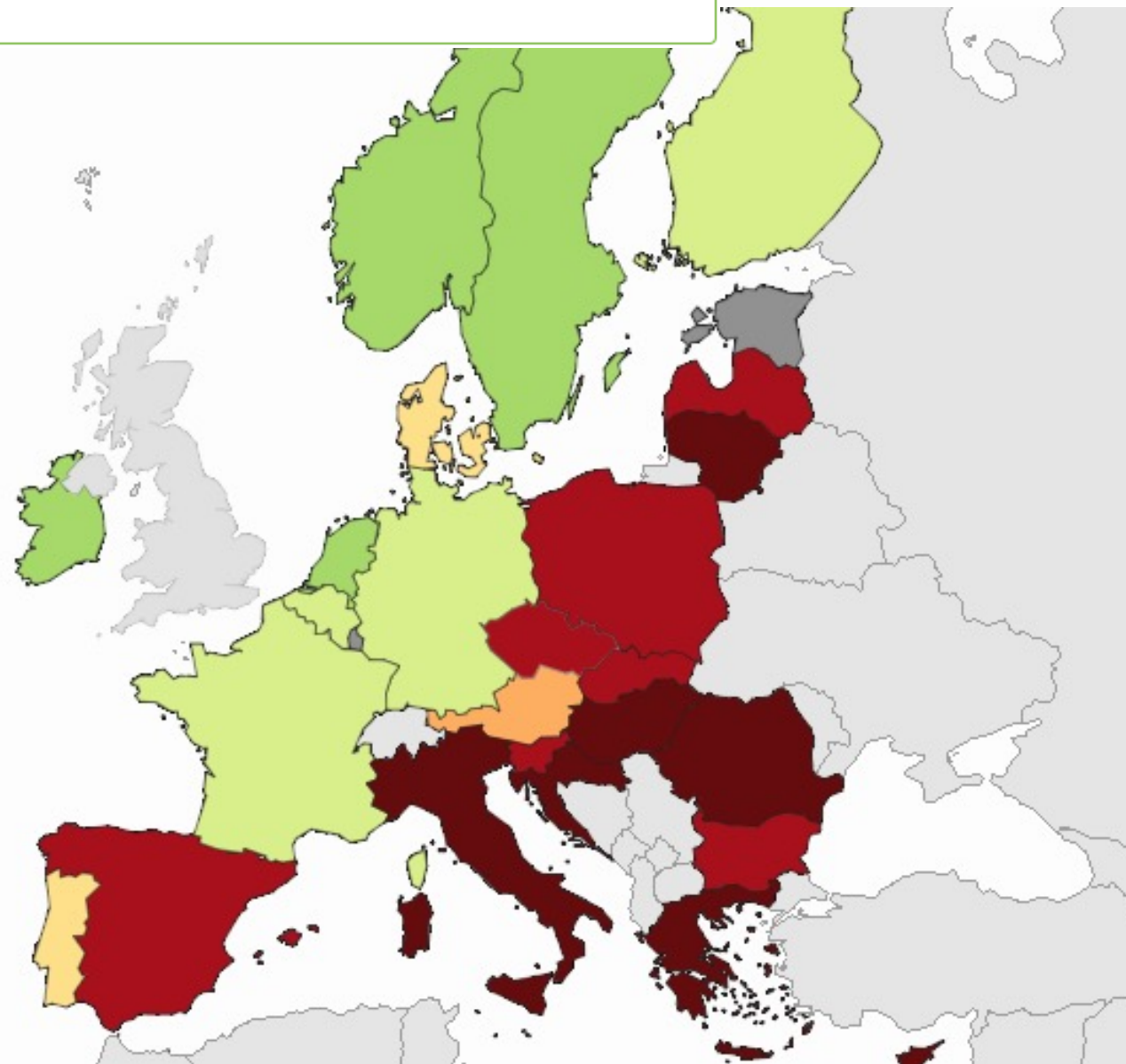
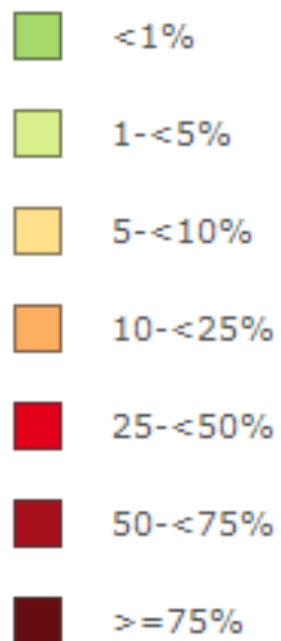
Recommendation	Strength of recommendation	Level of evidence
<b>Carbapenem-resistant <i>Acinetobacter baumannii</i> (CRAB)</b>		
<b><i>Recommendations on the choice of antibiotic treatment for CRAB</i></b>		
For patients with CRAB susceptible to sulbactam and HAP/VAP, we suggest ampicillin-sulbactam.	Conditional	Low
For patients with CRAB resistant to sulbactam, a polymyxin or high-dose tigecycline can be used if active <i>in vitro</i> . Lacking evidence, we cannot recommend on the preferred antibiotic.	No recommendation	
We conditionally recommend against ceftiderocol for the treatment of infections caused by CRAB.	Conditional	Low
<b><i>Recommendations on combination therapy for CRAB</i></b>		
For all patients with CRAB infections, we do not recommend polymyxin-meropenem combination therapy or polymyxin-rifampin combination therapy.	Strong	High/moderate
For patients with severe and high-risk CRAB infections, we suggest combination therapy including two <i>in vitro</i> active antibiotics among the available antibiotics (polymyxin, aminoglycoside, tigecycline, sulbactam combinations).	Conditional	Very low
For patients with CRAB infections with a meropenem MIC $\leq 8$ mg/L, we consider carbapenem combination therapy, using high-dose extended-infusion carbapenem dosing, as good clinical practice.	Good practice statement	Expert opinion
<b>All carbapenem-resistant Gram-negative bacteria</b>		
For pan-resistant CR-GNB (resistant also to polymyxins), treatment with the least resistant antibiotic/s based on MICs relative to the breakpoints is considered as good clinical practice.	Good practice statement	Expert opinion



# Surveillance Atlas of Infectious Diseases

Antimicrobial resistance ▼ Acinetobacter spp. ▼ Combined resistance (fluoroquinolones, aminoglycosides and carbapenems) ▼  
R - resistant isolates, percentage ▼ ▶ ◀◀ 2021 ▼ ▶▶

R - resistant isolates, percentage (%)



## Acinetobacter baumannii

<i>Antibiotici</i>		<i>MIC</i>	<i>MIC Breakpoint</i>	
			<i>S</i> ≤	<i>R</i> >
Cefiderocol	S		2	2
Amikacina	R	≥64	8	8
Ciprofloxacina	R	≥4	0.001	1
Colistina	S	≤0.5	2	2
Gentamicina	R	≥16	4	4
Meropenem	R	≥16	2	8
Trimetoprim/sulfametoxazolo	R	≥320	20	40

Come applicare nella *real life* le indicazioni delle LG?? Caso n°1



Materiale: Sangue v. periferica 1 aerobio

[51] Emocoltura germi aerobi:

Positivo

## 1 Acinetobacter baumannii

Materiale: Sangue v.periferica 2 anaerobio

[51] Emocoltura germi anaerobi:

Negativo

Materiale: Sangue v. periferica 3 aerobio

[51] Emocoltura germi aerobi:

Positivo

<i>Antibiotici</i>		<i>MIC</i>	<i>MIC Breakpoint</i>	
			<i>S</i> ≤	<i>R</i> >
Amikacina	R	≥64	8	8
Ciprofloxacina	R	≥4	0.001	1
Colistina	S	≤0.5	2	2
Gentamicina	R	≥16	4	4
Meropenem	R	≥16	2	8
Trimetoprim/sulfametoxazolo	S	≤20	20	40
Cefiderocol	R		2	2

# ESCMID guidelines

For patients with severe and high-risk CRAB infections, we suggest combination therapy including **two *in vitro* active antibiotics among the available antibiotics** (polymyxin, aminoglycoside, tigecycline, sulbactam combinations).

**OK**  
**Colistina + bactrim**

**... e la Tossicità renale ???**

**Caso trattato con:**  
**Colistina + ampi/sulba 9g → Colistina**

## Acinetobacter baumannii

Amikacina	R
Ciprofloxacina	R
Colistina	S
Gentamicina	R
Meropenem	R
Trimetoprim/sulfametoxazolo	S
Cefiderocol	R

### Question 3: What Is the Role of Ampicillin-Sulbactam for the Treatment of Infections Caused by CRAB?

#### *Suggested Approach*

High-dose ampicillin-sulbactam is a preferred therapy for CRAB infections when susceptibility has been demonstrated.

High-dose ampicillin-sulbactam remains a treatment consideration as a component of combination therapy even when susceptibility has not been demonstrated.



# antibiotics

## In Vitro Activity of Sulbactam–Durlobactam against Carbapenem-Resistant *Acinetobacter baumannii* Clinical Isolates: A Multicentre Report from Italy

**Table 1.** In vitro activities of sulbactam–durlobactam and comparators against 141 carbapenem-resistant *Acinetobacter baumannii* collected in Italy.

Antimicrobial Agent	Number of Isolates at Each MIC (mg/L)														MIC RANGE	MIC <sub>50</sub>	MIC <sub>90</sub>
	0.06	0.125	0,25	0.5	1	2	4	>4	8	16	32	64	128	>128			
SUL	/	/	/	/	/	2	8	–	27	45	33	8	13	5	0.06–>128	16	128
DUR	/	/	/	/	/	/	/	–	3	7	44	39	47	1	0.06–>128	64	128
SUL–DUR	/	4	25	51	30	14	6	–	4	2	/	/	/	5	0.06/4–>128/4	0.5	4
CST	/	7	6	12	20	19	22	55	–	–	–	–	–	–	0.06–>4	4	>4

/ = the number of isolates equal to zero. –, no values available. In SUL–DUR combination, DUR was at fixed concentration of 4 mg/L.

# CONCLUSIONS

**Wise use of classic anti-microbials (antimicrobial stewardship)**

**Wise use of new anti-microbial**

**MDR/XDR/DTR strains**

**Inhaled antibiotics (selected situations)**

**XDR strains**

**Combination treatment (maybe sometimes)**

**THE PRESENT**

**New antibiotics (now in phase I, II, III trials)**

**New Inhaled antibiotics**

**Biological agents**

**Vaccines**

**Phage therapy**

**THE FUTURE**