CONGRESO NACIONAL · 67 · BARCELONA 2022 · 24-26 NOVIEMBRE ·

ReFORMÚLaTE

CASOS CLÍNICOS SOBRE LAS NUEVAS INFECTIOUS DISEASE GUIDELINES

ESCMID GUIDELINES FOR THE TREATMENT OF INFECTIONS CAUSED BY MULTIDRUG-RESISTANT GRAM-NEGATIVE BACILLI

Pilar Retamar-Gentil

EEII, HUV Macarena

CIBER_INFECC

IBIS_Universidad de Sevilla, ES

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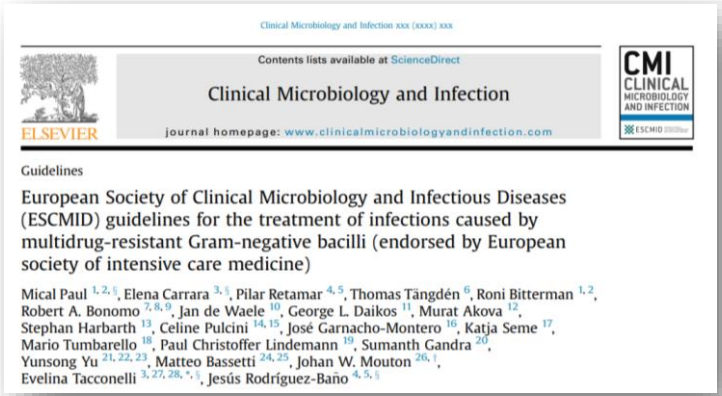
Conflicto de intereses…

Conferenciante: Menarini, Angelini, MSD

Advisor: Shionogui, Advanz.

Nuestra guía…



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ELSEVIER

CMI CLINICAL MICROBIOLOGY AND INFECTION

Guidelines

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)

Mical Paul [1, 2, §], Elena Carrara [3, §], Pilar Retamar [4, 5], Thomas Tängdén [6], Roni Bitterman [1, 2], Robert A. Bonomo [7, 8, 9], Jan de Waele [10], George L. Daikos [11], Murat Akova [12], Stephan Harbarth [13], Celine Pulcini [14, 15], José Garnacho-Montero [16], Katja Seme [17], Mario Tumbarello [18], Paul Christoffer Lindemann [19], Sumanth Gandra [20], Yunsong Yu [21, 22, 23], Matteo Bassetti [24, 25], Johan W. Mouton [26, †], Evelina Tacconelli [3, 27, 28, *, §], Jesús Rodríguez-Baño [4, 5, §]

Primero, revision sistemática de la(Dec 2019/Jul 2021)

Segundo, panel de expertos

Finalmente, recomendaciones discutidas hasta un consenso

PICO

- ✓ Population/participant: **hospitalized** patients (excluded: non complicated UTI/tracheobronchitis)
- ✓ Intervention: comparative randomized controlled trials (RCT)/observational studies
- ✓ Comparator/control: **EMA/FDA approved** antibiotics/any antibiotics
- ✓ Outcome: all-cause mortality (30 day); other: clinical cure, microbiological cure, resistances, relapse

Carbapenem-resistant Enterobacterales (CRE)

Recommendations on the choice of antibiotic treatment for CRE

For patients with severe infections due to CRE, we suggest meropenem-vaborbactam or ceftazidime-avibactam if active *in vitro*.

For patients with severe infections due to CRE carrying metallo-β-lactamases and/or resistant to all other antibiotics, including ceftazidime-avibactam and meropenem-vaborbactam, we conditionally recommend treatment with cefiderocol.

For patients with non-severe infections due to CRE, under the consideration of antibiotic stewardship, we consider the use of an old antibiotic, chosen from among the *in vitro* active on an individual basis and according to the source of infection, as good clinical practice. For patients with cUTI, we suggest aminoglycosides, including plazomicin, over tigecycline.

We suggest that tigecycline not be used for BSI and HAP/VAP; if necessary, in patients with pneumonia, clinicians may use high-dose tigecycline.

There is no evidence to recommend for or against the use of imipenem-relebactam and fosfomycin monotherapies for CRE at the time of writing.

Recommendations on combination therapy for CRE

For patients with CRE infections susceptible to and treated with ceftazidime-avibactam, meropenem-vaborbactam or cefiderocol, we do not recommend combination therapy.

For patients with severe infections caused by CRE carrying metallo-β-lactamases and/or resistant to new antibiotic monotherapies, we suggest aztreonam and ceftazidime-avibactam combination therapy.

For patients with severe infections caused by CRE susceptible *in vitro* only to polymyxins, aminoglycosides, tigecycline or fosfomycin, or in the case of non-availability of new BLBLI, we suggest treatment with more than one drug active *in vitro*. No recommendation for or against specific combination

We suggest that clinici
unless the meropene
may be used as part

In patients with non-se
consideration of anti
among the *in vitro* a
infection as good clinical practice

Infecciones graves
Infecciones no graves

Ceftazidima-avibactam
Meropenem-vaborbactan
Cefiderocol
(Imipenem-relebactam)
Meropenem
Aminoglicósidos (plazomicin)
Tigeciclina
Fosfomicina

/low

Conditional Moderate

Grado de evidencia

Fuerza de la recomendación

Conditional vs Strong Low vs Moderate

Good practice statement Expert opinion

Third-generation cephalosporin-resistant Enterobacterales (3GCephRE)

Recommendations on the choice of antibiotic treatment for 3GCephRE

For patients with BSI and severe infection due to 3GCephRE, we recommend a carbapenem (imipenem or meropenem) as targeted therapy

For patients with BSI due to 3GCephRE without septic shock, ertapenem instead of imipenem or meropenem may be used.

For patients with low-risk, non-severe infections due to 3GCephRE, under the consideration of antibiotic stewardship, we suggest piperacillin-tazobactam, amoxicillin/clavulanic acid or quinolones. It may be good practice to consider cotrimoxazole for non-severe cUTI.

For cUTI in patients without septic shock, we conditionally recommend aminoglycosides when active *in vitro* for short durations of therapy, or IV fosfomycin.

Among all patients with 3GCephRE infections, stepdown targeted therapy following carbapenems once patients are stabilized, using old BLBLI, quinolones, cotrimoxazole or other antibiotics based on the susceptibility pattern of the isolate, is good clinical practice.

We do not recommend tigecycline for infections caused by 3GCephRE.

Among all patients with 3GCephRE infections the new BLBLI are reserved antibiotics for extensively resistant bacteria and therefore, we consider it good clinical practice to avoid their use for infections caused by 3GCephRE, due to antibiotic stewardship considerations.

We suggest that cephamycins (e.g. cefoxitin, cefmetazole, flomoxef) and cefepime not be used for 3GCephRE infections.

For cefoperazone-sulbactam, ampicillin-sulbactam, ticarcillin-clavulanic acid, temocillin and mecillinam there is insufficient evidence for the management of patients with 3GCephRE infections at the time of writing and therefore no recommendation can be issued.

Infecciones graves
BC sin sepsis
Infecciones no graves, bajo riesgo

Meropenem, imipenem, ertapenem
Piperacilina-tazobactam
Amoxicilina-clavulánico
Quinolonas
Aminoglicósidos
Tigeciclina
Fosfomicina
Cotrimoxazol
Cefamixinas y cefepime

Preguntas…

Carbapenem-resistant Enterobacterales (CRE)

Recommendations on the choice of antibiotic treatment for CRE

For patients with severe infections due to CRE, we suggest meropenem-vaborbactam or ceftazidime-avibactam if active *in vitro*.	Conditional	Moderate/low
For patients with severe infections due to CRE carrying metallo-β-lactamases and/or resistant to all other antibiotics, including ceftazidime-avibactam and meropenem-vaborbactam, we conditionally recommend treatment with cefiderocol.	Conditional	Low
For patients with non-severe infections due to CRE, under the consideration of antibiotic stewardship, we consider the use of an old antibiotic, chosen from among the *in vitro* active on an individual basis and according to the source of infection, as good clinical practice. For patients with cUTI, we suggest aminoglycosides, including plazomicin, over tigecycline.	Good practice statement/conditional	Expert opinion/low
We suggest that tigecycline not be used for BSI and HAP/VAP; if necessary, in patients with pneumonia, clinicians may use high-dose tigecycline.	Conditional	Low
There is no evidence to recommend for or against the use of imipenem-relebactam and fosfomycin monotherapies for CRE at the time of writing.	No recommendation	

Recommendations on combination therapy for CRE

For patients with CRE infections susceptible to and treated with ceftazidime-avibactam, meropenem-vaborbactam or cefiderocol, we do not recommend combination therapy.	Strong	Low
For patients with severe infections caused by CRE carrying metallo-β-lactamases and/or resistant to new antibiotic monotherapies, we suggest aztreonam and ceftazidime-avibactam	Conditional	Moderate

consideration of antibiotic stewardship, we consider the use of monotherapy chosen from among the *in vitro* active old drugs, on an individual basis and according to the source of infection as good clinical practice

- ✓ ¿Cuál es el antibiótico de elección? (R CEF3ª, ECP)
- ✓ ¿Debemos usar tratamiento combinado? (ECP)

Ambler	Enzima	Cefto/taz	CAZ/AVI	ATM/AVI	MER/VAB	IMI/ REL	Cefiderocol	Plazomicina	Evaraciclina
A	ESBLs	SI	SI	SI	SI	SI	SI	SI	SI
	KPC	No	SI	SI	SI	SI	SI	SI	SI
B	MBL*	No	No	Si	No	No	SI	SI	SI
C	AmpC	SI	SI	SI	SI	SI	SI	SI	SI
D	OXA-48	No	SI	SI	No	No	SI	SI	SI

* VIM, NDM, IMP

CASO CLÍNICO 1

Antecedentes: Paciente de 42 años con litiasis renal e ITU de repetición.

NO RAM. No otros antecedentes de interés.

Ha presentado 3 episodios en último trimestre (*E.coli* MS, *E. coli* R AMC)

Tratamientos recibidos: cefuroxima, fosfomicina y ciprofloxacino.

Pendiente de litotricia.

CASO CLÍNICO 1

Episodio actual:

Acude a urgencias por fiebre de 24 horas y dolor renal derecho.

A la exploración se encuentra consciente, temperatura 38.5˚C, 101 lpm, 18 rpm, PA: 139/77 mmHg.

En las pruebas complementarias presenta:

Hb: 12,9 gr/dl, leucocitos: 19.450 cls/dl, plaquetas 345.000, glucosa 120 mg/dl, creatina 0,9 mg/dl. PCR: 213 mg/dl.

Eco abdominal: litiasis en cáliz derecho y discreto líquido perirrenal.

Se obtiene urocultivo y hemocultivo.

Inician tratamiento con: ceftriaxona 1 gr/24 horas.

CASO CLÍNICO 1

Muestra: Sangre

Cultivo de bacterias: Se aísla: ***(1) Escherichia coli***

ANTIBIOGRAMA	(1) S/I/R	CMI(µg/ml)
Ampicilina	R	>8
Amoxicilina/clavulánico	**S**	**<=8**
Piperacilina/tazobactam	**S**	**<=8**
Cefuroxima	R	>8
Cefotaxima	R	>32
Ceftazidima	R	16
Cefepime	R	>8
Aztreonam	R	>4
Ertapenem	**S**	**<=0.12**
Imipenem	**S**	**<=1**
Meropenem	**S**	**<=0.12**
Gentamicina	**S**	**<=2**
Tobramicina	**S**	**<=2**
Amikacina	**S**	**<=8**
Ciprofloxacino	R	>1
Trimetroprim/sulfametoxazol	R	>4/76
Fosfomicina	**S**	**<=16**

CTX-M-15

Lista de problemas:

- Pielonefritis
- Paciente sano
- Foco “fácil complicado”
- **ITU complicada (BC sin sepsis)**

CASO CLÍNICO 1…¿Tratamiento de elección?

1. Meropenem 2 gr q8
2. Ertapenem 1 gr iv qd.
3. Fosfomicina 4gr iv q6.
4. Amikacina 1 gr qd.
5. Amoxicilina-clavulánico 1 gr iv q8.

Third-generation cephalosporin-resistant Enterobacterales (3GCephRE)

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Among all patients with 3GCephRE infections, stepdown targeted therapy following carbapenems once patients are stabilized, using old BLBLI, quinolones, cotrimoxazole or other antibiotics based on the susceptibility pattern of the isolate, is good clinical practice.

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Among all patients with 3GCephRE infections the new BLBLI are reserved antibiotics for extensively resistant bacteria and therefore, we consider it good clinical practice to avoid their use for infections caused by 3GCephRE, due to antibiotic stewardship considerations.

We suggest that cephamycins (e.g. cefoxitin, cefmetazole, flomoxef) and cefepime not be used for 3GCephRE infections.

For cefoperazone-sulbactam, ampicillin-sulbactam, ticarcillin-clavulanic acid, temocillin and mecillinam there is insufficient evidence for the management of patients with 3GCephRE infections at the time of writing and therefore no recommendation can be issued.

Nuestro caso…
BC sin sepsis
Infecciones no graves, bajo riesgo

Strong	Moderate
Conditional	Moderate
Conditional/good practice statement	Moderate/expert opinion
Conditional/strong	Moderate/high
Good practice statement	Expert opinion

Nuestras opciones….
Meropenem
Ertapenem
Amoxicilina-clavulánico
Aminoglicósidos
Fosfomicina

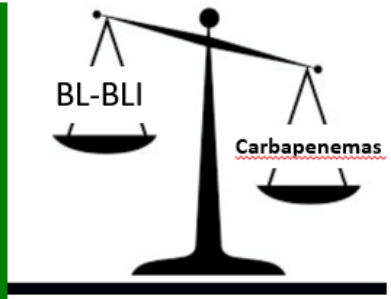
CASO CLÍNICO: evidencias proCARBAPENEM

BLEE

AMC-PTZ

Rodriguez_Baño CID 2015
VardaKas JAC 2012
Shiber JAC 2015
Gutierrez-Gutierrez AAC 2016*
Gudiol AAC 2017

Rodriguez-Baño 2019



Carbapenemas

Paterson&Bonomo CMR 2005

Harris JAMA 2018

Pip-tazo (4,5 g/8h, 30¨m) vs meropenem (1 g/8h, 30 m)

Pip-tazo no demostró NO ser inferior

Otros…

Empiric Therapy With Carbapenem-Sparing Regimens for Bloodstream Infections due to Extended-Spectrum β-Lactamase–Producing Enterobacteriaceae: Results From the INCREMENT Cohort Palacios-Baena CID 2017

Rodriguez-Baño JAMA 2019

- ✓ Grupo de meropenem: + ITU, menos sepsis…
- ✓ Grupo PipTaz: más comorbilidad.
- ✓ Piptaz en 30 min
- ✓ Mortalidad relacionada no analizada.
- ✓ Outcome microbiológicos a favor de PIPTAZ
- ✓ Contaminación de tratamiento previo

CASO CLÍNICO: otras evidencias

BLEE

Otros antibióticos…

Empiric Therapy With Carbapenem-Sparing Regimens for Bloodstream Infections due to Extended-Spectrum β-Lactamase–Producing Enterobacteriaceae: Results From the INCREMENT Cohort

Palacios-Baena CID 2017

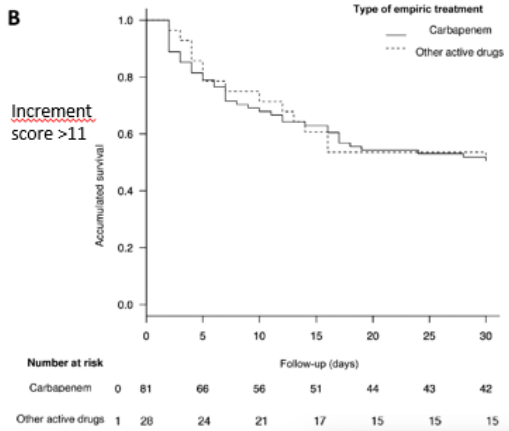


Table 2. Thirty-Day Mortality Associated With Empiric Treatment Received

Empiric Therapy	Deaths/Treated	High-Risk Score[a]
Carbapenem as only active drug	42/226 (18.6)	32/66 (48.5)
Carbapenem combined with other active drug	9/23 (39.1)	8/15 (53.3)
Cephalosporin as only active drug	2/7 (28.6)	1/2 (50)
Aminoglycoside as only active drug[b]	9/41 (21.9)	8/16 (50)
Fluoroquinolone as only active drug	2/19 (10.5)	2/2 (100)
Trimethoprim-sulfamethoxazole as only active drug	0/4 (0)	0/1 (0)
Tigecycline as only active drug	1/2 (50)	1/2 (50)
Others used as only active drug[c]	2/10 (20)	2/4 (50)
Other combinations[d]	0/4 (0)	0/1 (0)

Journal of Antimicrobial Chemotherapy (2007) **60**, 247–257
doi:10.1093/jac/dkm193
Advance Access publication 11 June 2007

JAC

Efficacy and safety of aminoglycoside monotherapy: systematic review and meta-analysis of randomized controlled trials

CASO CLÍNICO: otras evidencias

JAMA Network | Open

Original Investigation | Infectious Diseases

Effectiveness of Fosfomycin for the Treatment of Multidrug-Resistant *Escherichia coli* Bacteremic Urinary Tract Infections
A Randomized Clinical Trial

Sojo-Dorado et al. JAMA Open 2022

Table 2. Patients Reaching CMC and Reasons for Not Reaching It

	Patients, No./total No. (%)			
	Receiving fosfomycin	Receiving comparator	Risk difference (1-sided 95% CI)[a]	*P* value, 1-sided
CMC at TOC among MITT (measures of success)				
All patients	48/70 (68.6)	57/73 (78.0)	−9.4 (−21.5 to ∞)	.10
Patients with ceftriaxone-susceptible isolates[b]	25/31 (80.6)	27/31 (87.0)	−6.4 (−21.7 to ∞)	.24
Patients with ceftriaxone-resistant isolates[b]	23/39 (59.0)	30/42 (71.4)	−12.4 (−29.8 to ∞)	.12
Reasons for not reaching CMC at TOC among MITT (measures of failure)				
Clinical or microbiological failure				
All patients	10/70 (14.3)	14/73 (19.7)	−5.4 (−∞ to 4.9)	.19
Patients with ceftriaxone-susceptible isolates[b]	3/31 (9.7)	4/31 (12.9)	−3.2 (−∞ to 10.0)	.34
Patients with ceftriaxone-resistant isolates[b]	7/39 (17.9)	10/42 (23.8)	−8.9 (−∞ to 6.9)	.25
Other reasons				
Withdrawn because of adverse events	6/70 (8.5)[c]	0/73 (0)	8.5 (−∞ to 13.9)	.006
Missed assessment at TOC	3/70 (4.2)	2/73 (2.7)	1.5 (−∞ to 6.5)	.31
TOC assessed but urine culture at TOC not available	3/70 (4.2)	0/73 (0)[d]	4.2 (−∞ to 8.1)	.03

CASO CLÍNICO 2

Paciente de 63 años

Antecedentes: NO RAM. HTA y DM (tratamientos con enalapril y metformina).

Colangiocarcinoma con prótesis biliar plástica en junio/22

3 episodios de colangitis aguda desde entonces, recambios de prótesis hasta colocación de metálica (necesidad de ingreso).

Tratamientos recibidos: meropenem, piperacilina/tazobactam, ceftriaxona, ciprofloxacino, amoxicilina/clavulánico y profilaxis con cotrimoxazol entre cada episodio.

CASO CLÍNICO 2

Episodio actual:

Acude a urgencias por fiebre de 48 horas, dolor en el hipocondrio derecho.

A la exploración se encuentra consciente, temperatura 38.5˚C, 101 lpm, 18 rpm, PA: 99/57 mmHg.

En las pruebas complementarias presenta:

Hb: 10,9 gr/dl, leucocitos: 18.450 cls/dl, plaquetas 345.000, glucosa 230 mg/dl, creatina 1,6 mg/dl, Bl D 2 gr/dl. PCR: 237 mg/dl.

TAC abdominal: absceso en el lóbulo hepático izquierdo (8 x 9 cm).

Inician tratamiento con: meropenem 1 gr/8. Se pide drenaje mediante radiología intervencionista y CPRE

CASO CLÍNICO 2

Muestra: Absceso aspiración.Hígado

Tinción de Gram: Negativo.

Cultivo de bacterias: Se aísla:

(1) Klebsiella pneumoniae

ANTIBIOGRAMA	(1) S/I/R	CMI(µg/ml)
Ampicilina	R	>8
Amoxicilina/clavulánico	R	>32
Piperacilina/tazobactam	R	>16
Cefuroxima	R	>8
Cefotaxima	R	>32
Ceftazidima	R	4
Cefepime	R	>8
Ceftazidima/avibactam	**S**	**<=2**
Ceftolozano/tazobactam	R	4
Aztreonam	R	>4
Ertapenem	R	>1
Imipenem	R	>8
Meropenem	R	>32
Gentamicina	**S**	**<=2**
Tobramicina	**S**	**<=2**
Amikacina	**S**	**<=8**
Ciprofloxacino	R	>1
Levofloxacino	R	>1
Trimetroprim/sulfametoxazol	**S**	**<=2/38**

KPC-2 + CTX-M-15

Lista de problemas:

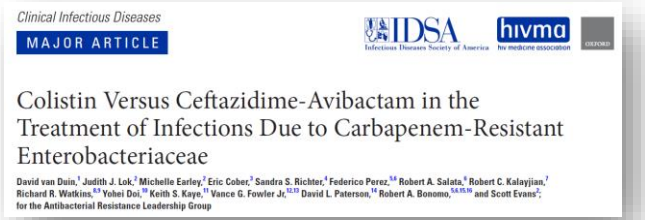
- SOFA≥2
- Paciente frágil
- Foco difícil de tratar
- **Infección grave**

CASO CLÍNICO 3…¿Tratamiento de elección?

1. Meropenem 2 gr q8 perfusión extendida (p.e.) + amikacina 1 gr qd
2. Ceftazidima-avibactam 2 gr q8 p.e.
3. Preguntaría CMI de meropenem-vaborbactam
4. Preguntaría CMI de colistina
5. Amikacina 1 gr qd

Evidencias…..ceftazidima-avibactam

Estudios pivotales CRE
Información retrospectiva, observacional, KPC


Clinical Infectious Diseases
MAJOR ARTICLE

Colistin Versus Ceftazidime-Avibactam in the Treatment of Infections Due to Carbapenem-Resistant Enterobacteriaceae

David van Duin, Judith J. Lok, Michelle Earley, Eric Cober, Sandra S. Richter, Federico Perez, Robert A. Salata, Robert C. Kalayjian, Richard R. Watkins, Yohei Doi, Keith S. Kaye, Vance G. Fowler Jr, David L. Paterson, Robert A. Bonomo, and Scott Evans; for the Antibacterial Resistance Leadership Group

CR_*K. pneumoniae* (46% BC)
Mortalidad ajustada a 30 días:
9% vs 32% (9%–35%; P = .001)


Clinical Infectious Diseases
MAJOR ARTICLE

Efficacy of Ceftazidime-Avibactam Salvage Therapy in Patients With Infections Caused by *Klebsiella pneumoniae* Carbapenemase–producing *K. pneumoniae*

Mario Tumbarello, Enrico Maria Trecarichi, Alberto Corona, Francesco Giuseppe De Rosa, Matteo Bassetti, Cristina Mussini, Francesco Menichetti, Claudio Viscoli, Caterina Campoli, Mario Venditti, Andrea De Gasperi, Alessandra Mularoni, Carlo Tascini, Giustino Parruti, Carlo Pallotto, Simona Sica, Ercole Concia, Rosario Cultrera, Gennaro De Pascale, Alessandro Capone, Spinello Antinori, Silvia Corcione, Elda Righi, Angela Raffaella Losito, Margherita Digaetano, Francesco Amadori, Daniele Roberto Giacobbe, Giancarlo Ceccarelli, Ernestina Mazza, Francesca Raffaelli, Teresa Spanu, Roberto Cauda, and Pierluigi Viale

KPC-producing *K. pneumoniae* BC
Ceftazidima-avibactam tras 7 de mejor terapia disponible
Propensity-score_Mortalidad a 30 d (36.5% vs 55.8%, P = 0.005)

Van Duin CID 2018; Shields AAC 2017; Caston Int J Inf Dis 2017; Tumbarello CID 2019; Alradaddi BMC Inf Dis 2019

Evidencias meropenem-vaborbactam

Infect Dis Ther (2018) 7:439–455
https://doi.org/10.1007/s40121-018-0214-1

ORIGINAL RESEARCH

Effect and Safety of Meropenem–Vaborbactam versus Best-Available Therapy in Patients with Carbapenem-Resistant Enterobacteriaceae Infections: The TANGO II Randomized Clinical Trial

Wunderick, Inf Dis Ther 2018

Table 2 Efficacy endpoints among all patients with confirmed CRE infections (mCRE-MITT)

	M–V (n = 32) n (%)	BAT (n = 15) n (%)	Difference[a] (95% CI)	P value	Relative difference[b]
Efficacy endpoints					
Clinical cure at EOT	21 (65.6)	5 (33.3)	32.3 (3.3–61.3)	0.03	97.0
Clinical cure at TOC	19 (59.4)	4 (26.7)	32.7 (4.6–60.8)	0.02	122.5
Microbiologic cure[c] at EOT	21 (65.6)	6 (40.0)	25.6 (− 4.1 to 55.4)	0.09	64.0
Microbiologic cure[c] at TOC	17 (53.1)	5 (33.3)	19.8 (− 9.7 to 49.3)	0.19	59.5
Day-28 mortality	5 (15.6)	5 (33.3)	− 17.7 (− 44.7 to 9.3)	0.20	− 53.2
	M–V (n = 23) n (%)	**BAT (n = 15) n (%)**	**Difference[a] (95% CI)**	**P value**	**Relative difference[b]**
Sensitivity analysis of clinical cure at TOC and all-cause mortality at day 28 across all infection types (mCRE-MITT) excluding prior antibiotic failure[d]					
Clinical cure at TOC	16 (69.6)	4 (26.7)	42.9 (13.7–72.1)	0.004	160.7
Day-28 all-cause mortality	1 (4.3)	5 (33.3)	− 29.0 (− 54.3 to -3.7)	0.02	− 87.1

Evidencias tratamiento combinado

35 estudios estimaban mortalidad

(34/35) “considerable risk of bias” (“high” en 12, “moderate” en 14; y “low” en 9).

Una droga activa vs 2 drogas activas: 7 estudios

A favor de la combinación en pacientes graves

Tumbarello, JAC 2015; Gutierrez_Gutierrez, Lancet Inf Dis 2017; Falcone, CMI 2016

Combinación que incluye carbapenem

Meropenem MIC ≤ 8 mg/dl (Tumbarello, JAC 2015)

AIDA and OVERCOME trials (HAP/VAP and BSI): COL vs MER+COL

Subanalisis de infecciones por CRE: no differencias en mortalidad a 28 días

Paul, Lancet Infect Dis 2018; Kaye, presentation at 31th ECCMID Basel 2021

CASO CLÍNICO 3

Paciente de 83 años

Antecedentes: HTA y DM (tratamientos con enalapril y metformina), ITUs de repetición tratadas con múltiples AB (cefalosporinas, quinolonas, A/C). Residencia de ancianos

Episodio actual:

Acude a urgencias por dolor abdominal y vómitos. Sin fiebre.

A la exploración se encuentra consciente, temperatura 38.5˚C, 101 lpm, 18 rpm, PA: 140/89 mmHg.

En pruebas complementarias presenta: Hb: 10,9 gr/dl, leucocitos: 18.450 cls/dl, plaquetas 345.000, glucosa 230 mg/dl, creatina 1,6 mg/dl, Bl D 2 gr/dl. PCR: 350 mg/dl.

Se obtiene hemocultivo y urocultivo e inicia tratamiento con meropenem 1 gr/8 horas

CASO CLÍNICO 3

MICROBIOLOGÍA

Muestra: Orina (media)

Cultivo de bacterias: Se aíslan > 100.000 U.F.C./ml de:

(1) Klebsiella pneumoniae

ANTIBIOGRAMA	(1)	
	S/I/R	CMI(µg/ml)
Ampicilina	R	>8
Amoxicilina/clavulánico	R	>32
Piperacilina/tazobactam	R	>16
Cefuroxima	R	>8
Cefotaxima	R	>32
Ceftazidima	R	4
Cefepime	R	>8
Aztreonam	R	>4
Ertapenem	R	>1
Imipenem	I	2
Meropenem	I	1
Gentamicina	R	>4
Tobramicina	R	>4
Amikacina	**S**	**<=8**
Ciprofloxacino	R	>1
Trimetroprim/sulfametoxazol	R	>4/76
Fosfomicina	**S**	32
Nitrofurantoina	**S**	**<=64**

CTX-M-15+OXA-48

Lista de problemas:

No sepsis

Insuficiencia renal

ITU

Infección leve

CASO CLÍNICO 3…¿Tratamiento de elección?

1. Meropenem 2 gr q8 PE
2. Meropenem 2 gr q8 PE+ Fosfomicina 4 gr q6
3. Preguntaría CMI de Ceftazidima-avibactam
4. Amikacina 1 gr qd
5. Tigeciclina 100 mg qd (2nd día: 50 mg qd)

CASO CLÍNICO 4

Varón de 78 años. Diabetes.

ITU de repetición (3 episodios en un año, 1 ingreso: fosfomicina, ceftriaxona, ciprofloxacino)

Espondilolistesis.

Episodio actual:

Artrodesis lumbar.

Durante ingreso: ITU asociado a sonda: piperacilina-tazobactam 7 días

2 semanas más tarde: infección de la artrodesis e ingresa.

T: 38,5ºC, **TA 149/78**, **97 pm,** 16 rpm. Dolor lumbar.

13.700 leucocitos (90% PMN), lactato 1.8 mmol/L, creat **1,6 mg/dL, PCR**: **278**

Se toman HC. Se inicia tratamiento con Vancomicina 1 gr q12 y meropenem 2gr qd.

CASO CLÍNICO 4

Muestra: Sangre

Cultivo de bacterias: Se aísla:

(1) Klebsiella pneumoniae

ANTIBIOGRAMA	(1)	
	S/I/R	CMI(µg/ml)
Ampicilina	R	>8
Amoxicilina/clavulánico	R	>32
Piperacilina/tazobactam	R	>16
Cefuroxima	R	>8
Cefotaxima	R	>32
Ceftazidima	R	>32
Cefepime	R	>8
Aztreonam	R	>4
Ertapenem	R	1
Imipenem	I	<=1
Meropenem	I	1
Gentamicina	**S**	**<=2**
Tobramicina	R	>4
Amikacina	I	<=8
Ciprofloxacino	R	>1
Trimetroprim/sulfametoxazol	R	>4/76

VIM-1, OXA-48, CTX-M-15, SHV-28

Lista de problemas:

¿No sepsis??

Bacteriemia

Infección profunda de herida quirúrgica

Infección severa

CASO CLÍNICO 4…¿Tratamiento de elección?

1. Ceftazidime-avibactam 2 gr q8 PE + Aztreonam 1 gr q8
2. Meropenem 2 gr q8 PE + Gentamicina 240 qd
3. Preguntaría CMI de cefiderocol
4. Gentamicina 240 mgr qd

Evidencias de cefiderocol

Efficacy and safety of cefiderocol or best available therapy for the treatment of serious infections caused by carbapenem-resistant Gram-negative bacteria (CREDIBLE-CR): a randomised, open-label, multicentre, pathogen-focused, descriptive, phase 3 trial

Matteo Bassetti, Roger Echols, Yuko Matsunaga, Mari Ariyasu, Yohei Doi, Ricard Ferrer, Thomas P Lodise, Thierry Naas, Yoshihito Niki, David L Paterson, Simon Portsmouth, Julian Torre-Cisneros, Kiichiro Tsuyuguchi, Richard G Wunderink, Teutee D Niyonzo

	Nosocomial pneumonia		Bloodstream infections or sepsis		Complicated urinary tract infections		Overall	
	Cefiderocol (n=45)	Best available therapy (n=22)	Cefiderocol (n=30)	Best available therapy (n=17)	Cefiderocol (n=26)	Best available therapy (n=10)	Cefiderocol (n=101)	Best available therapy (n=49)
Day 14	11 (24%; 12·9–39·5)	3 (14%; 2·9–34·9)	5 (17%; 5·6–34·7)	1 (6%; 0·1–28·7)	3 (12%; 2·4–30·2)	2 (20%; 2·5–55·6)	19 (19%; 11·7–27·8)	6 (12%; 4·6–24·8)
Day 28	14 (31%; 18·2–46·6)	4 (18%; 5·2–40·3)	7 (23%; 9·9–42·3)	3 (18%; 3·8–43·4)	4 (15%; 4·4–34·9)	2 (20%; 2·5–55·6)	25 (25%; 16·7–34·3)	9 (18%; 8·8–32·0)
End of study	19 (42%; 27·7–57·8)	4 (18%; 5·2–40·3)	11 (37%; 19·9–56·1)	3 (18%; 3·8–43·4)	4 (15%; 4·4–34·9)	2 (20%; 2·5–55·6)	34 (34%; 24·6–43·8)	9 (18%; 8·8–32·0)

Data are n (%; 95% CI) by clinical diagnosis and overall. Percentages were calculated using n as the denominator, where n was the number of patients in the safety population who had the specified clinical diagnosis and known vital status at each timepoint.

Table 5: **All-cause mortality in the safety population**

Basseti, Lancet Inf Dis 2021

POST_HOC analisis: *CR-K. pneumoniae*:
mortalidad 6/28 (21.4%) con cefiderocol vs 4/15 (26.7%) con MTD

Evidencia de tratamiento combinado: Nuevos fármacos

5 cohortes retrospectivas: 824 pacientes (USA, España e Italia)

No diferencia en mortalidad/fracaso clínico en infecciones causadas por **KPC and OXA-48**

King, AAC 2017; Tumbarelllo, CID 2019; Shields, AAC 2018; De la Calle, JAC 2019; Tumbarello, CID 2021

Estudio observacional (Falcone, CID 2021)

102 pacientes con BC por ECP productor de MBL (82**NDM**_ 20 **VIM**)

Ceftazidime-avibactam + aztreonam vs combinación de drogas activas

PS_analisis: ceftazidime-avibactam-aztreonam y mortalidad a 30 días (HR 0.37, 95% CI 0.13e0.74), moderada evidencia for ceftazidime-avibactam

Mensajes para llevar a casa

Muy importante determinar foco, gravedad y riesgo del paciente antes de tomar una decisión en cuanto AB.

En infecciones por **E R cef 3ª**: carbapenemes para infecciones graves y considerar **alternativas en leves (PTZ/AMC/fosfo/amika)**

En infecciones por **ECP** considerar los nuevos fármacos para infecciones graves o combinaciones con meropenem si no hay acceso a los mismos (CFT_AV + AZT).
En **leves pensar en alternativas (AMK, cipro, CMX, tige…)**

Si estabilidad clínica alcanzada (48-72 horas): **desescalar**


PROA_Macarena
5.327 Tweets
CONTIGO
Servicio Enfermedades Infecciosas
Equipo PROA
HUM
Siguiendo
PROA_Macarena
@PROAmacarena Te sigue
Grupo #PROA (Programa Optimización Antibioterapia) / Servicio Enfermedades Infecciosas, Hospital Virgen Macarena, Sevilla. #AntimicrobialStewardship.
Sevilla, España
hospitalmacarena.es/activos/antibi...
Se unió en noviembre de 2015
816 Siguiendo
5.251 Seguidores
SHORTEN-2 trial, PROA Hospital de Valme y 68 más de las cuentas que sigues siguen a este usuario

67 · CONGRESO NACIONAL · 24-26 NOVIEMBRE · BARCELONA 2022 ·

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Gracias por su atención

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Eskerrik asko zure arretagatik

Grazas pola súa atención