

# Infecciones graves ocasionadas por Gram positivos. UPDATE

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# **Neumonía nosocomial**

**Bacteriemia / endocarditis**

**Infecciones de piel y partes blandas**

**Infección osteoarticular**

**Infecciones del SNC**

**Endoftalmitis**

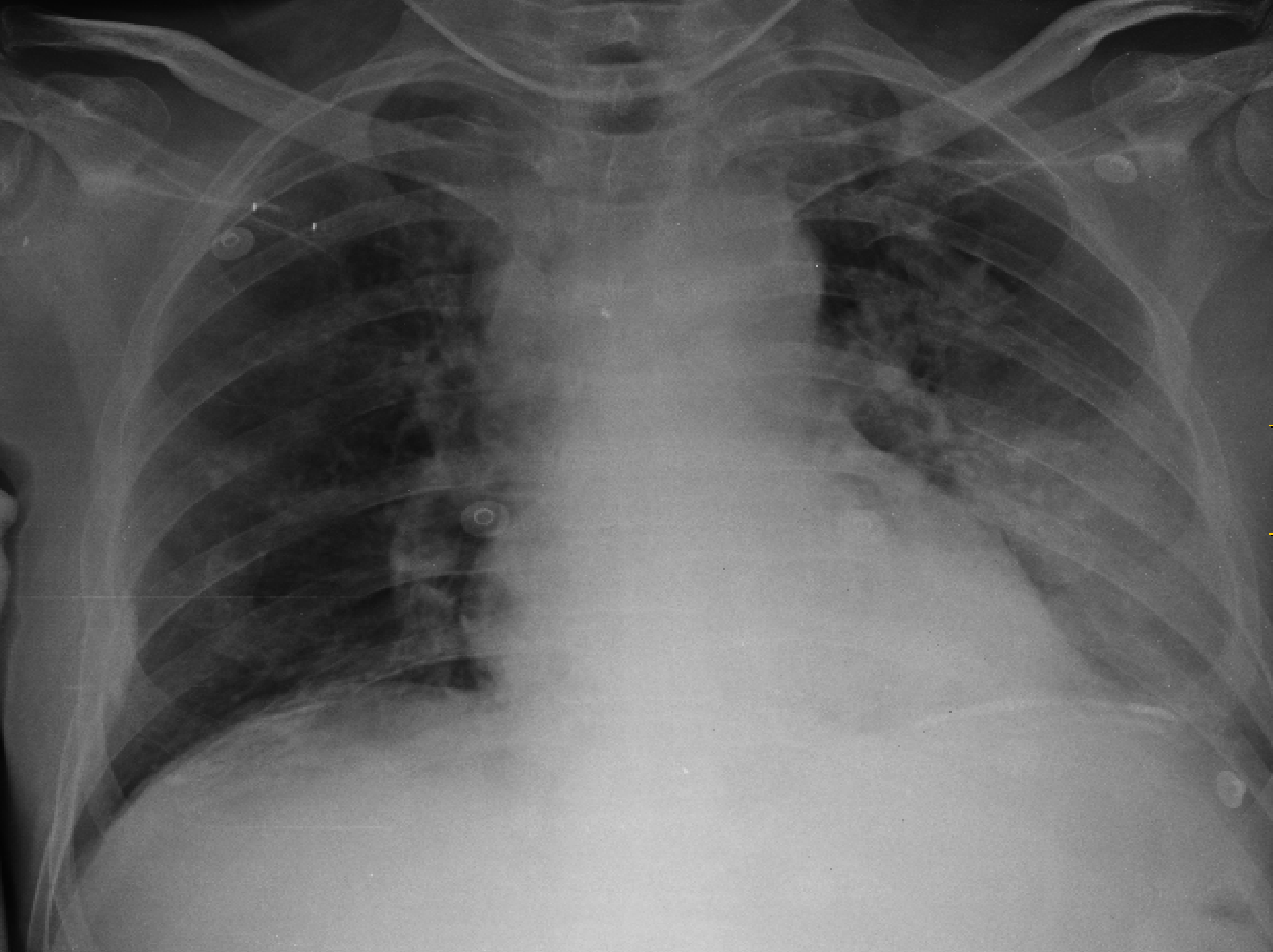
Varón de 60 años con antecedentes de infección por VIH y N. Laringe.

fiebre

espectoración purulenta

PCR: 22 mg/dL

7-10



Varón de 60 años con antecedentes de infección por VIH y N. Laringe.

fiebre

espectoración purulenta

PCR: 22 mg/dL, Cr: 2.4 mg/dL

7-10

Febricular

PCR: 14 mg/dL

12-10

HC

SARM TC:12h

CIM<sub>vanco</sub>: 1 mg/L

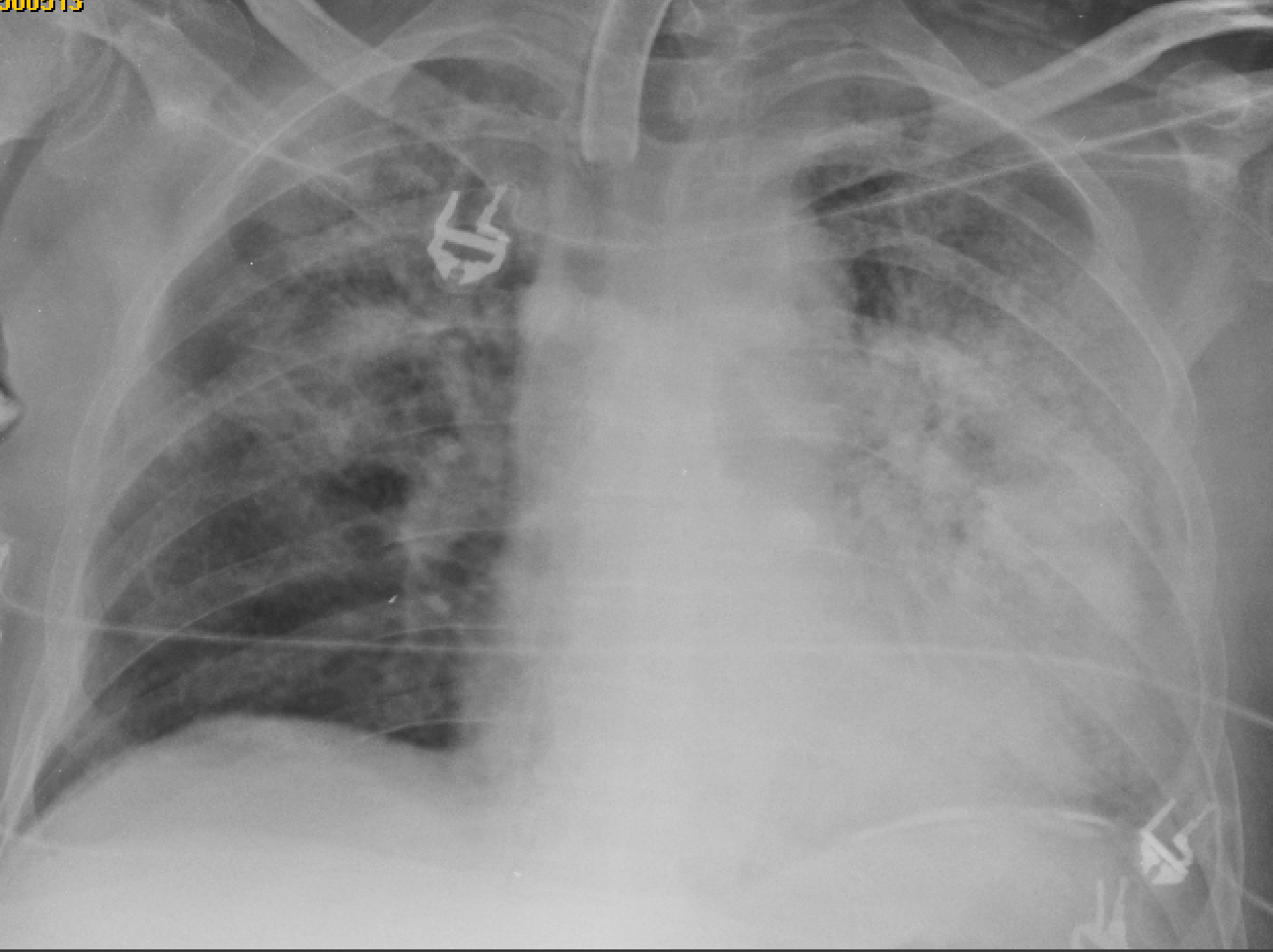
Mero 1g/8h

Vanco 1g/24h

C<sub>max</sub>: 12 mg/L

C<sub>min</sub>: 2 mg/L

1250 mg/12h



Varón de 60 años con antecedentes de infección por VIH y N. Laringe.

fiebre

espectoración purulenta

PCR: 22 mg/dL, Cr: 2.4 mg/dL

Febril

PCR: 14 mg/dL

7-10

9-10

12-10

14-10

HC: SARM TC:12h

HC

SARM TC: 33h

CIM<sub>vanco</sub>: 1 mg/L

Mero 1g/8h

Vanco 1g/24h

C<sub>max</sub>: 12 mg/L

C<sub>max</sub>: 23 mg/L

C<sub>min</sub>: 2 mg/L

C<sub>min</sub>: 7 mg/L

1250 mg/12h

1000 mg/8h

Linezolid

600 mg/12h

## Infección documentada por SARM

$\leq 1$

$> 1$

**vancomicina**

15 mg/Kg 12-8h iv,  
medir conc. sérica a  
las 48h y ajustar el  
valle a 15 mg/L

**linezolid**

- Neumonía
- IPPB
- Infección OA
- SNC
- Endoftalmitis

**daptomicina**

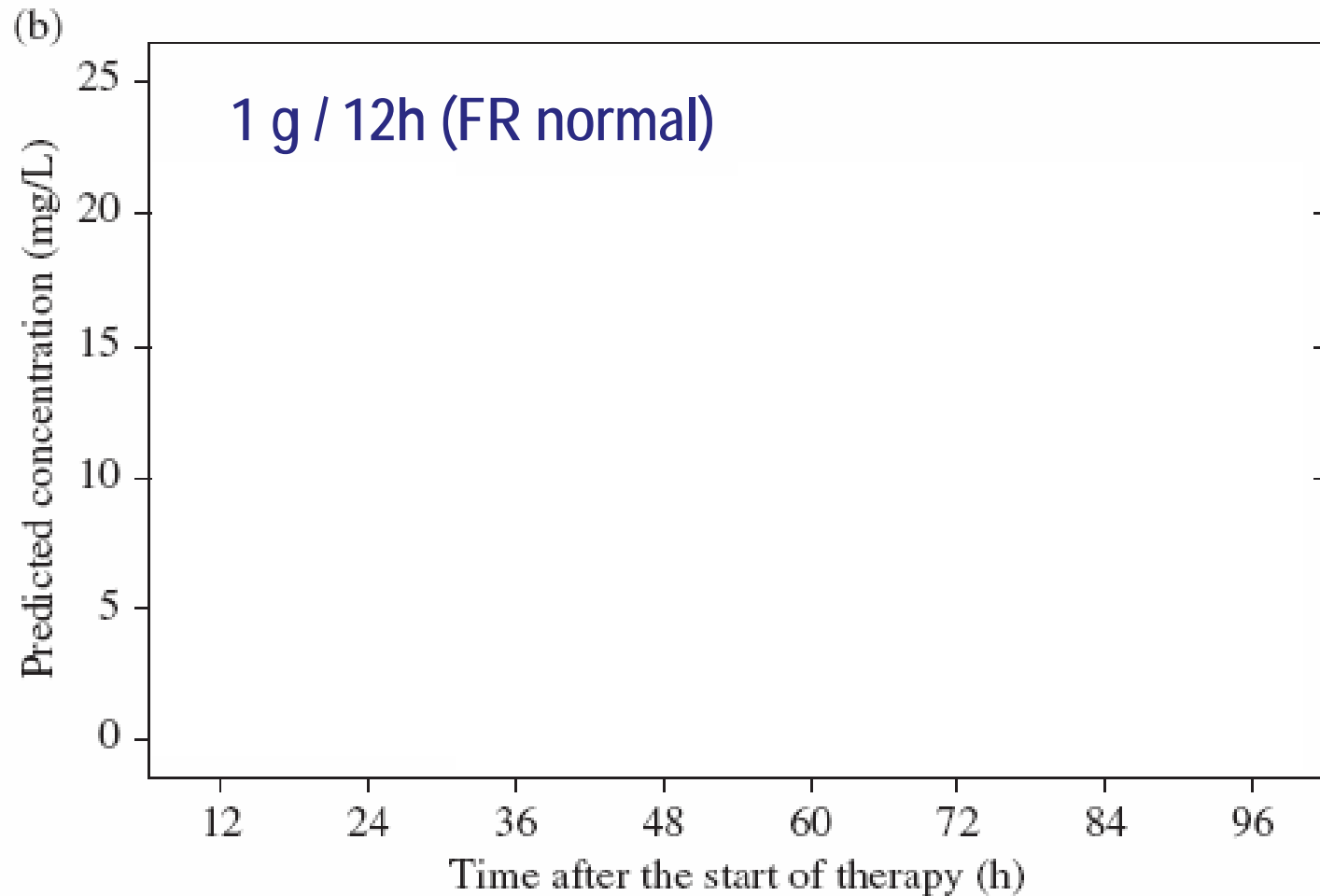
- Endocarditis
- Bacteriemia



Thompson AH, et al.

**Development and evaluation of vancomycin dosage guidelines designed to achieve new target concentrations**

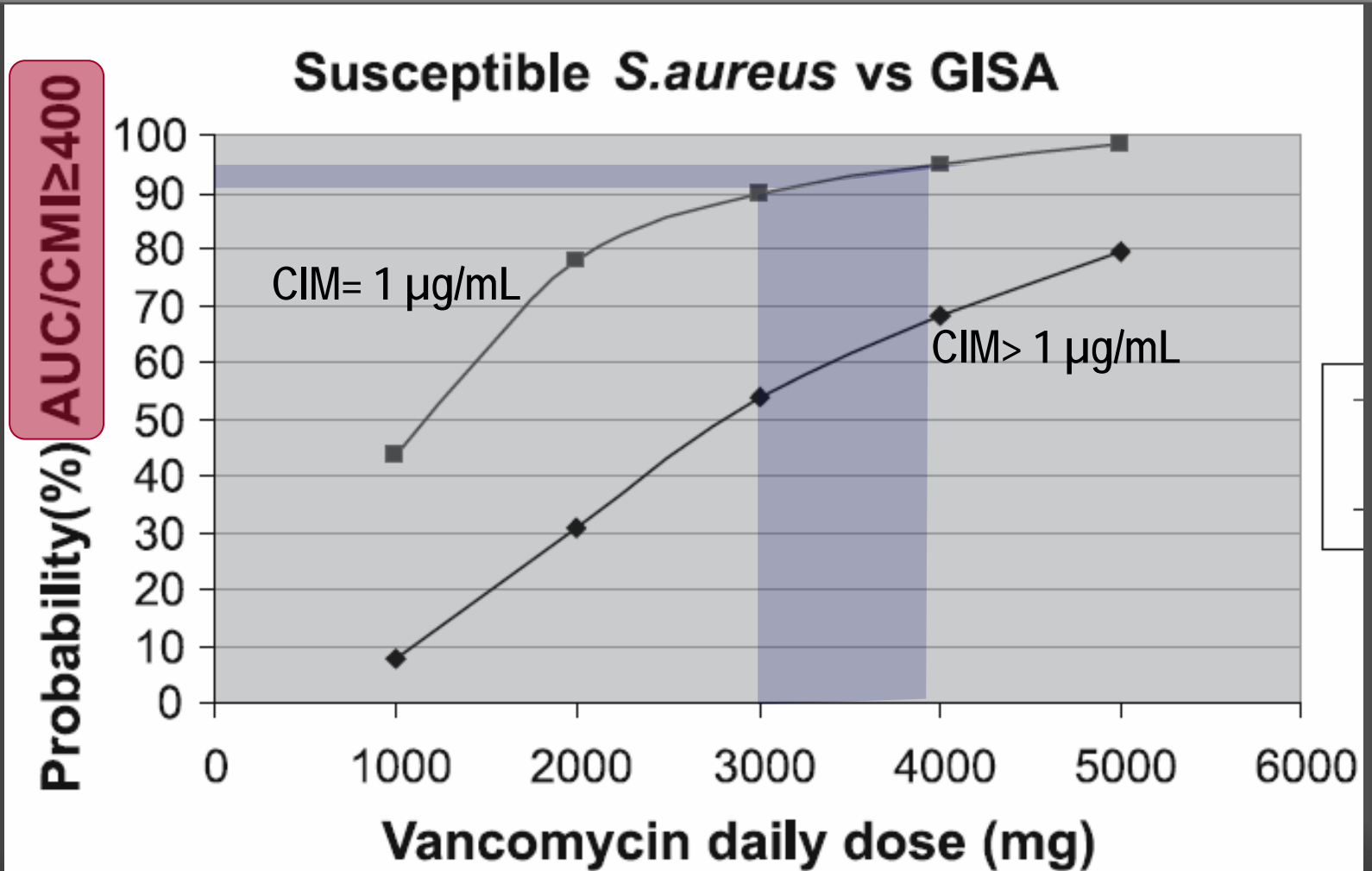
*J Antimicrob Agents* 2009; 63: 1050-57



Del Mar M *et al.*

# Pharmacokinetic/pharmacodynamic analysis of vancomycin in ICU patients

*Intensive Care Med* 2007;33:279-85



Kalil A, et al.

**Linezolid versus vancomycin or teicoplanin for nosocomial pneumonia: A systematic review and meta-analysis**

*Crit Care Med* 2010; 38:000-000

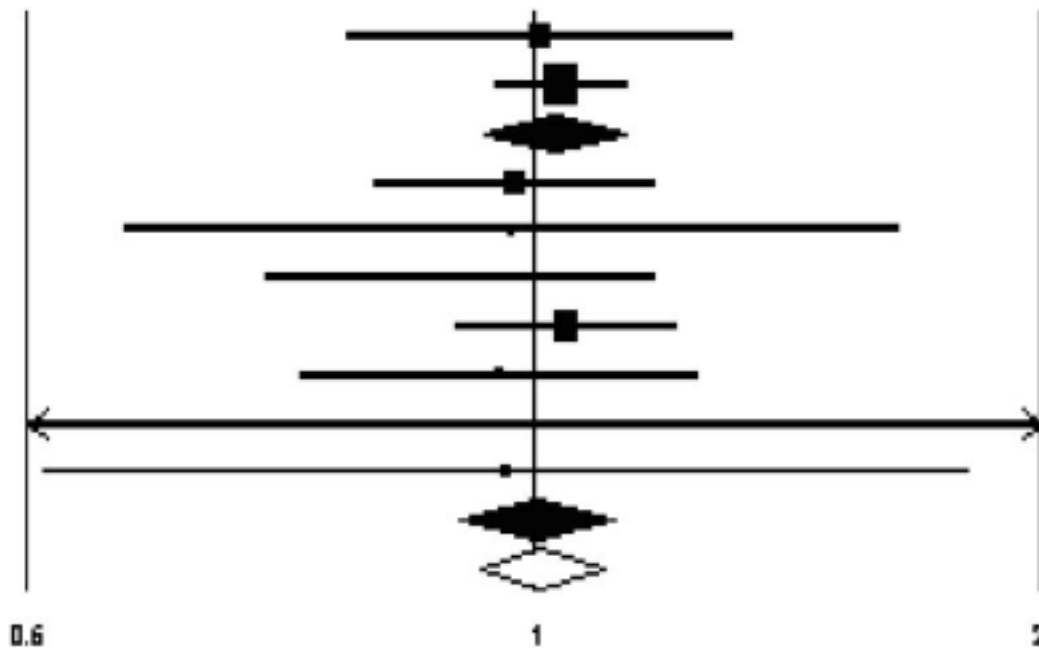
Study, Year	Total Sample Size	Mean Age (Treatment/Control)	Type of Infection
Rubinstein E, 2001 (21)	402	63/61	Pneumonias
Stevens DL, 2002 (22)	460	64/60	MRSA infections, including pneumonias
Kaplan SL, 2003 (23)	316	2.2/2.9	Gram-positive infections, including pneumonias
Wunderink R, 2003 (24)	623	63/62	Pneumonias
Cepeda JA, 2004 (19)	204	59/57	Gram-positive infections, including pneumonias
Wilcox M, 2004 (20)	430	53/55	Gram-positive infections, including pneumonias
Jaksic B, 2006 (25)	421	48/47	Neutropenic fever, including pneumonias
Kohno S, 2007 (26)	151	68/67	MRSA infections, including pneumonias
Wunderink R, 2008 (27)	50	56/55	MRSA pneumonias

Kalil A, et al.

# Linezolid versus vancomycin or teicoplanin for nosocomial pneumonia: A systematic review and meta-analysis

*Crit Care Med* 2010; 38:000-000

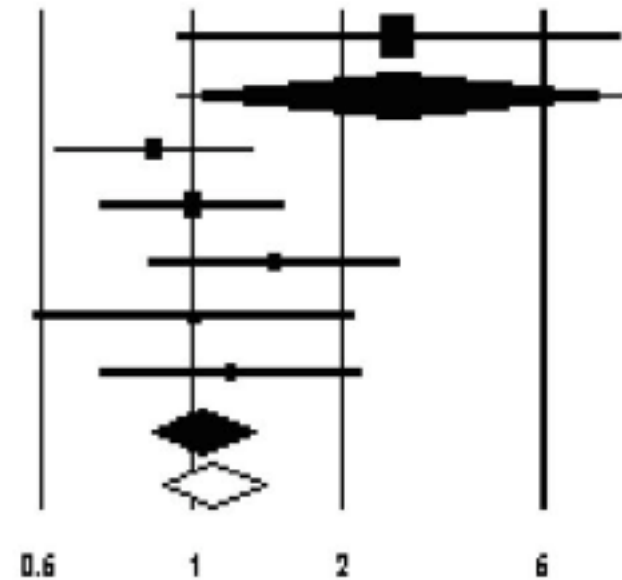
curación clínica



vancomycin

linezolid

erradicación (SARM)



vancomycin

linezolid

Kalil A, et al.

# Linezolid versus vancomycin or teicoplanin for nosocomial pneumonia: A systematic review and meta-analysis

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Wunderick . et al.

**Analysis of 2 doble-blind studies of patients with  
MRSA nosocomial pneumonia**

*Chest 2003;124:1789-1797.*

Tratamiento	NN por SARM	
	Curación (%)	Supervivencia, %
Vancomicina* (n=62)	22 (35.5)	63.5
Linezolid (n=61)	36 (59)	80
Valor - p	0.009	0.03

\* CIM ≤ 2 mg/L

Kollef MH . et al.

**Clinical cure and survival in GP VAP: retrospective analysis of 2-  
doble blind studies comparing linezolid with vancomycin.**

*Int Care Med 2004;30:388-94.*

Tratamiento	NAVM por SARM	
	% Curación	% Supervivencia
Vancomicina* (n=47)	21.2	61.7
Linezolid (n=44)	62.2	84.1
Valor - p	0.001	0.02

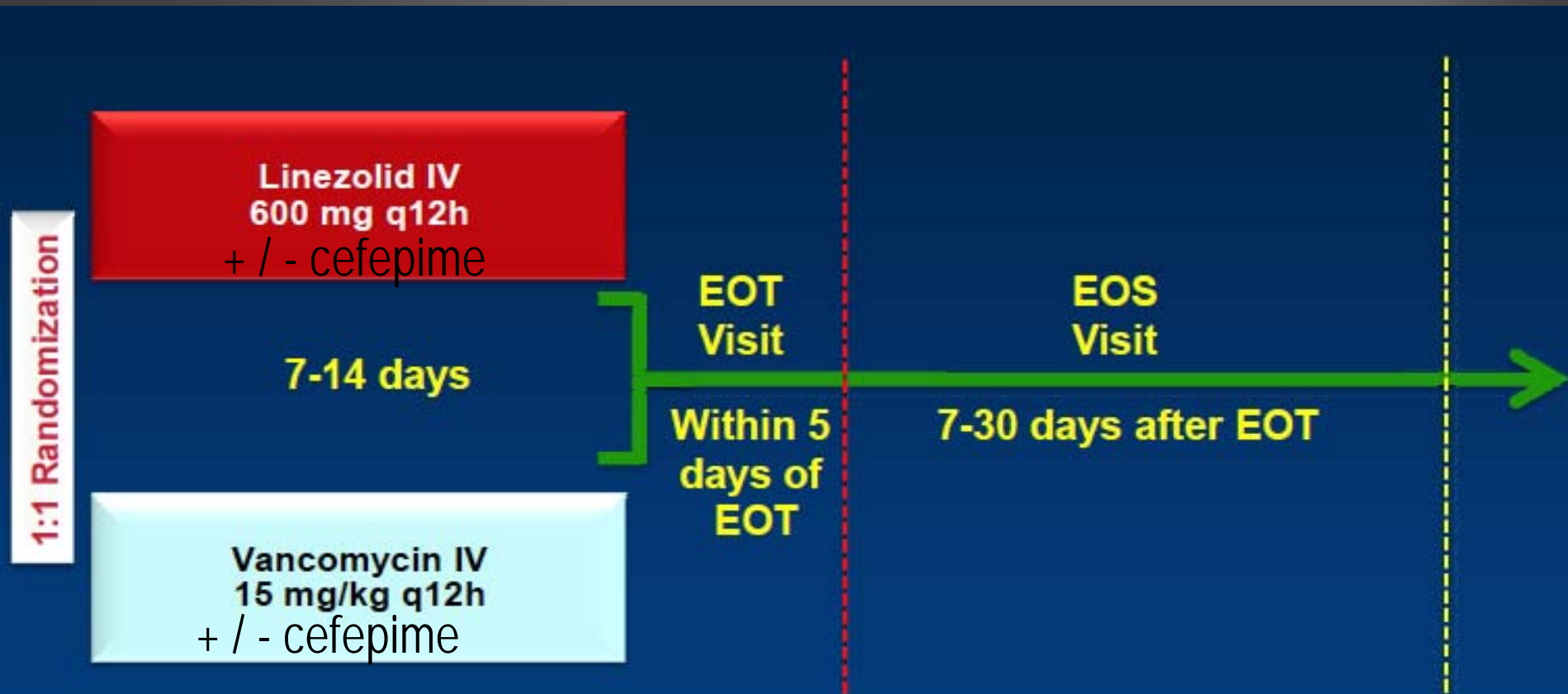
\* CIM  $\leq$  2 mg/L (80%, 1 mg/L)

Kunkel M. et al.

# Nosocomial Pneumonia With Suspected Or Proven Methicillin-Resistant *Staphylococcus aureus* (MRSA) (ZEPHYR)

IDSA 2010 (ClinicalTrials.gov identifier: NCT00084266)

Diseño: estudio aleatorizado y doble ciego





Kunkel M. et al.

**Nosocomial Pneumonia With Suspected Or Proven Methicillin-Resistant *Staphylococcus aureus* (MRSA) (ZEPHYR)**

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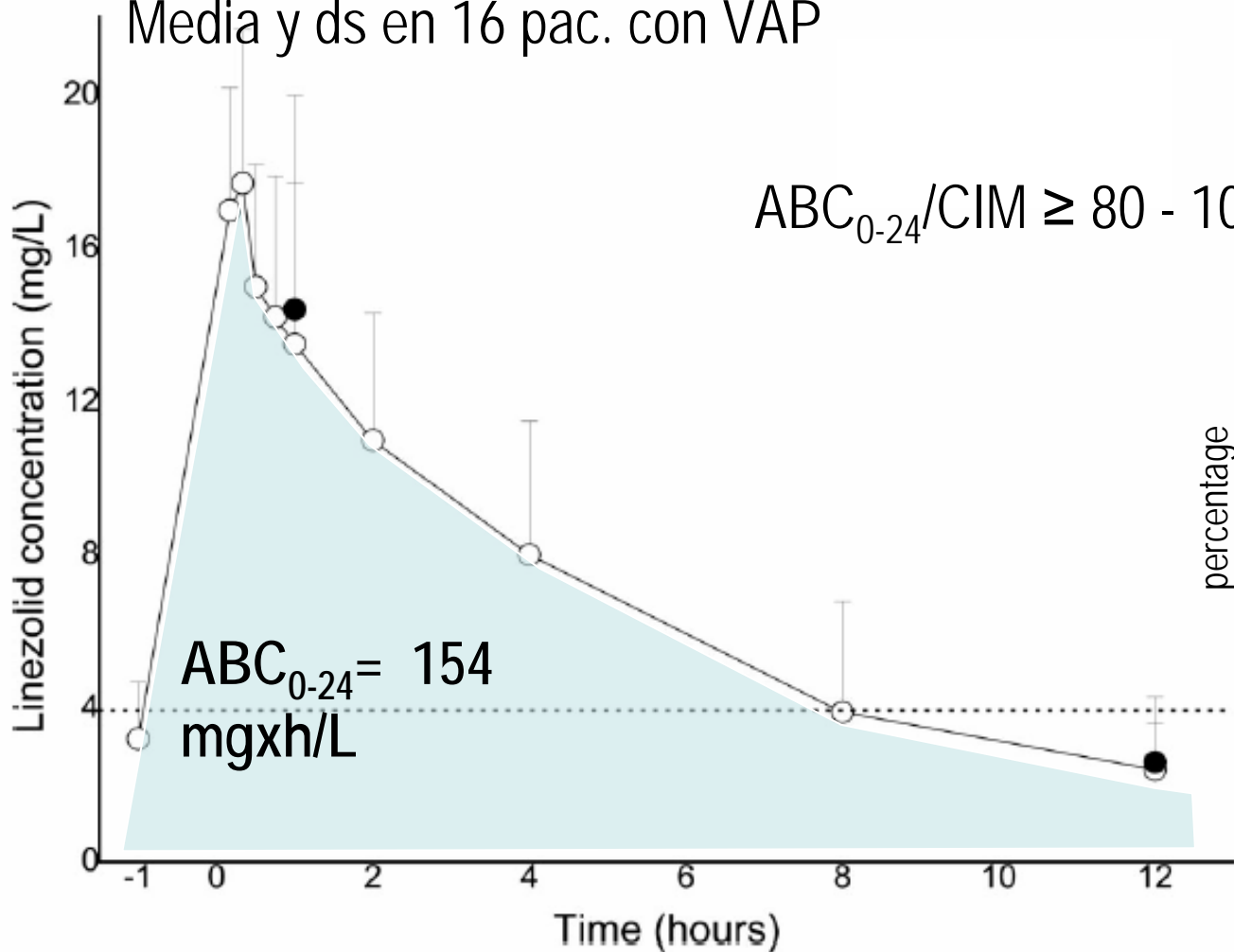
características	Linezolid n=172	Vancomicina n=176	P
Edad media	60.7	61.6	-
APACHE II	17.2	17.4	-
IOT+VM (%)	125 (68.3)	140 (74.5)	-
Curación PP EOS (30d)	95 (57.6)	81 (46.6)	0.04
Curación/mejoría PP EOT	150 (83.3)	130 (69.9)	0.002
Erradicación PP EOT	149 (81.9)	114 (60.6)	0.001
Anemia	30 (5.2)	42 (7.2)	-
Insuf. Renal	23 (3.8)	42 (7.8)	-
Trombocitopenia	8 (1.3)	13 (2.2)	-

Boselli E, et al

# Pharmacokinetics and intrapulmonary concentrations of linezolid administered to critically ill patients with VAP

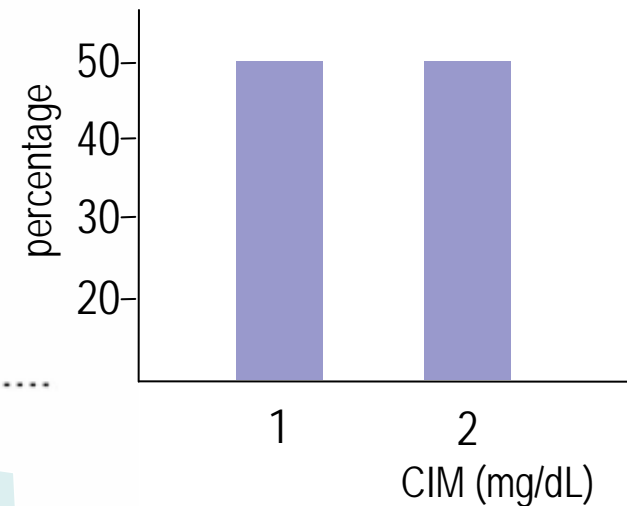
*Crit Care Med 2005; 33: 1529-33*

Media y ds en 16 pac. con VAP



$$154 / 1 = 154$$

$$154 / 2 = 77$$

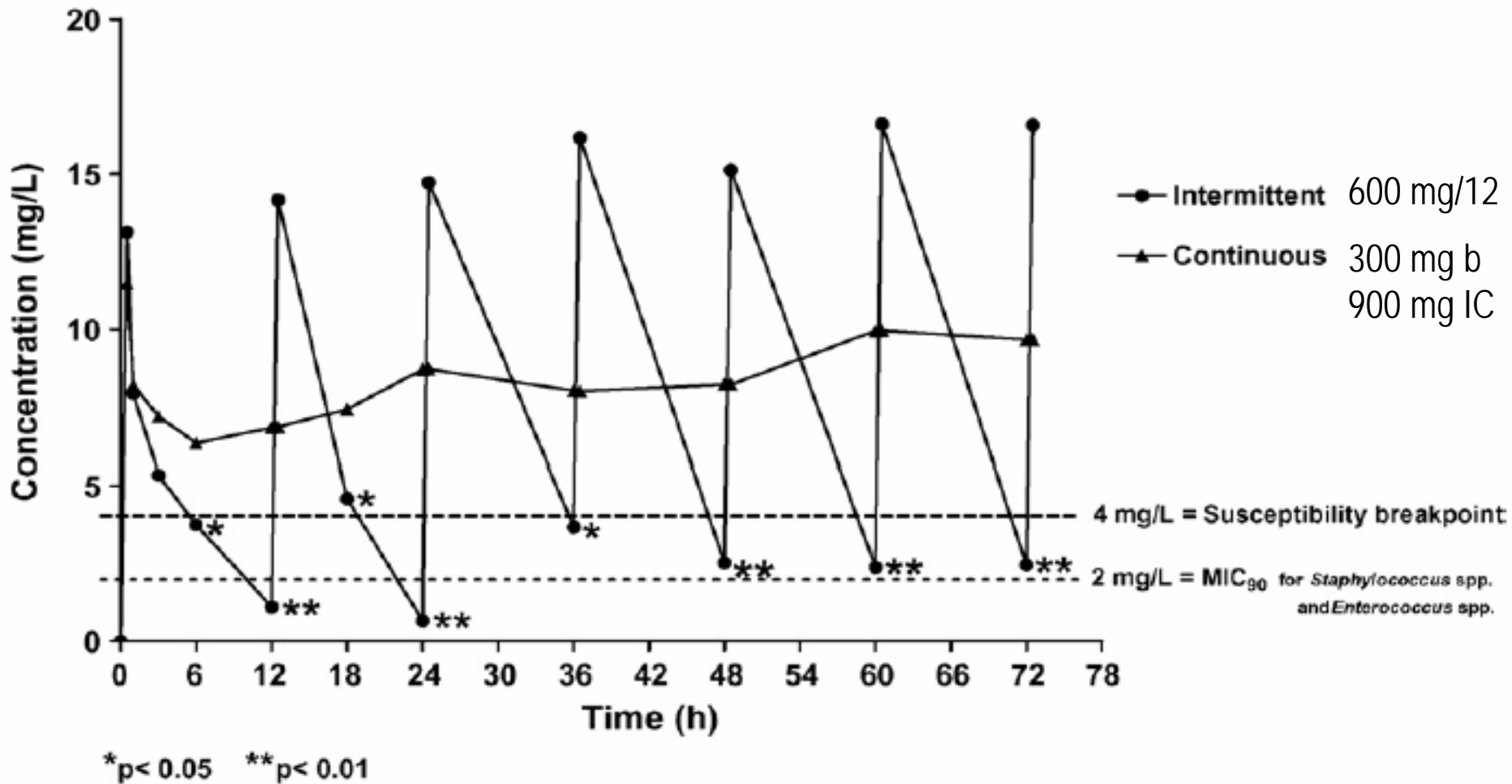


Picazo JJ. EIMC 2010

Chiara Adembri, et al

# Linezolid pharmacokinetic/pharmacodynamic profile in critically ill septic patients: intermittent versus continuous infusion

*Int J Antimicrob Agents* 2008; 31: 122-9



**Neumonía nosocomial**

**Bacteriemia / endocarditis**

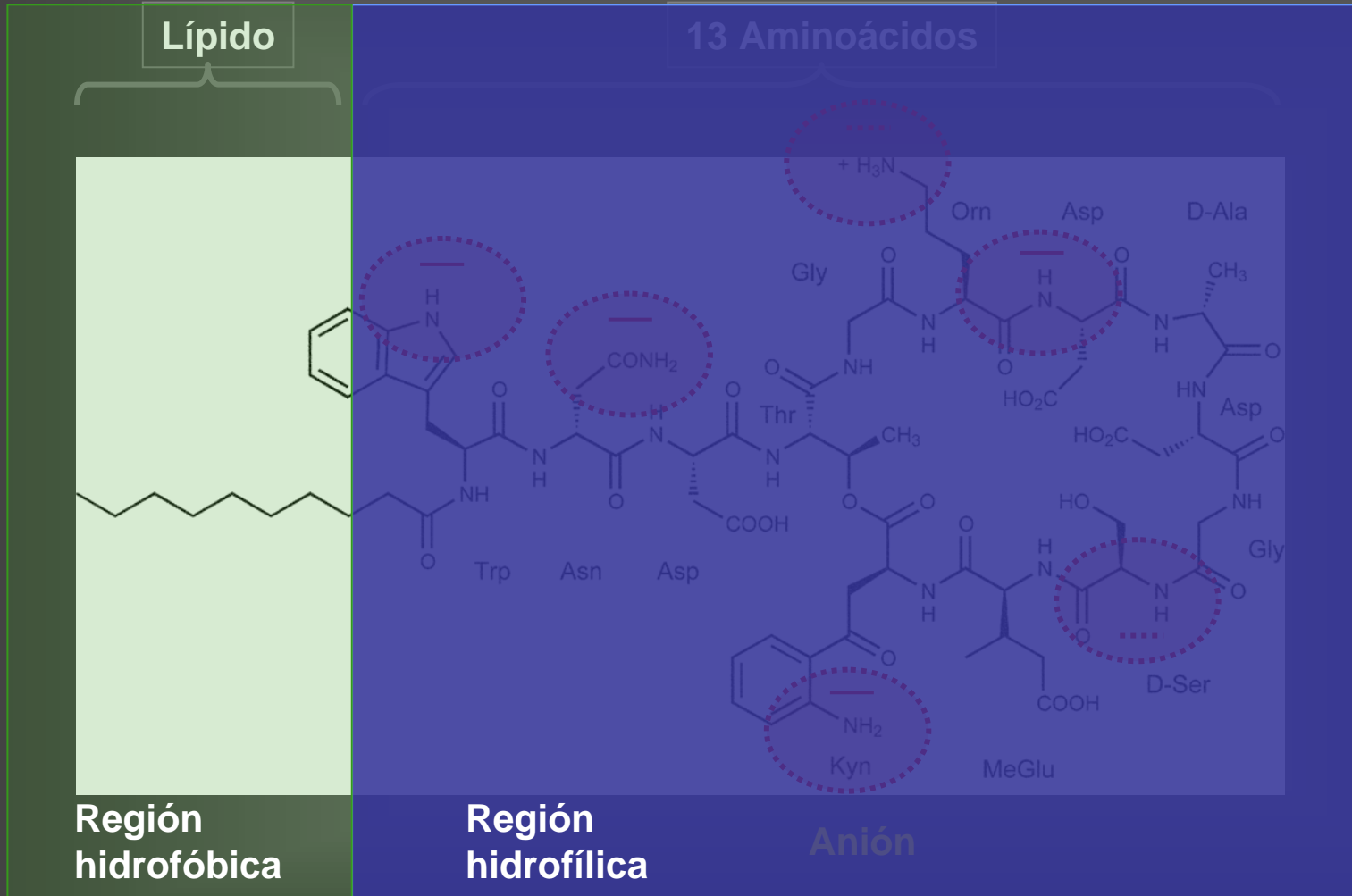
**Infecciones de piel y partes blandas**

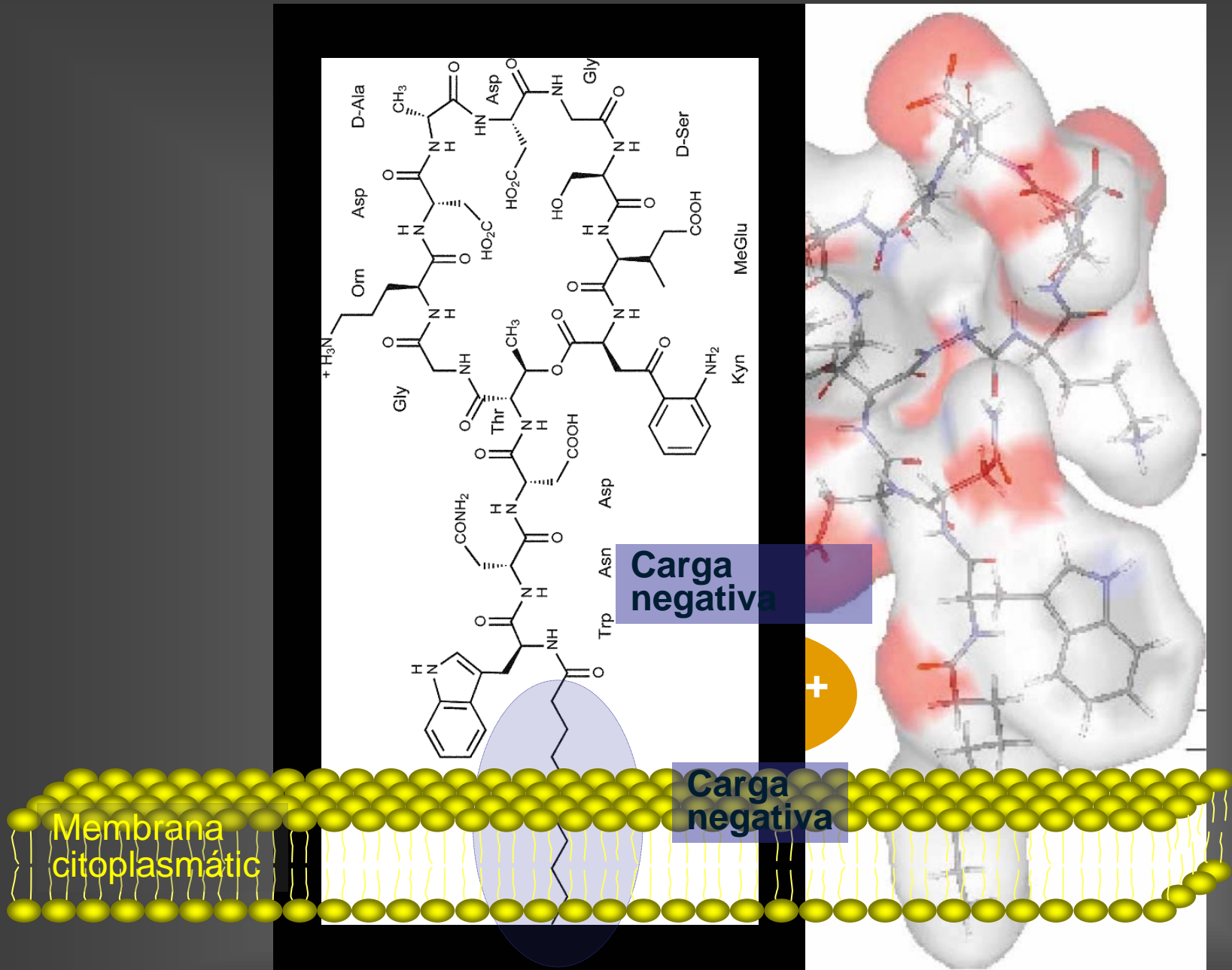
**Infección osteoarticular**

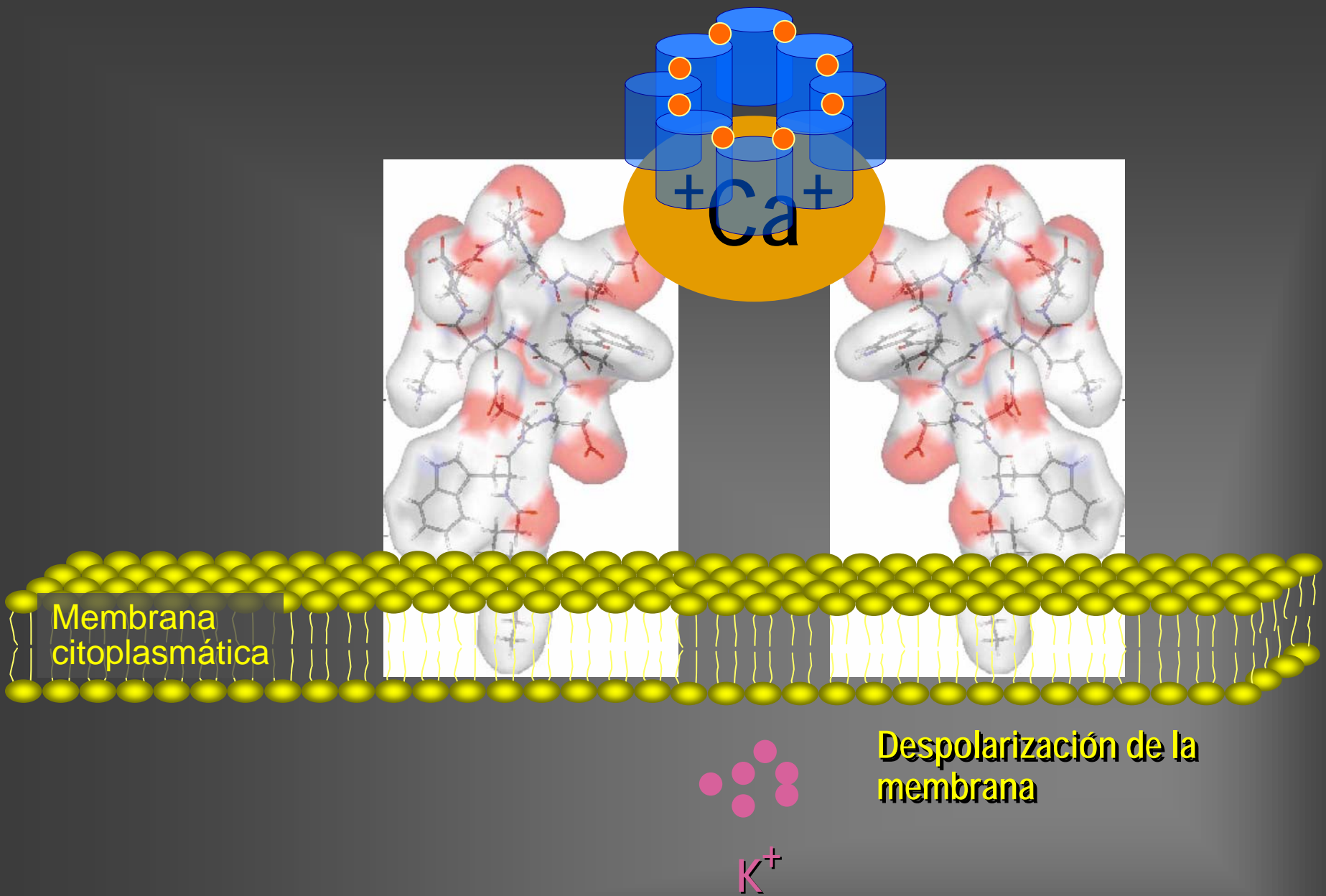
**Infecciones del SNC**

**Endoftalmitis**

# Daptomicina (lipopéptido)







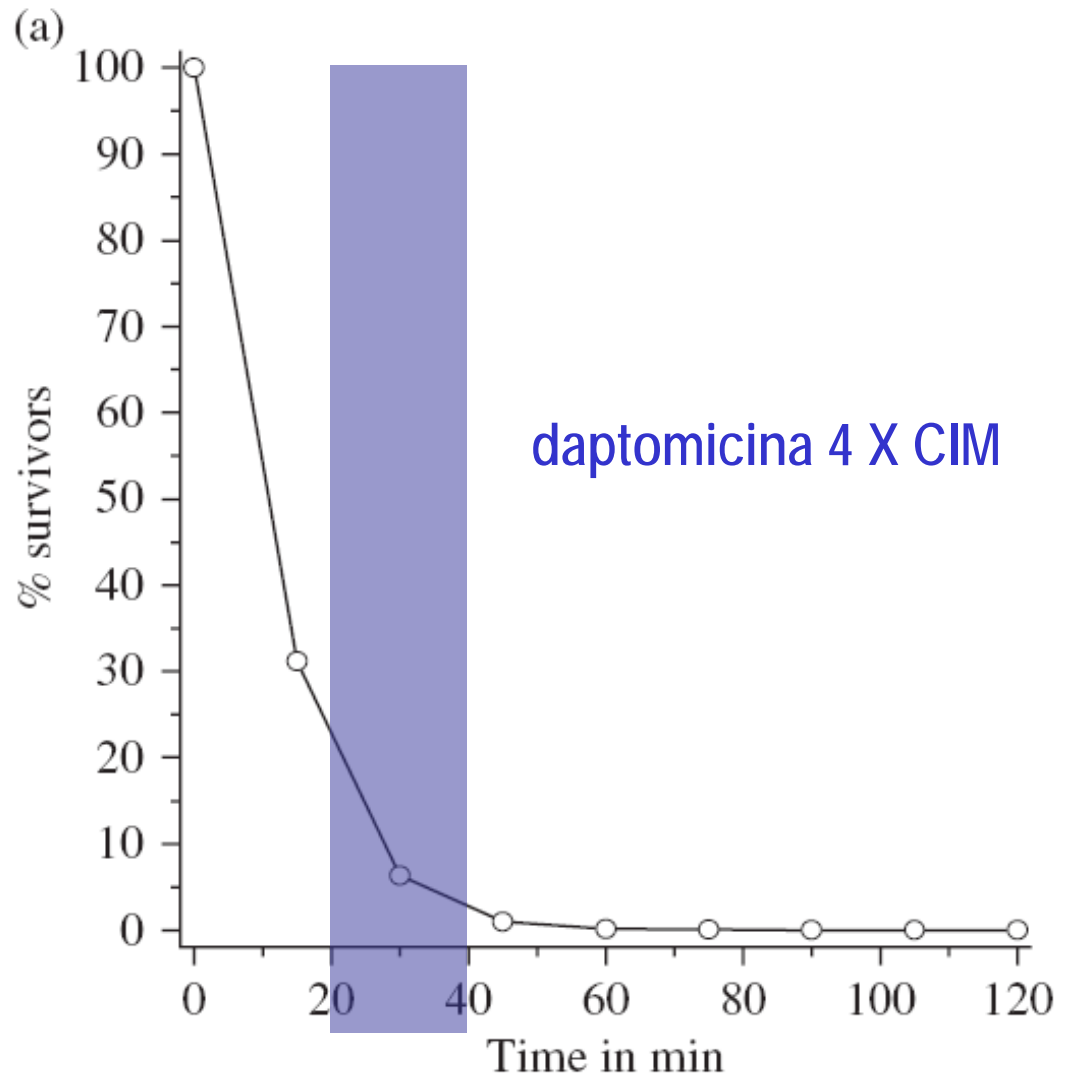
Straus SK, Hancock REW. *Biochim Biophys Acta* 2006;1758:1215–1223

Hobbs JK *et al.* *J Antimicrob Chemother* 2008;62:1003–1008

*Hobbs JK, Miller K, O'Neill A and Chopra I*

**Consequences of daptomycin-mediated membrane damage in *S. aureus***

*J Antimicrob Chemother*  
2008; 62: 1003–1008

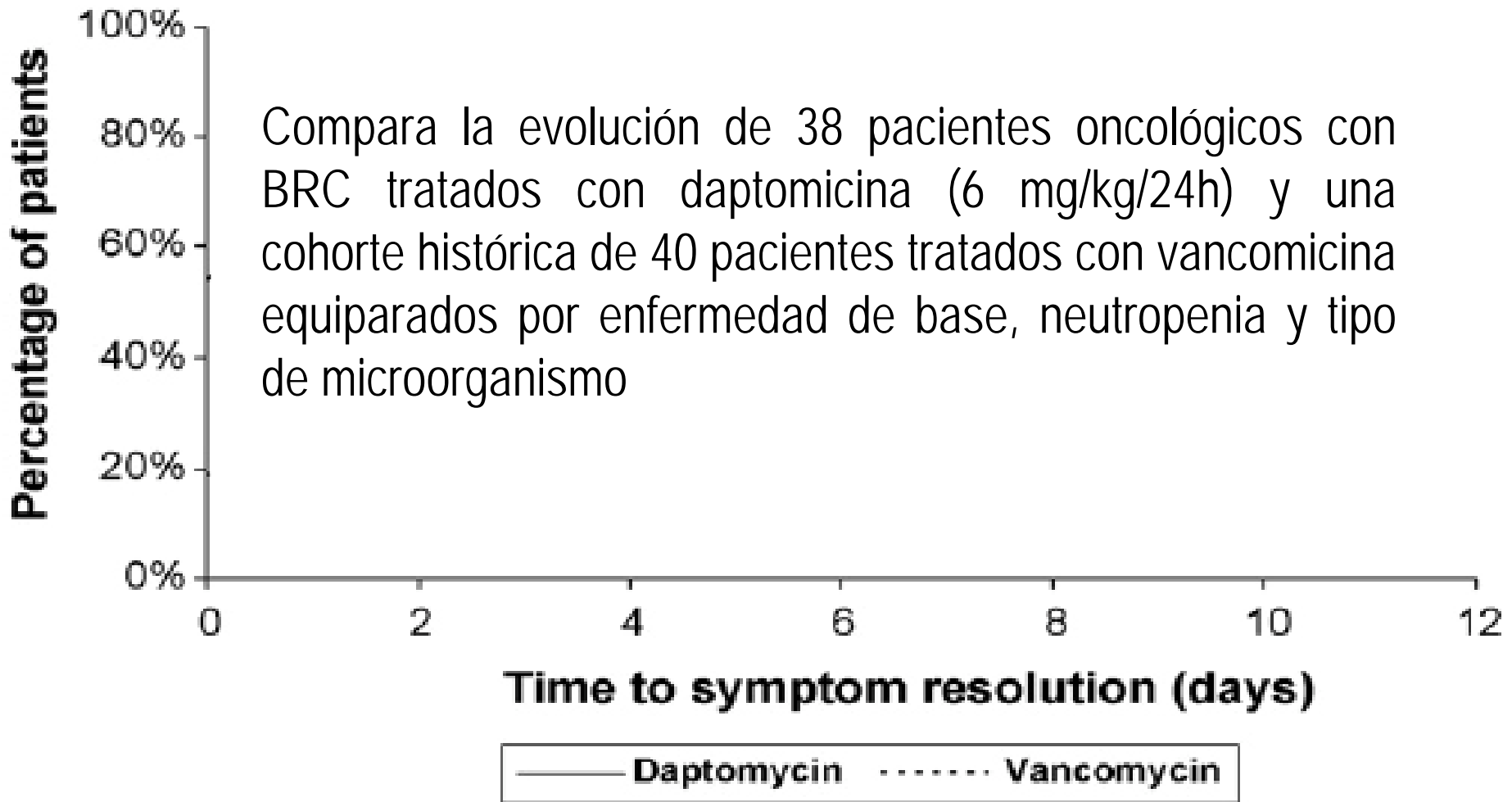




*Anne-Marie Chaftari, et al*

## **Efficacy and safety of daptomycin in the treatment of Gram-positive catheter-rel bloodstream infections in cancer patients**

*Int J Antimicrob Agents 2010; 36: 182-6*



*Anne-Marie Chaftari, et al*

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variables	Daptomicina (n=38)	vancomicina( $n_p=$ 40)	
Síntomas a las 48h	28 / 37 (76)	20 / 38 (53)	0.04
HC - a las 48h	29 / 37 (78)	11 / 32 (34)	<0.001
HC - a los 7 días	34 / 37 (92)	27 / 32 (84)	0.46
Respuesta global*	25 /37 (68)	11 /34 (32)	0.003

\* Curación clínica y microbiológica a las 72h, no recidiva, no complicación tardía y mortalidad relacionada a 30 días

# Daptomycin versus Standard Therapy for Bacteremia and Endocarditis Caused by *Staphylococcus aureus*

Vance G. Fowler, Jr., M.D., M.H.S., Helen W. Boucher, M.D., G. Ralph Corey, M.D., Elias Abrutyn, M.D., Adolf W. Karchmer, M.D., Mark E. Rupp, M.D., Donald P. Levine, M.D., Henry F. Chambers, M.D.,

*New Engl J Med 2006; 355: 363*

Criteria	Daptomycin	Standard Therapy	Absolute Difference in Success Rates
	no. of patients/total no. (%)		% (95% CI)*
Overall success (intention to treat)	53/124 (42.7)	48/122 (39.3)	3.4 (-8.9 to 15.7)
Final diagnosis: right-sided endocarditis plus complicated bacteremia			
Overall	34/79 (43.0)	30/77 (39.0)	4.1 (-11.3 to 19.5)
MSSA	20/49 (40.8)	21/48 (43.8)	-2.9 (-16.7 to 10.9)
MRSA	14/30 (46.7)	9/29 (31.0)	15.7 (-1.1 to 32.5)
Final diagnosis: uncomplicated bacteremia			
Overall	18/32 (56.2)	16/29 (55.2)	1.0 (-10.1 to 12.1)
MSSA	12/21 (57.1)	11/17 (64.7)	-7.6 (-38.6 to 23.5)
MRSA	6/10 (60.0)	5/11 (45.5)	14.5 (-27.7 to 56.8)

**2 g/4h**

— cloxacilina +  
— gentamicina

**daptomicina 6 mg/kg/24h**

*Matteo Bassetti, et al*

**High-dose daptomycin in documented  
*Staphylococcus aureus* infections**

*Int J Antimicrob Agents 2010; 36: 459-61*

Characteristic	≤ 6 mg/kg	> 6 mg/kg
Age (years) [median (10–90th percentile)]		
Gender male [n (%)]	14 (64)	24 (77)
Duration of hospitalisation (days) [median (10–90th percentile)]	15 (8.3–54.4)	23 (11–32)
APACHE II score [median (10–90th percentile)]	12 (7.3–22.4)	16 (9–21.8)
Underlying conditions [n (%)]		
Diabetes mellitus	3 (14)	5 (16)
Peripheral vascular disease	3 (14)	6 (19)
Immunocompromised	2 (9.1)	5 (16)
Neutropenia	1 (4.5)	3 (10)
Type of infection [n (%)]		
Uncomplicated BSI	10 (45)	7 (23)
Complicated BSI	3 (14)	8 (26)
cSSTI	3 (14)	5 (16)
Left-sided endocarditis	2 (9.1)	4 (13)
Right-sided endocarditis	2 (9.1)	5 (16)
Osteomyelitis	2 (9.1)	2 (6.5)
Type of <i>S. aureus</i> [n (%)]		
MRSA	19 (86)	27 (87)
MSSA	3 (14)	4 (13)
Duration of therapy (days) [median (10–90th percentile)]	13.5 (10–51.3)	19 (14–52.2)

**Éxito clínico**

**73%**

**94%**

**Éxito microbiológico**

**68%**

**93%**

*Kullar R, et al*

**High dose daptomycin for infective endocarditis**

*ECCMID 2010, Wien. Abstract 512*

characteristics      RS- endocarditis (n=23)      LS-endocarditis (n=20)

<u>Dosis (mg/kg/día)*</u>	9.7	9.9
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curación

<b>MRSA</b>	13 (81%)	9 (90%)
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<b>VRE</b>	1 (100)	3 (75)
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CPK > 150 UI/L **	13%	15%
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\* La dosis alta se mantuvo 8-12 días

\*\* En ningún caso fue necesario interrumpir el tratamiento

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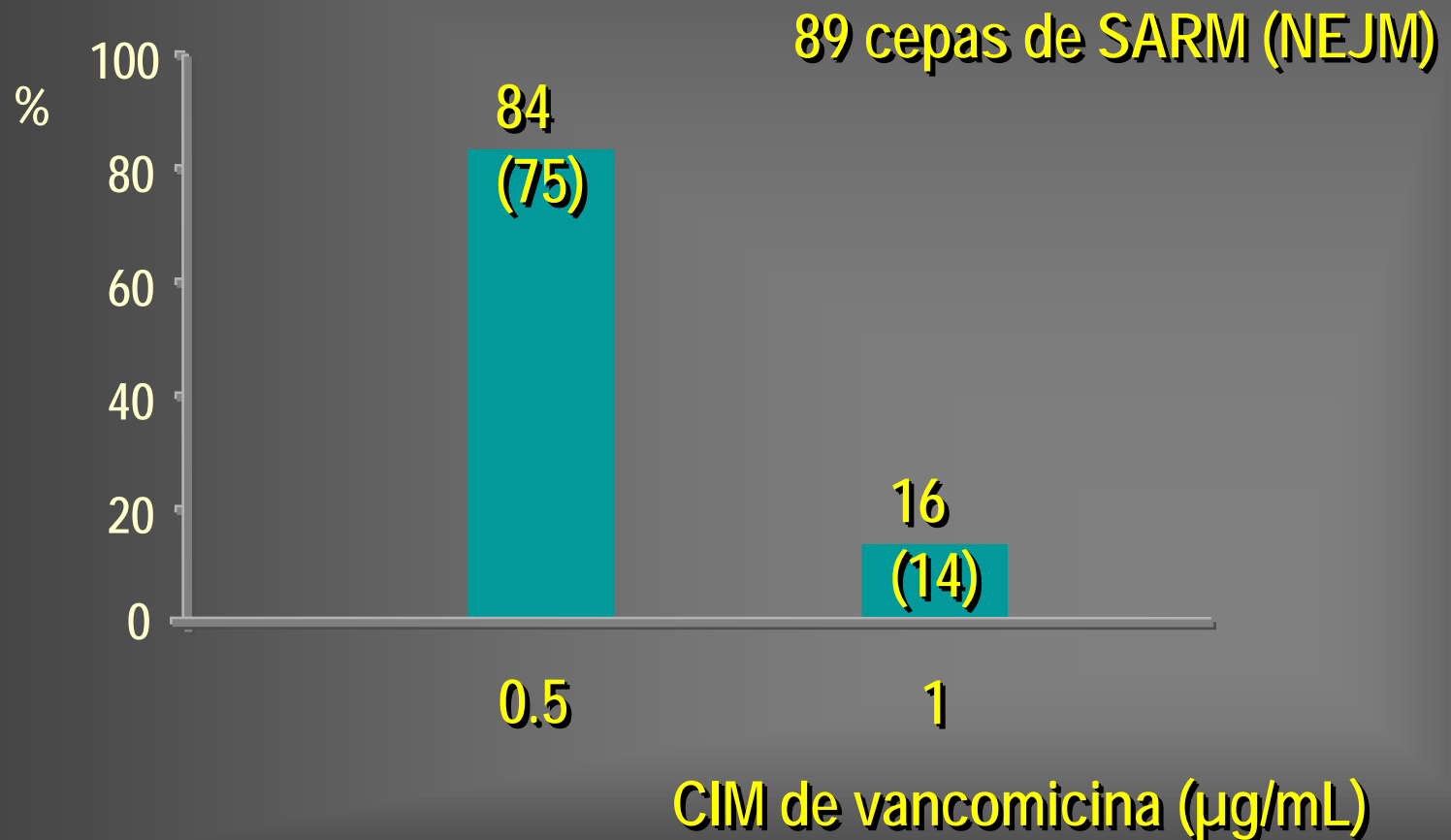
— vancomicina +  
— gentamicina

daptomicina 6 mg/kg/24h

*McCalla C et al.*

**Microbiological and genotypic analysis of methicillin-resistant *Staphylococcus aureus***

*Antimicrob Agents Chemother* 2008; 52: 3441-3443



*Kiyan PO, et al*

**Daptomycin versus vancomycin for MRSA bacteremia with reduced in vitro susceptibility to vancomycin\***

*ECCMID 2010, Wien. Abstract 514*

características	dapto (n=37)	vanco (n=74)	P
Edad (ds)	50 (13)	51 (15)	
APACHE II (ds)	14 (7)	14 (7)	
UCI	24%	21%	
Inmunosupresión	24%	7%	0.01
Vanco MIC=2 mg/L	54%	15%	0.01
Fracaso (%)	14%	28%	0.06
Mortalidad 30-d (%)	3%	16%	0.06

\* CIM > 1 mg/L



*Kiyan PO, et al*

**Daptomycin versus vancomycin for MRSA bacteremia with reduced in vitro susceptibility to vancomycin\***

*ECCMID 2010, Wien. Abstract 514*

foco	% de fracaso	
	dapto (n=37)	vanco (n=74)
Catéter	14	14
Piel y PB	14	17
Endocarditis	10	39
Cuerpo extraño	33	75
Otros	0	20

\* CIM > 1 mg/L