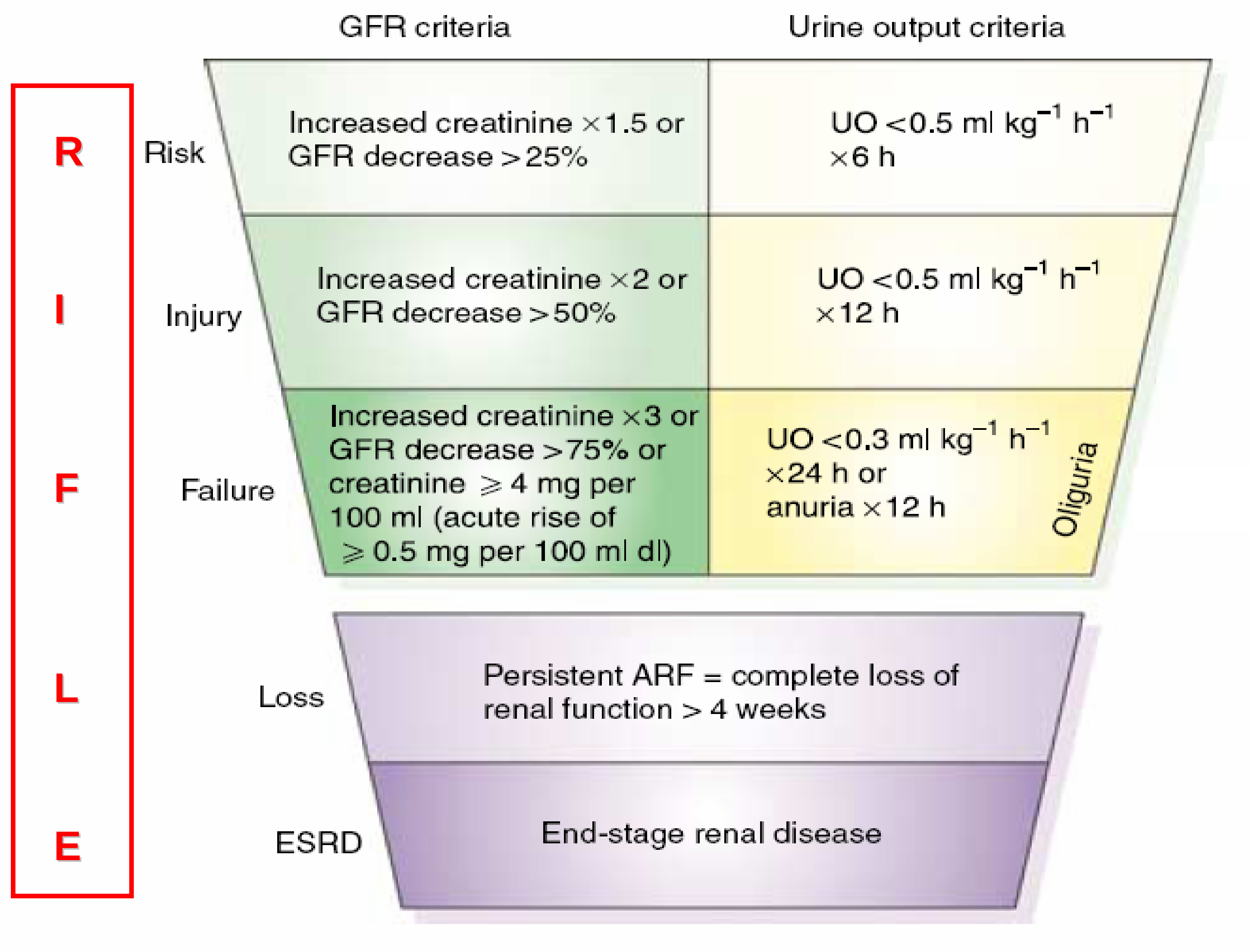
USO DE LOS ANTIBIOTICOS
EN PACIENTES CON DETERIORO RENAL

Manuel Landecho
Unidad de médicos hospitalistas-Área de hospitalización especial
Servicio de Medicina Interna
Clínica Universidad de Navarra

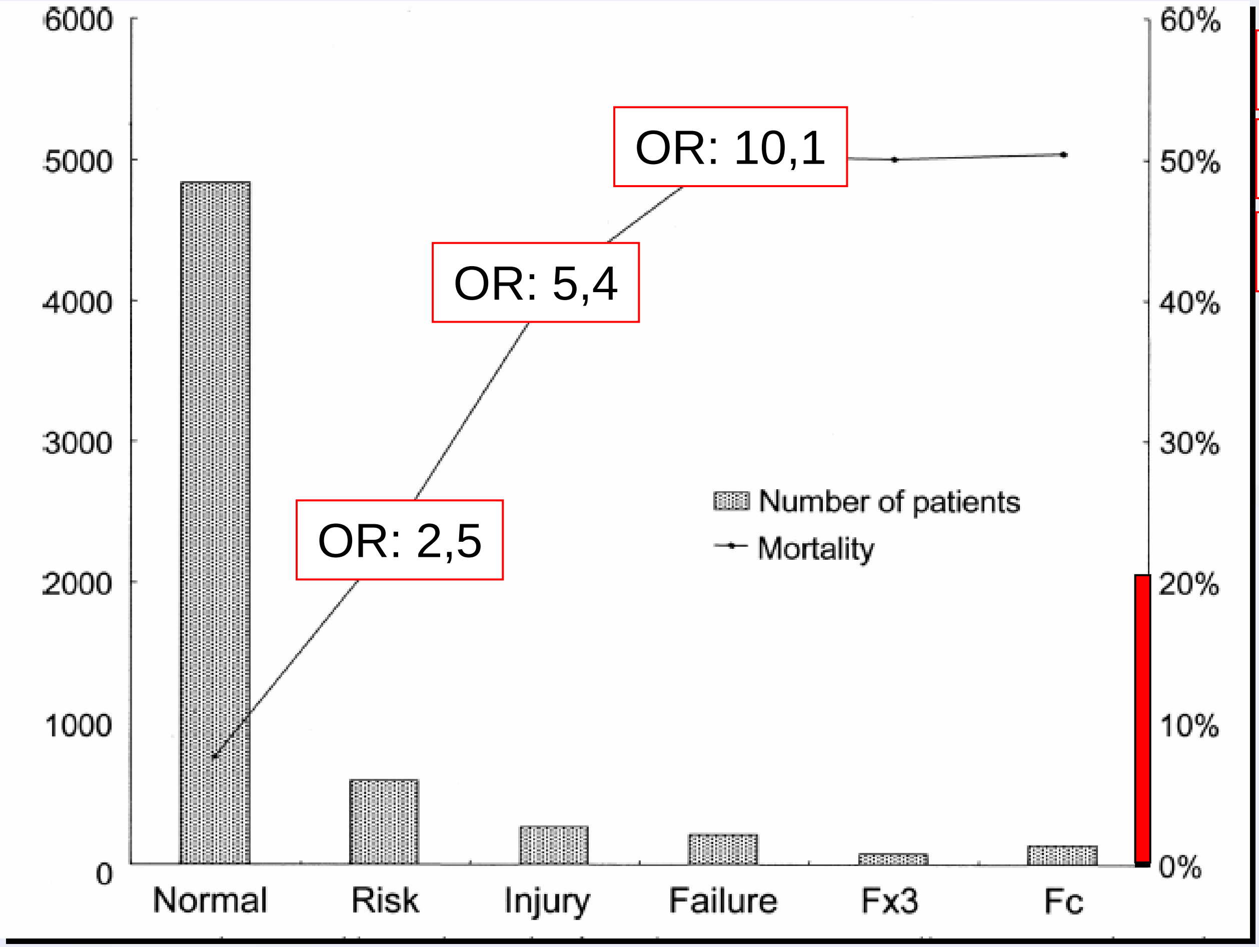
DEFINICIÓN DE DAÑO RENAL AGUDO: ESCALA RIFLE



		GFR criteria	Urine output criteria
R	Risk	Increased creatinine ×1.5 or GFR decrease >25%	UO <0.5 ml kg^{-1} h^{-1} ×6 h
I	Injury	Increased creatinine ×2 or GFR decrease >50%	UO <0.5 ml kg^{-1} h^{-1} ×12 h
F	Failure	Increased creatinine ×3 or GFR decrease >75% or creatinine ⩾ 4 mg per 100 ml (acute rise of ⩾ 0.5 mg per 100 ml dl)	UO <0.3 ml kg^{-1} h^{-1} ×24 h or anuria ×12 h Oliguria
L	Loss	Persistent ARF = complete loss of renal function > 4 weeks	
E	ESRD	End-stage renal disease	

Critical Care 2004, 8:R204-R212

ESCALA RIFLE PREDICE MORTALIDAD INTRAHOSPITALARIA



OR: 10,1

OR: 5,4

OR: 2,5

R: 2,5(2,15-2,98)

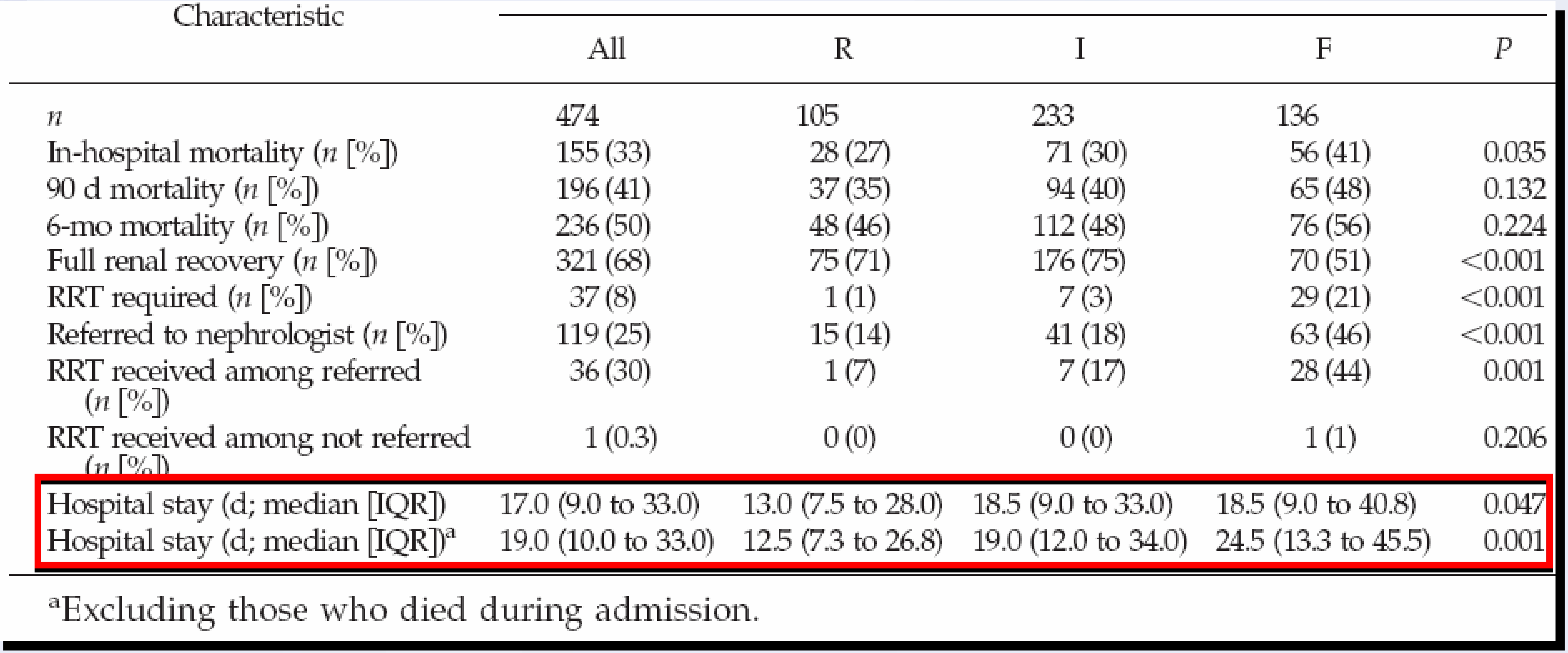
I: 5,4(4,54-6,47)

F: 10,1(8,32-12,32)

prevalencia acumulada próxima al 20%

Crit Care Med 2006 Vol. 34, No. 7

ESCALA RIFLE PREDICE INGRESOS PROLONGADOS

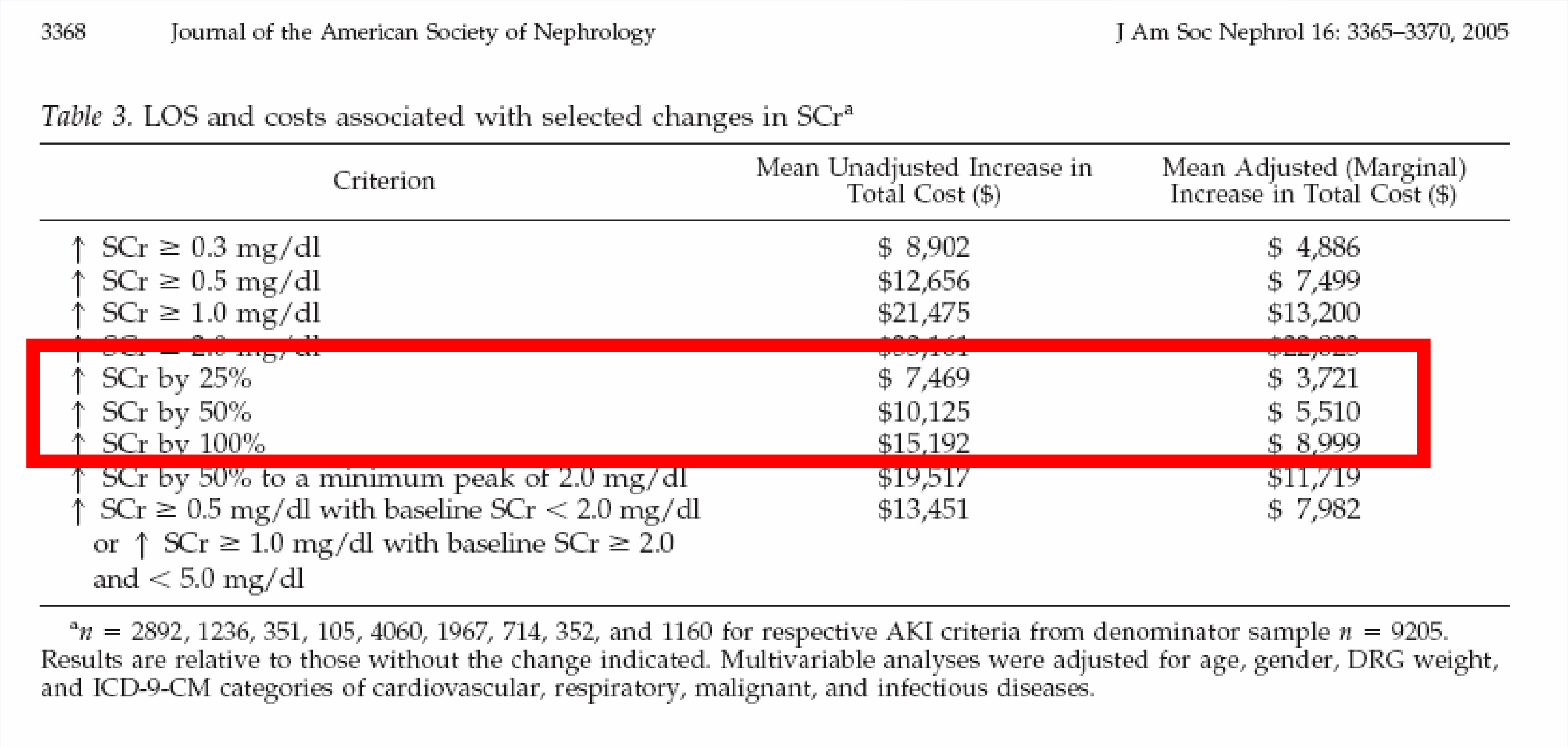


Characteristic	All	R	I	F	*P*
n	474	105	233	136	
In-hospital mortality (*n* [%])	155 (33)	28 (27)	71 (30)	56 (41)	0.035
90 d mortality (*n* [%])	196 (41)	37 (35)	94 (40)	65 (48)	0.132
6-mo mortality (*n* [%])	236 (50)	48 (46)	112 (48)	76 (56)	0.224
Full renal recovery (*n* [%])	321 (68)	75 (71)	176 (75)	70 (51)	<0.001
RRT required (*n* [%])	37 (8)	1 (1)	7 (3)	29 (21)	<0.001
Referred to nephrologist (*n* [%])	119 (25)	15 (14)	41 (18)	63 (46)	<0.001
RRT received among referred (*n* [%])	36 (30)	1 (7)	7 (17)	28 (44)	0.001
RRT received among not referred (*n* [%])	1 (0.3)	0 (0)	0 (0)	1 (1)	0.206
Hospital stay (d; median [IQR])	17.0 (9.0 to 33.0)	13.0 (7.5 to 28.0)	18.5 (9.0 to 33.0)	18.5 (9.0 to 40.8)	0.047
Hospital stay (d; median [IQR])[a]	19.0 (10.0 to 33.0)	12.5 (7.3 to 26.8)	19.0 (12.0 to 34.0)	24.5 (13.3 to 45.5)	0.001

[a] Excluding those who died during admission.

J Am Soc Nephrol 18: 1292–1298, 2007.

FRA PREDICE INCREMENTO DE COSTES



3368 Journal of the American Society of Nephrology J Am Soc Nephrol 16: 3365–3370, 2005

Table 3. LOS and costs associated with selected changes in SCr[a]

Criterion	Mean Unadjusted Increase in Total Cost ($)	Mean Adjusted (Marginal) Increase in Total Cost ($)
↑ SCr ≥ 0.3 mg/dl	$ 8,902	$ 4,886
↑ SCr ≥ 0.5 mg/dl	$12,656	$ 7,499
↑ SCr ≥ 1.0 mg/dl	$21,475	$13,200
↑ SCr ≥ 2.0 mg/dl	$33,161	$22,023
↑ SCr by 25%	$ 7,469	$ 3,721
↑ SCr by 50%	$10,125	$ 5,510
↑ SCr by 100%	$15,192	$ 8,999
↑ SCr by 50% to a minimum peak of 2.0 mg/dl	$19,517	$11,719
↑ SCr ≥ 0.5 mg/dl with baseline SCr < 2.0 mg/dl or ↑ SCr ≥ 1.0 mg/dl with baseline SCr ≥ 2.0 and < 5.0 mg/dl	$13,451	$ 7,982

[a] n = 2892, 1236, 351, 105, 4060, 1967, 714, 352, and 1160 for respective AKI criteria from denominator sample n = 9205. Results are relative to those without the change indicated. Multivariable analyses were adjusted for age, gender, DRG weight, and ICD-9-CM categories of cardiovascular, respiratory, malignant, and infectious diseases.

J Am Soc Nephrol 16: 3365–3370, 2005.

¿HAY MANERA DE PREDECIR EL DESARROLLO DE FRA?
ANTECEDENTES PERSONALES (1)

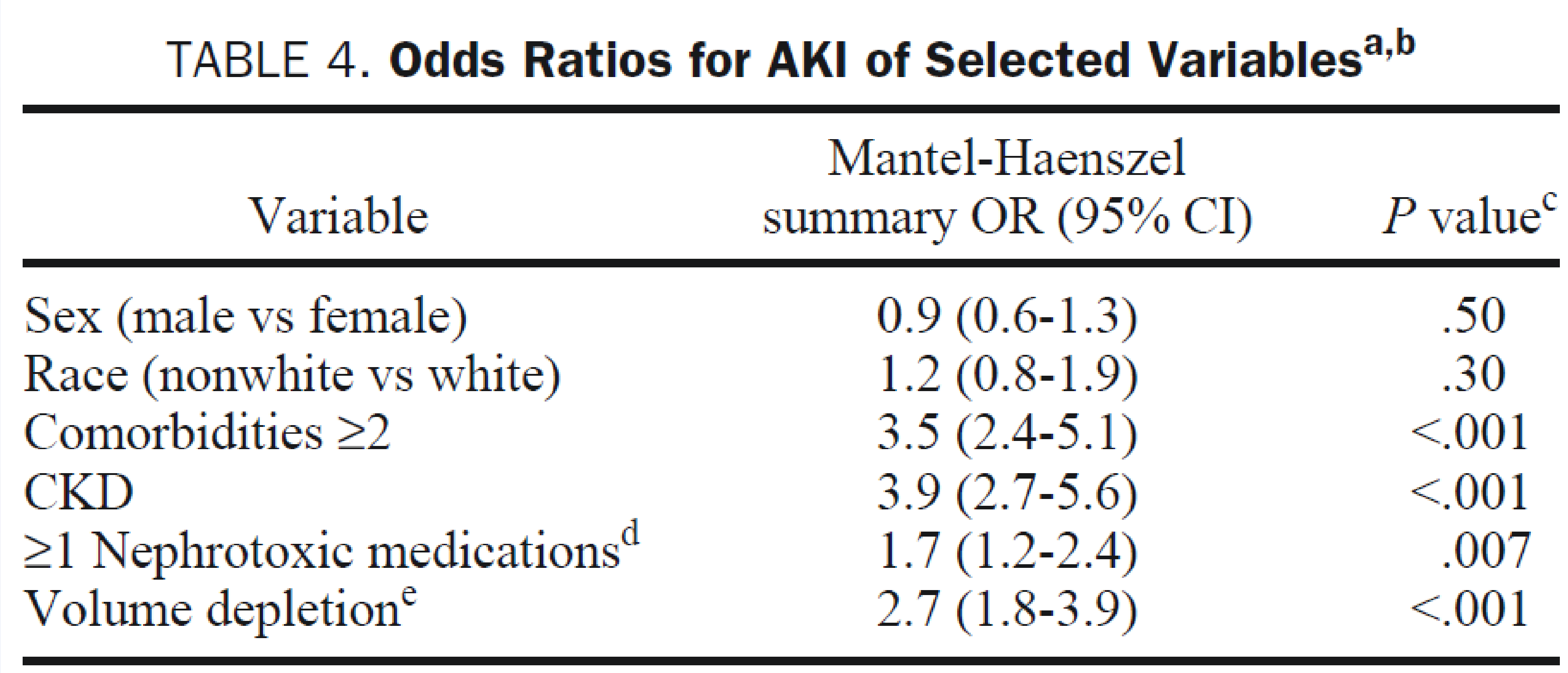
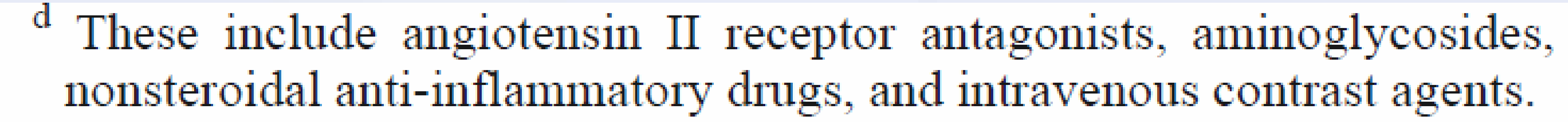


TABLE 4. **Odds Ratios for AKI of Selected Variables**[a,b]

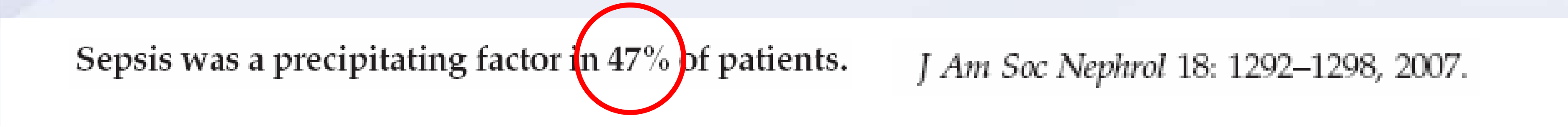
Variable	Mantel-Haenszel summary OR (95% CI)	*P* value[c]
Sex (male vs female)	0.9 (0.6-1.3)	.50
Race (nonwhite vs white)	1.2 (0.8-1.9)	.30
Comorbidities ≥2	3.5 (2.4-5.1)	<.001
CKD	3.9 (2.7-5.6)	<.001
≥1 Nephrotoxic medications[d]	1.7 (1.2-2.4)	.007
Volume depletion[e]	2.7 (1.8-3.9)	<.001



[d] These include angiotensin II receptor antagonists, aminoglycosides, nonsteroidal anti-inflammatory drugs, and intravenous contrast agents.

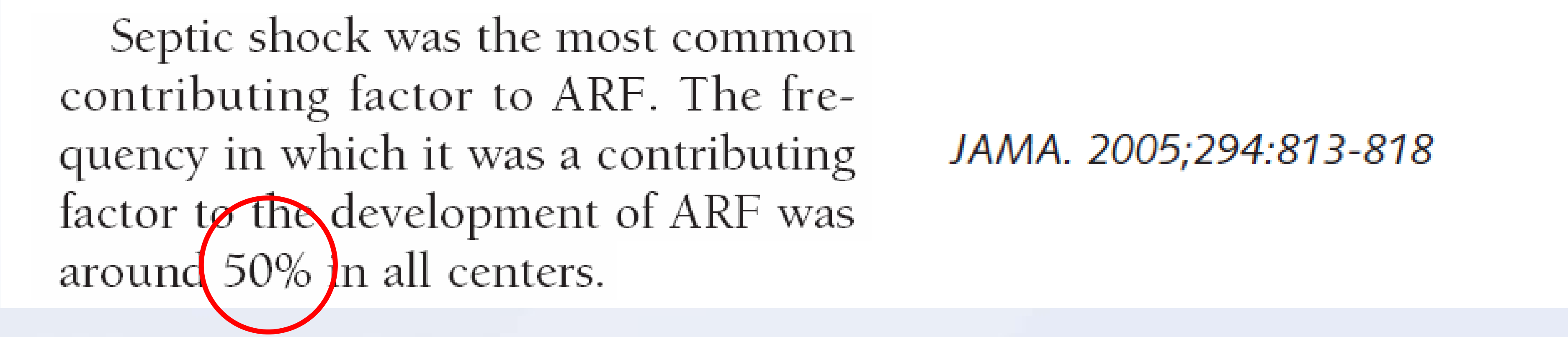
Mayo Clin Proc. 2009;84(5):410-416

¿HAY MANERA DE PREDECIR EL DESARROLLO DE FRA?
MOTIVOS DE INGRESO



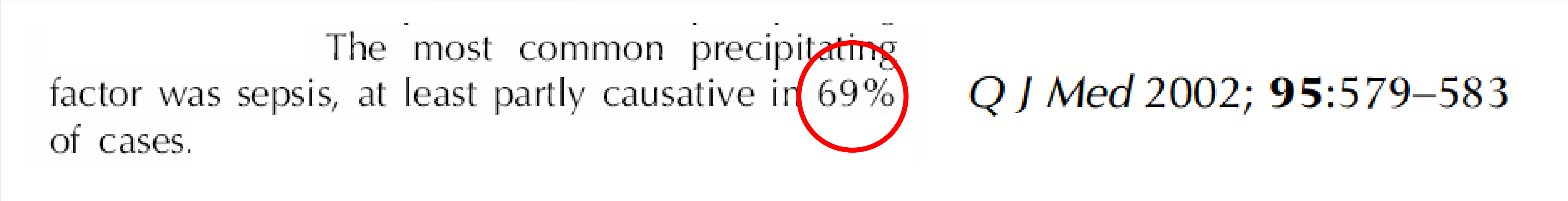
Sepsis was a precipitating factor in 47% of patients.

J Am Soc Nephrol 18: 1292–1298, 2007.



Septic shock was the most common contributing factor to ARF. The frequency in which it was a contributing factor to the development of ARF was around 50% in all centers.

JAMA. 2005;294:813-818



The most common precipitating factor was sepsis, at least partly causative in 69% of cases.

Q J Med 2002; **95**:579–583

¿Y QUÉ HAY QUE HACER?

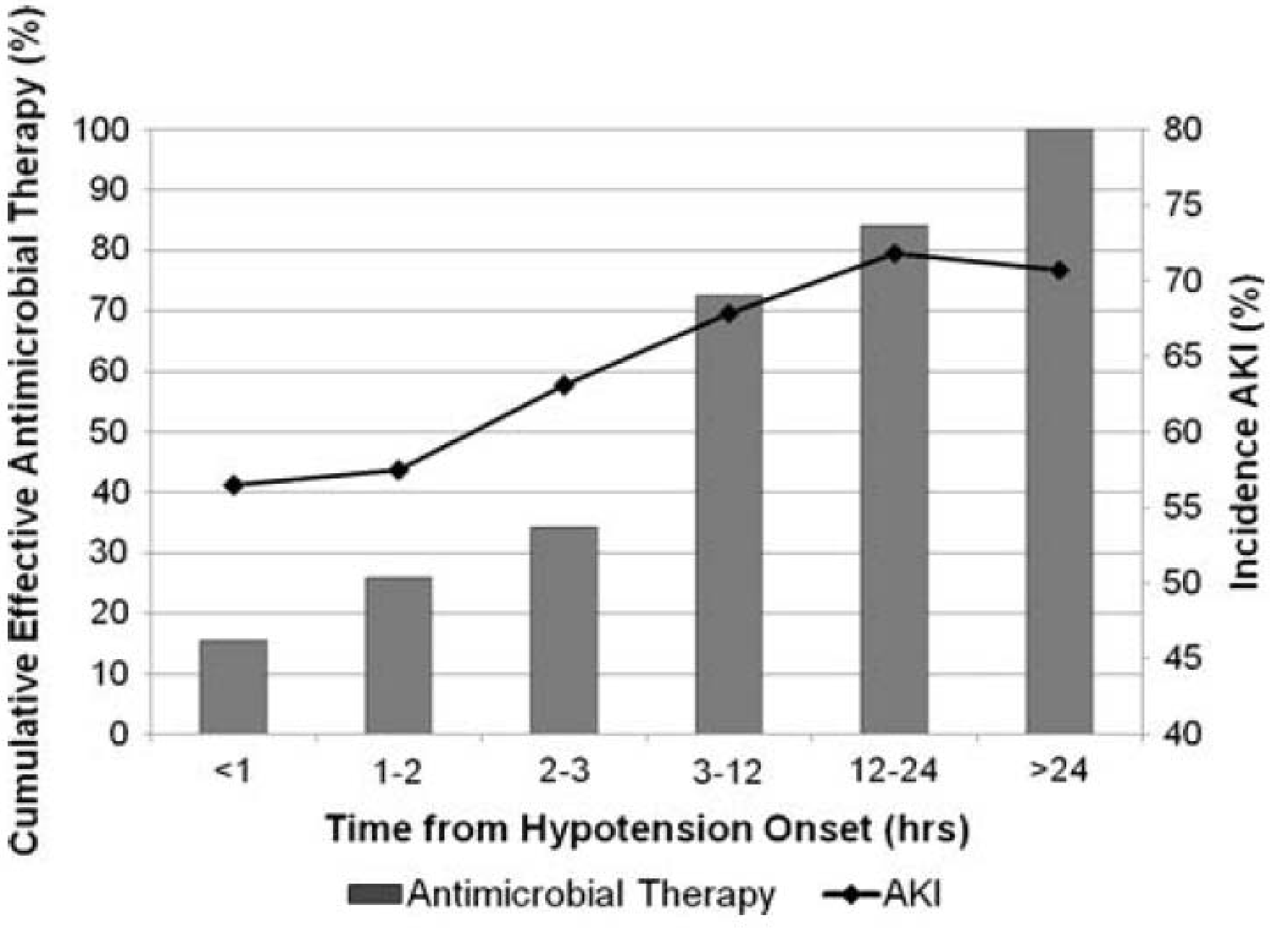


Fig. 2 Cumulative effective antimicrobial therapy following onset of hypotension and associated incidence of AKI

Intensive Care Med (2009) 35:871–881

¿QUÉ ALTERNATIVAS HAY?

- PENICILINAS
- QUINOLONAS
- MACRÓLIDOS
- AMINOGLUCÓSIDOS

- GLUCOPÉPTIDOS
- DAPTOMICINA
- TIGECICLINA
- LINEZOLID

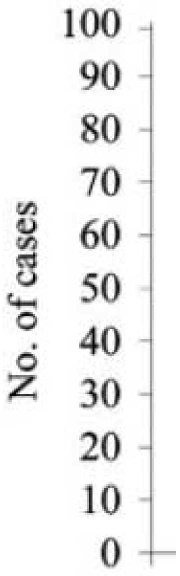
PENICILINAS/ QUINOLONAS/ MACRÓLIDOS

- Limitado por el perfil de sensibilidades frente a algunos G+ habituales (SARM, *Staph. coagulasa negativos, Enterococos*)

- Mantienen actividad frente a G- habituales (*Pseudomonas, E.coli* …)

- En general poco nefrotóxicas.

VANCOMICINA (1): ¿es eficaz?



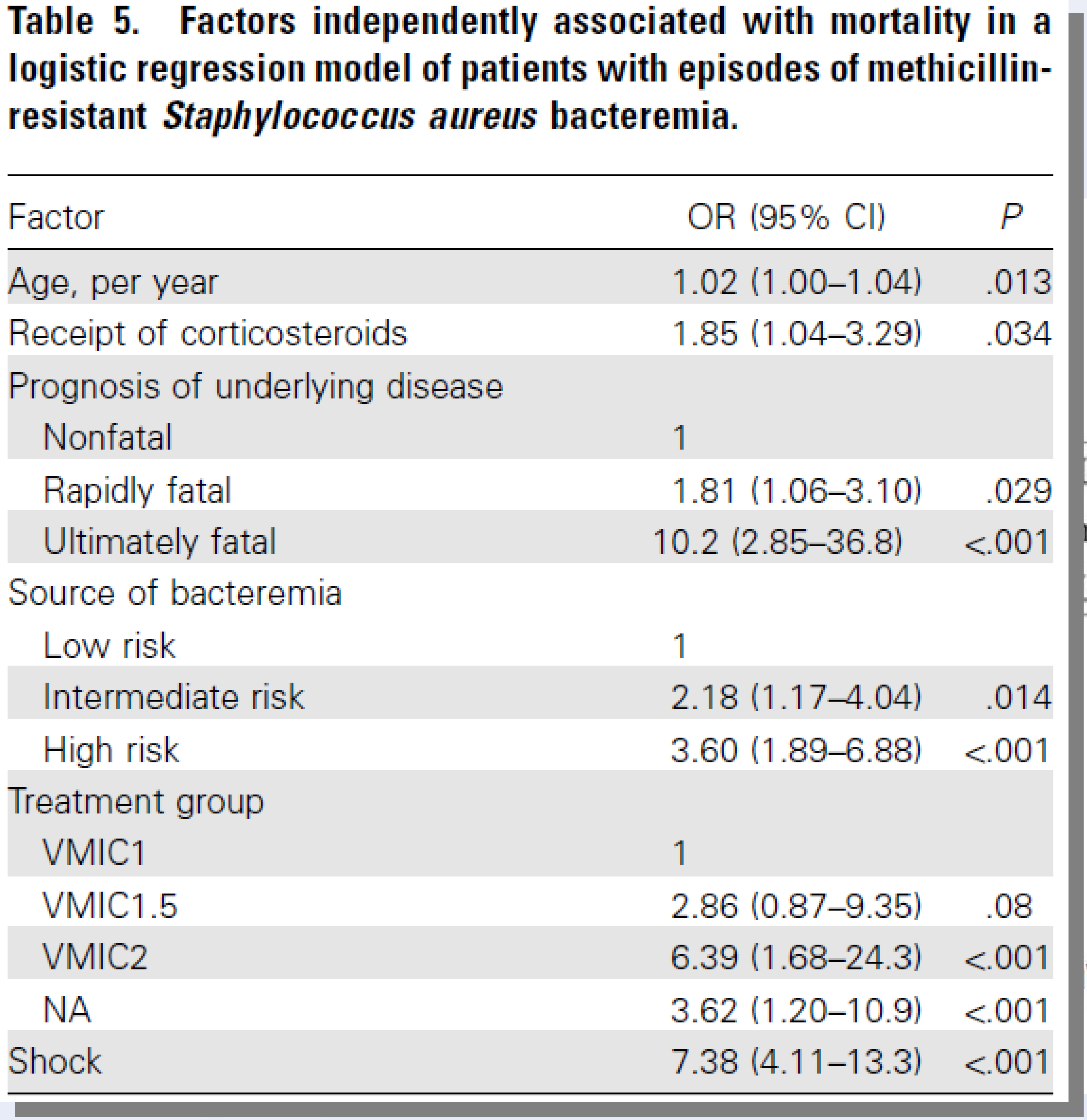


Table 5. Factors independently associated with mortality in a logistic regression model of patients with episodes of methicillin-resistant *Staphylococcus aureus* bacteremia.

Factor	OR (95% CI)	*P*
Age, per year	1.02 (1.00–1.04)	.013
Receipt of corticosteroids	1.85 (1.04–3.29)	.034
Prognosis of underlying disease		
Nonfatal	1	
Rapidly fatal	1.81 (1.06–3.10)	.029
Ultimately fatal	10.2 (2.85–36.8)	<.001
Source of bacteremia		
Low risk	1	
Intermediate risk	2.18 (1.17–4.04)	.014
High risk	3.60 (1.89–6.88)	<.001
Treatment group		
VMIC1	1	
VMIC1.5	2.86 (0.87–9.35)	.08
VMIC2	6.39 (1.68–24.3)	<.001
NA	3.62 (1.20–10.9)	<.001
Shock	7.38 (4.11–13.3)	<.001

Figure 1 ycin
MIC of th

Clinical Infectious Diseases 2008;46:193–200

VANCOMICINA (2): ¿es segura?

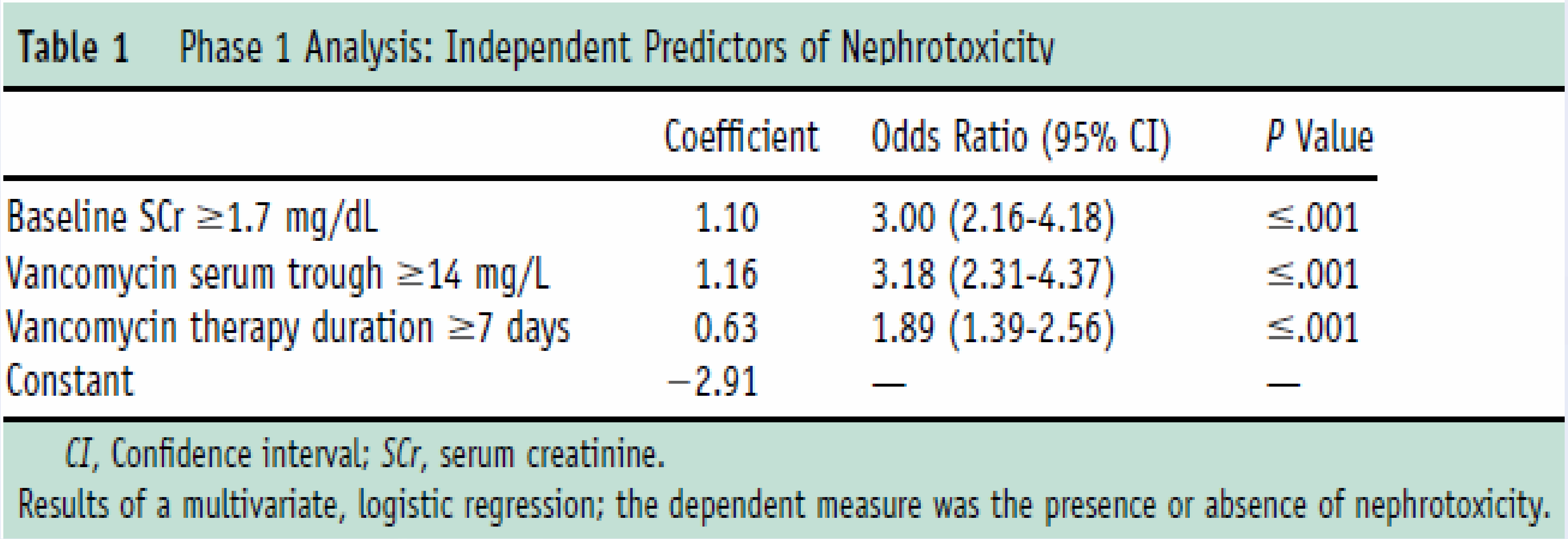


Table 1 Phase 1 Analysis: Independent Predictors of Nephrotoxicity

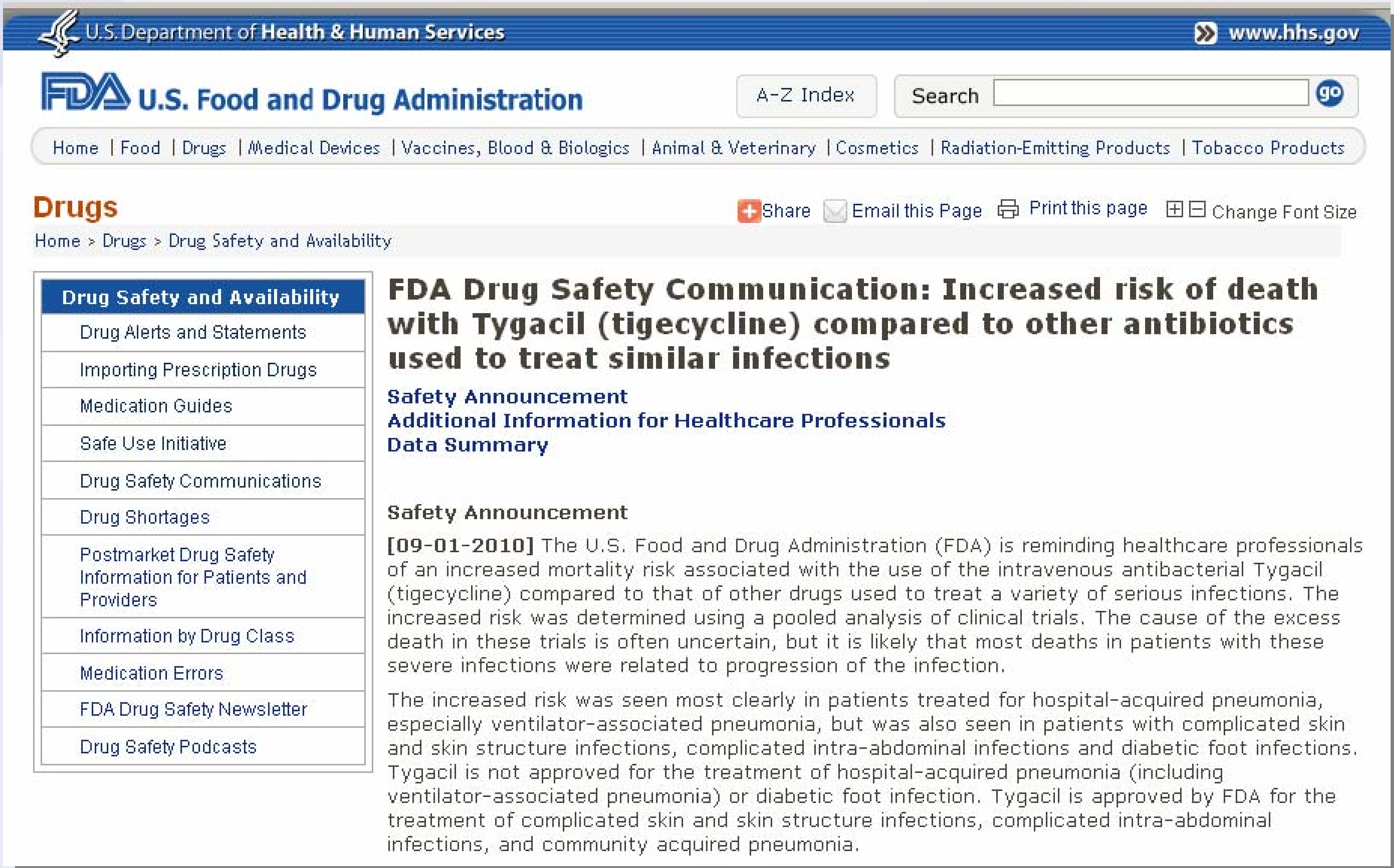
	Coefficient	Odds Ratio (95% CI)	*P* Value
Baseline SCr ≥1.7 mg/dL	1.10	3.00 (2.16-4.18)	≤.001
Vancomycin serum trough ≥14 mg/L	1.16	3.18 (2.31-4.37)	≤.001
Vancomycin therapy duration ≥7 days	0.63	1.89 (1.39-2.56)	≤.001
Constant	−2.91	—	—

CI, Confidence interval; *SCr*, serum creatinine.

Results of a multivariate, logistic regression; the dependent measure was the presence or absence of nephrotoxicity.

Adaptado de: The American Journal of Medicine, Vol 123, No 12, December 2010

TIGECICLINA: ¿es eficaz?


U.S. Department of Health & Human Services
www.hhs.gov
FDA U.S. Food and Drug Administration
A-Z Index
Search
go
Home | Food | Drugs | Medical Devices | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Radiation-Emitting Products | Tobacco Products
Drugs
Share
Email this Page
Print this page
Change Font Size
Home > Drugs > Drug Safety and Availability
Drug Safety and Availability
Drug Alerts and Statements
Importing Prescription Drugs
Medication Guides
Safe Use Initiative
Drug Safety Communications
Drug Shortages
Postmarket Drug Safety Information for Patients and Providers
Information by Drug Class
Medication Errors
FDA Drug Safety Newsletter
Drug Safety Podcasts

FDA Drug Safety Communication: Increased risk of death with Tygacil (tigecycline) compared to other antibiotics used to treat similar infections

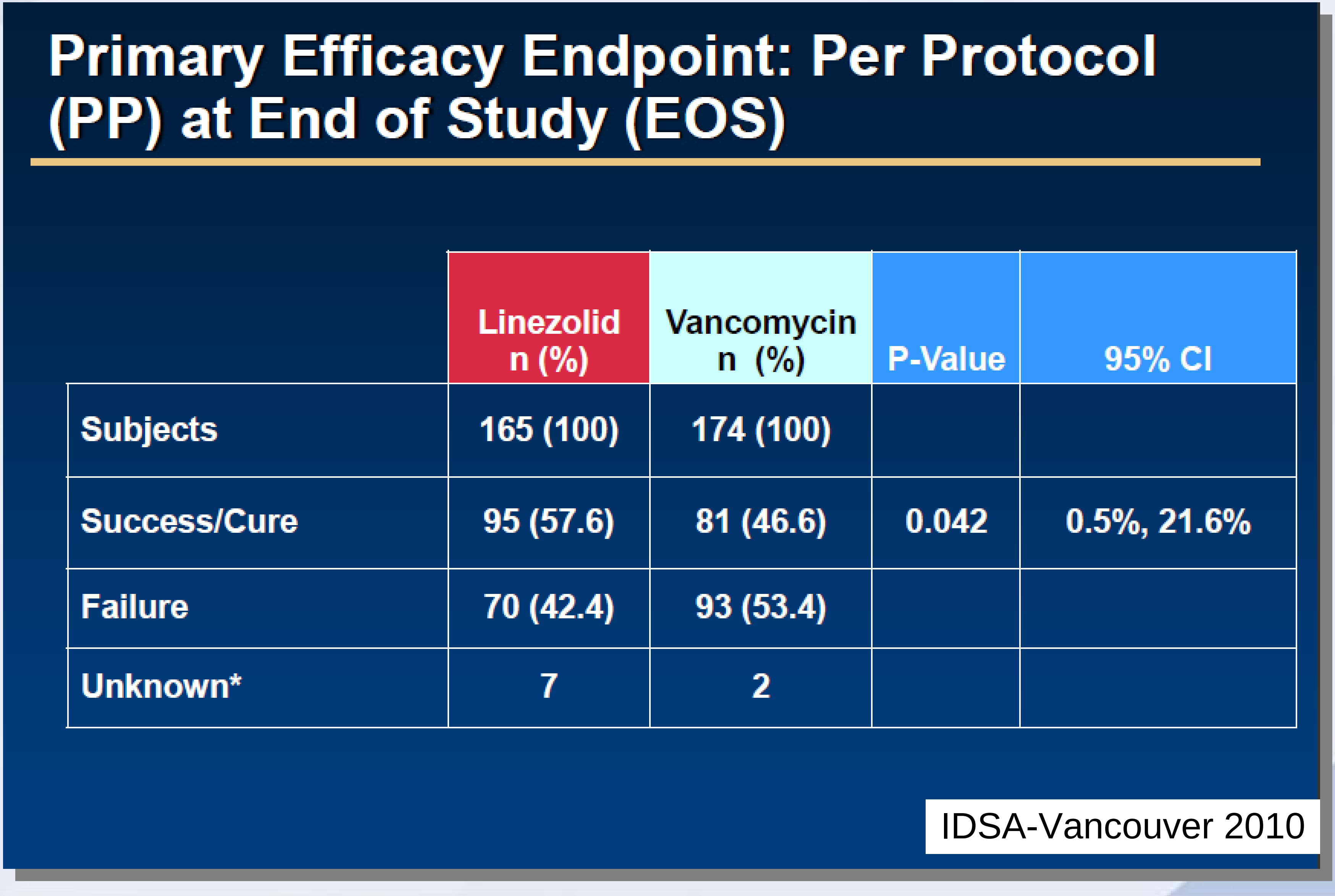
Safety Announcement
Additional Information for Healthcare Professionals
Data Summary

Safety Announcement

[09-01-2010] The U.S. Food and Drug Administration (FDA) is reminding healthcare professionals of an increased mortality risk associated with the use of the intravenous antibacterial Tygacil (tigecycline) compared to that of other drugs used to treat a variety of serious infections. The increased risk was determined using a pooled analysis of clinical trials. The cause of the excess death in these trials is often uncertain, but it is likely that most deaths in patients with these severe infections were related to progression of the infection.

The increased risk was seen most clearly in patients treated for hospital-acquired pneumonia, especially ventilator-associated pneumonia, but was also seen in patients with complicated skin and skin structure infections, complicated intra-abdominal infections and diabetic foot infections. Tygacil is not approved for the treatment of hospital-acquired pneumonia (including ventilator-associated pneumonia) or diabetic foot infection. Tygacil is approved by FDA for the treatment of complicated skin and skin structure infections, complicated intra-abdominal infections, and community acquired pneumonia.

LINEZOLID (1): ¿es eficaz?

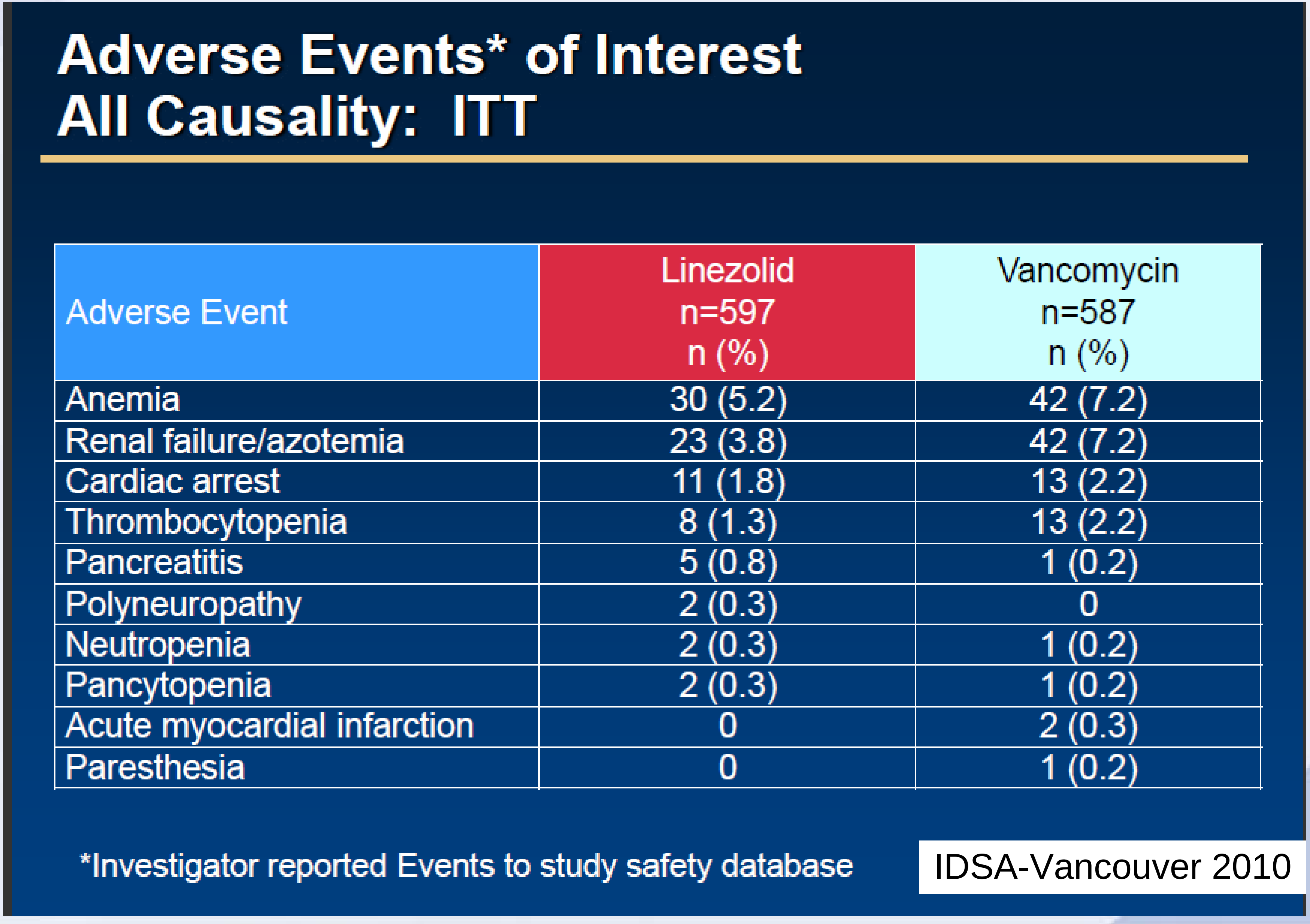


Primary Efficacy Endpoint: Per Protocol (PP) at End of Study (EOS)

	Linezolid n (%)	Vancomycin n (%)	P-Value	95% CI
Subjects	165 (100)	174 (100)		
Success/Cure	95 (57.6)	81 (46.6)	0.042	0.5%, 21.6%
Failure	70 (42.4)	93 (53.4)		
Unknown*	7	2		

IDSA-Vancouver 2010

LINEZOLID (2): ¿es seguro?



Adverse Events* of Interest
All Causality: ITT

Adverse Event	Linezolid n=597 n (%)	Vancomycin n=587 n (%)
Anemia	30 (5.2)	42 (7.2)
Renal failure/azotemia	23 (3.8)	42 (7.2)
Cardiac arrest	11 (1.8)	13 (2.2)
Thrombocytopenia	8 (1.3)	13 (2.2)
Pancreatitis	5 (0.8)	1 (0.2)
Polyneuropathy	2 (0.3)	0
Neutropenia	2 (0.3)	1 (0.2)
Pancytopenia	2 (0.3)	1 (0.2)
Acute myocardial infarction	0	2 (0.3)
Paresthesia	0	1 (0.2)

*Investigator reported Events to study safety database

IDSA-Vancouver 2010

LINEZOLID (3) : ¿es seguro?

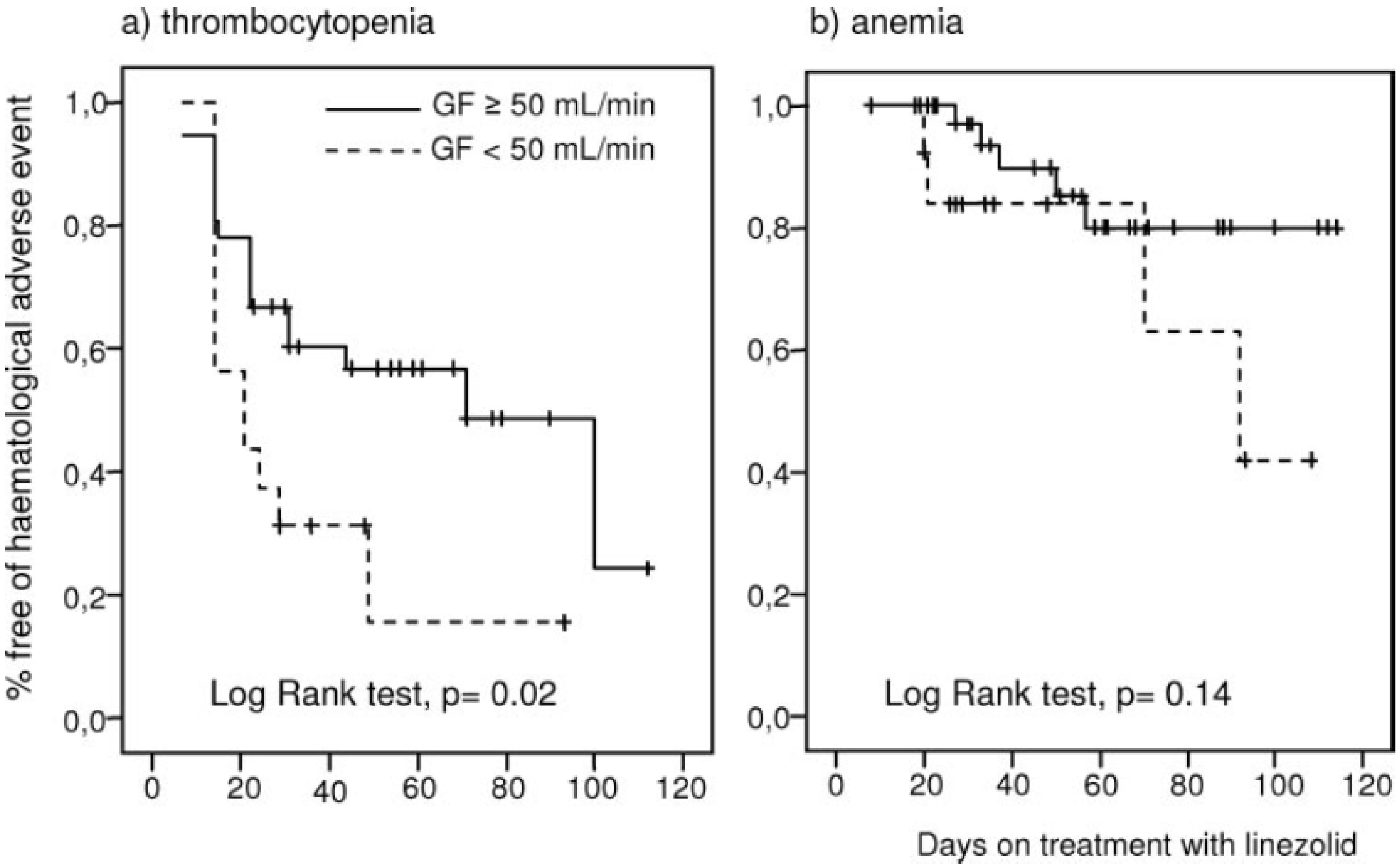
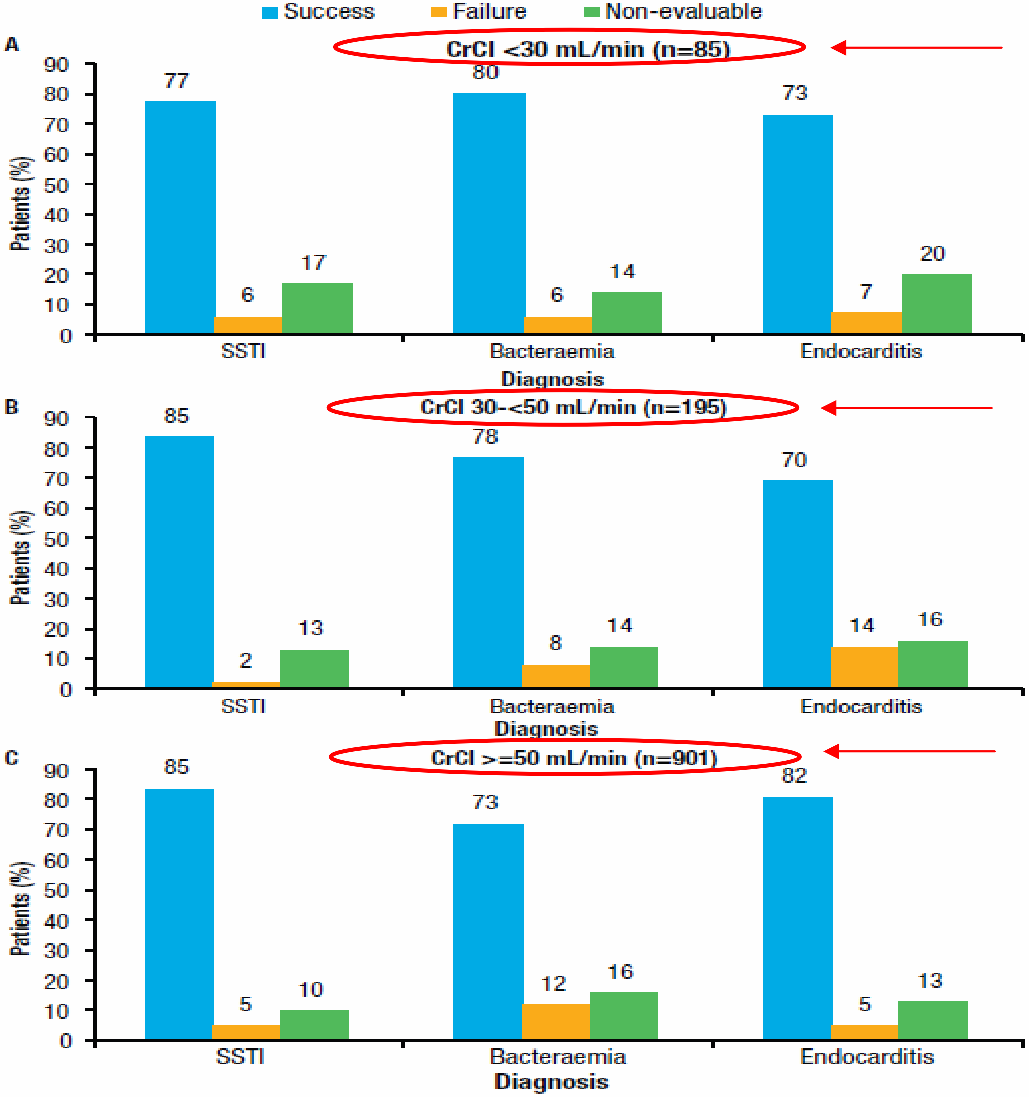


FIG. 3. Cumulative probability of hematological adverse events according to GFR.

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2007, p. 2559–2563 Vol. 51, No. 7

DAPTOMICINA (1): ¿es eficaz?



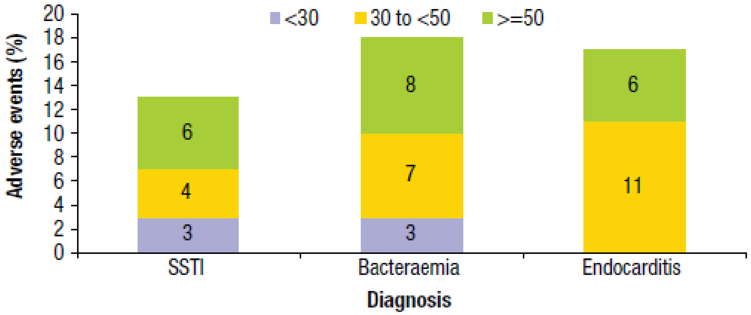
Clinical outcome (success, failure and non-evaluable) by different diagnosis were assessed at the end of DAP therapy for the at creatinine clearance (CrCl) levels <30 mL/min (A); 30-<50 mL/min (B), and ≥ 50 mL/min (C); SSTI: skin and soft tissue infe

Safety and effectiveness of daptomycin in patients with renal insufficiency not requiring renal replacement therapy

Gonzalez-Ruiz A[1], Lamp KC[2], Lin M-Y[2] and Chaves RL[3]

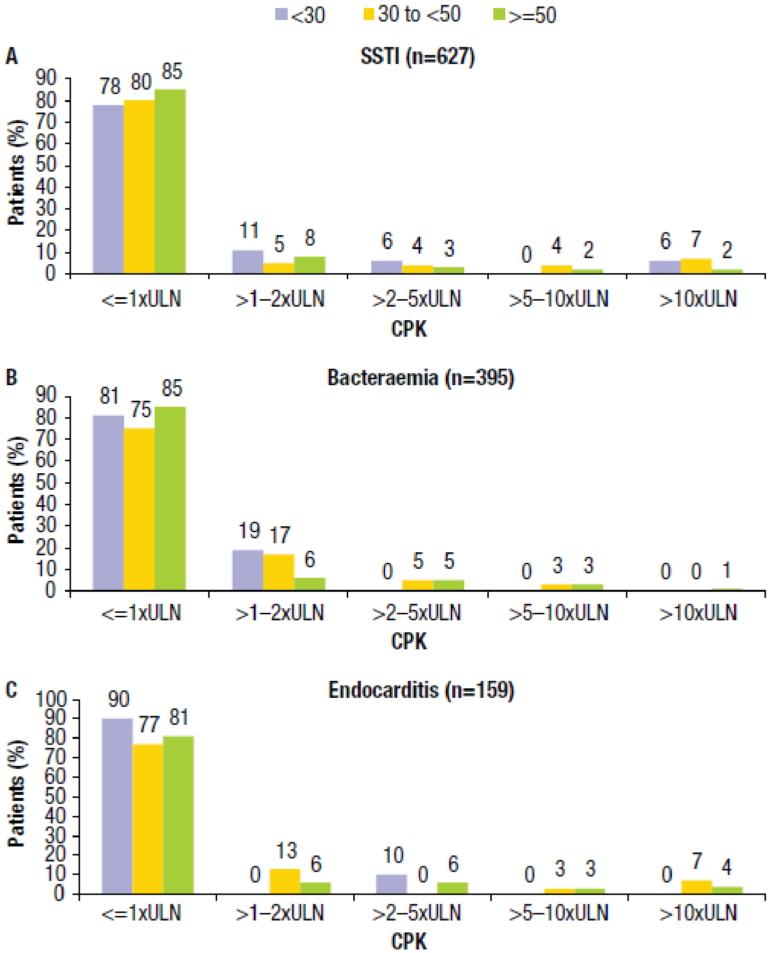
[1]Darent Valley Hospital, Microbiology Department, Kent, UK; [2]Cubist Pharmaceuticals, Lexington, MA, US; [3]Novartis Pharma AG, Basel, Switzerland

DAPTOMICINA (2): ¿es segura?



Adverse events (AEs) reported with different diagnosis for the patients at CrCl levels <30, 30-<50, and ≥ 50 mL/min.

Figure 3. Adverse events related to study medication



Highest CPK measured during treatment for different diagnosis of patients at CrCl levels <30, 30-<50, and ≥ 50 mL/min.

Figure 2. Serum creatine phosphokinase (CPK) during DAP therapy

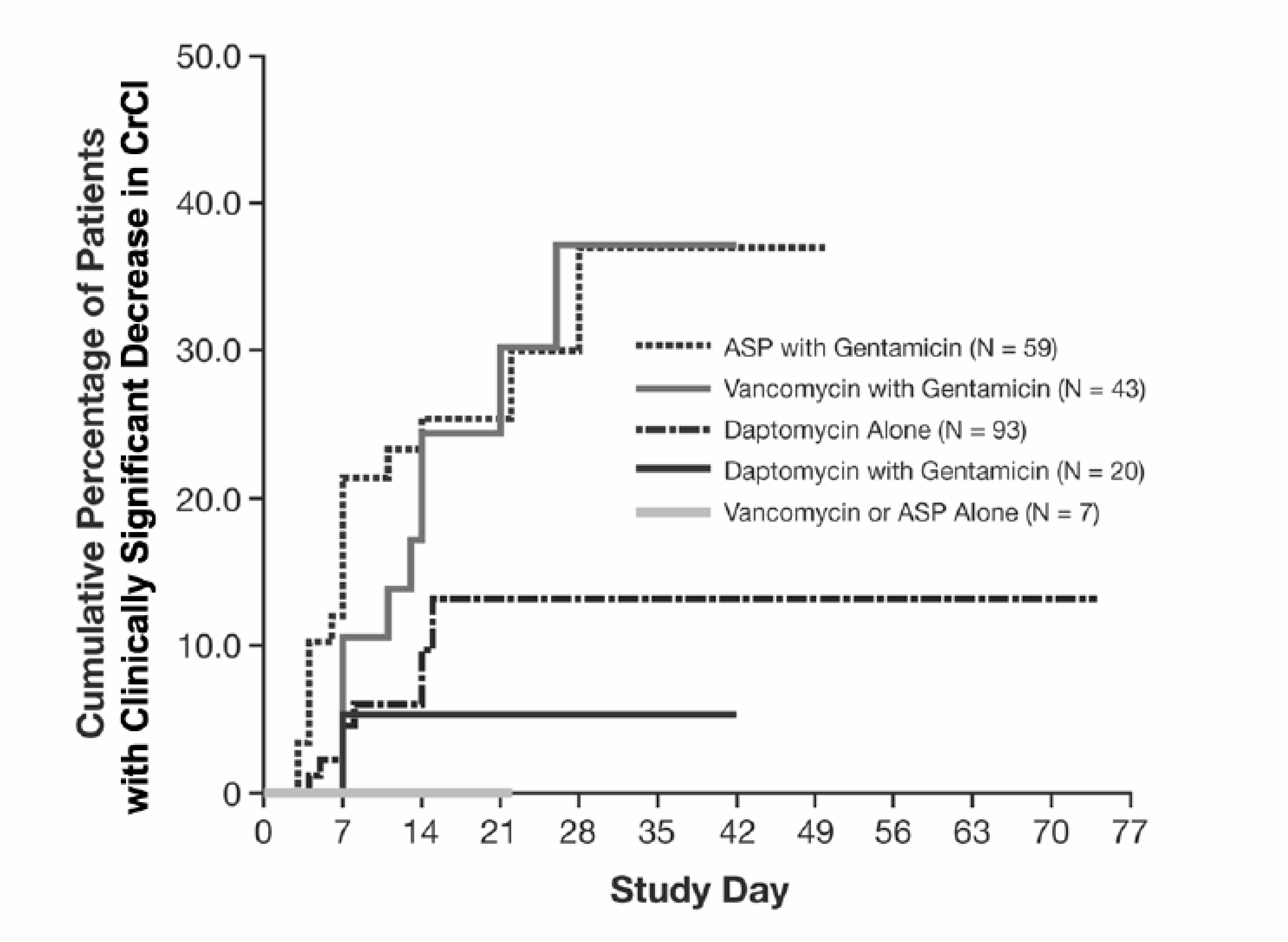
20th European Congress of Clinical Microbiology and Infectious Diseases

Safety and effectiveness of daptomycin in patients with renal insufficiency not requiring renal replacement therapy

Gonzalez-Ruiz A[1], Lamp KC[2], Lin M-Y[2] and Chaves RL[3]

[1]Darent Valley Hospital, Microbiology Department, Kent, UK; [2]Cubist Pharmaceuticals, Lexington, MA, US; [3]Novartis Pharma AG, Basel, Switzerland

DAPTOMICINA (3) ¿y cuando se asocia a otros nefrotóxicos?



Clinical Infectious Diseases 2009; 48:713–21

AMINOGLICÓSIDOS … esos otros nefrotóxicos

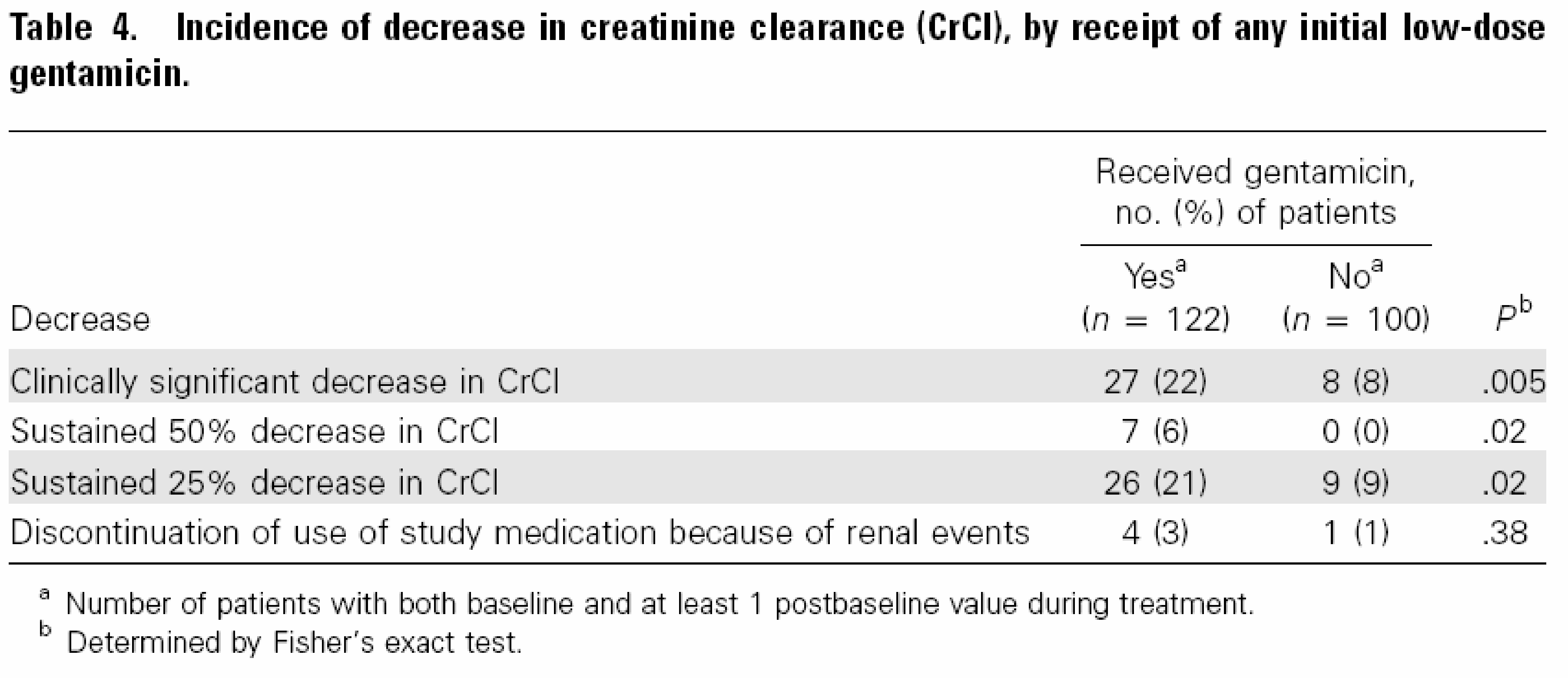


Table 4. Incidence of decrease in creatinine clearance (CrCl), by receipt of any initial low-dose gentamicin.

	Received gentamicin, no. (%) of patients		
Decrease	Yes[a] (n = 122)	No[a] (n = 100)	P[b]
Clinically significant decrease in CrCl	27 (22)	8 (8)	.005
Sustained 50% decrease in CrCl	7 (6)	0 (0)	.02
Sustained 25% decrease in CrCl	26 (21)	9 (9)	.02
Discontinuation of use of study medication because of renal events	4 (3)	1 (1)	.38

[a] Number of patients with both baseline and at least 1 postbaseline value during treatment.
[b] Determined by Fisher's exact test.

Clinical Infectious Diseases 2009; 48:713–21

CONCLUSIONES

El deterioro agudo de la función renal se asocia con:

- Aumento de la mortalidad intrahospitalaria
- Ingresos prolongados
- Incremento significativo de costes

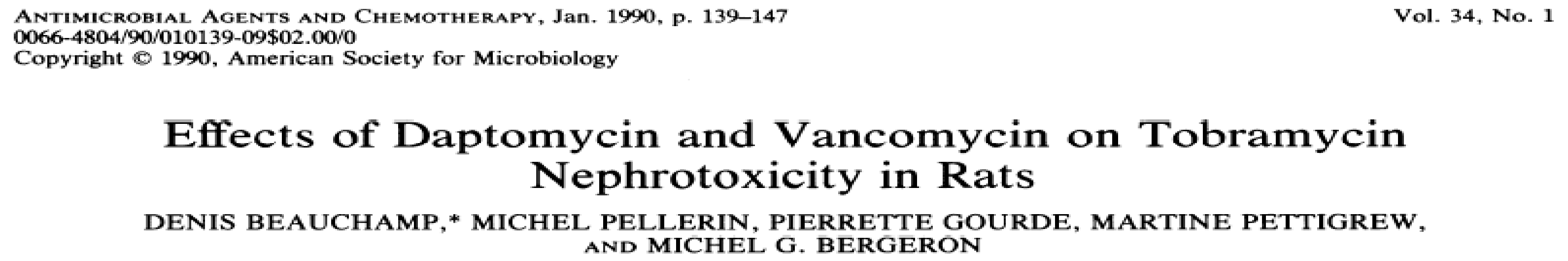
El deterioro renal agudo se produce fundamentalmente en el contexto de la sepsis

- En pacientes pluripatológicos
- Cuando existe enfermedad renal previa
- Cuando se asocian otros fármacos nefrotóxicos

En el contexto del deterioro de la función renal, cuando se sospeche la presencia de G+, una elección individualizada del tratamiento podría tener implicaciones en el pronóstico :

- Bacteriemia, endocarditis, celulitis complicada: DAPTOMICINA
- Infección de órgano (neumonía, meningitis …): LINEZOLID (no indicado en bacteriemia)
- PENICILINAS: para secuenciar siempre según antibiograma
- TIGECICLINA: 3º lugar. Infecciones polimicrobianas.

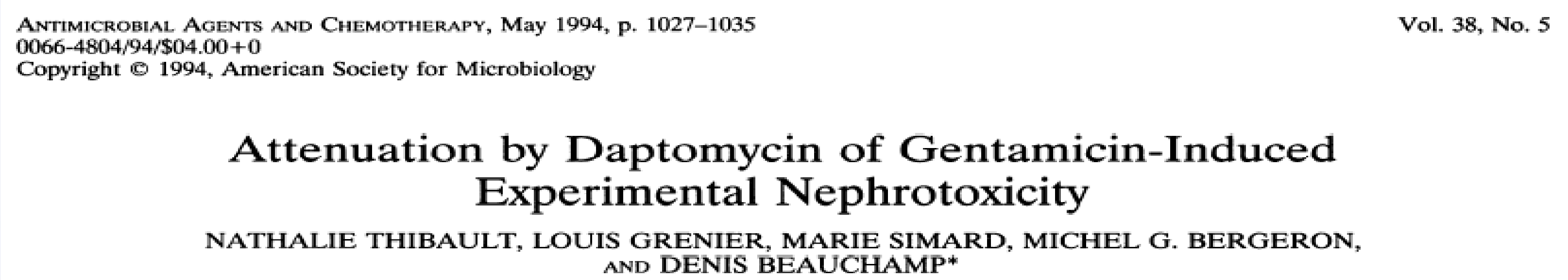
DAPTOMICINA ¿y cuando se asocia a otros nefrotóxicos?



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 1990, p. 139–147 Vol. 34, No. 1
0066-4804/90/010139-09$02.00/0
Copyright © 1990, American Society for Microbiology

Effects of Daptomycin and Vancomycin on Tobramycin Nephrotoxicity in Rats

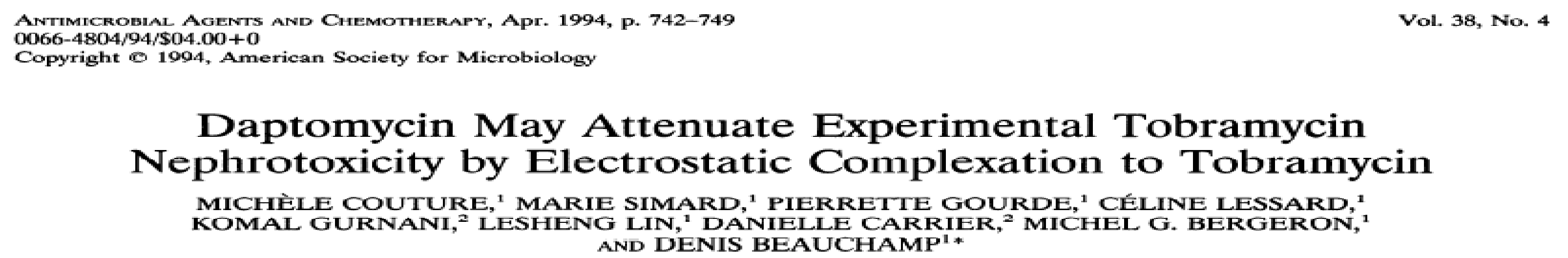
DENIS BEAUCHAMP,* MICHEL PELLERIN, PIERRETTE GOURDE, MARTINE PETTIGREW,
AND MICHEL G. BERGERON



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, May 1994, p. 1027–1035 Vol. 38, No. 5
0066-4804/94/$04.00+0
Copyright © 1994, American Society for Microbiology

Attenuation by Daptomycin of Gentamicin-Induced Experimental Nephrotoxicity

NATHALIE THIBAULT, LOUIS GRENIER, MARIE SIMARD, MICHEL G. BERGERON,
AND DENIS BEAUCHAMP*



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 1994, p. 742–749 Vol. 38, No. 4
0066-4804/94/$04.00+0
Copyright © 1994, American Society for Microbiology

Daptomycin May Attenuate Experimental Tobramycin Nephrotoxicity by Electrostatic Complexation to Tobramycin

MICHÈLE COUTURE,[1] MARIE SIMARD,[1] PIERRETTE GOURDE,[1] CÉLINE LESSARD,[1]
KOMAL GURNANI,[2] LESHENG LIN,[1] DANIELLE CARRIER,[2] MICHEL G. BERGERON,[1]
AND DENIS BEAUCHAMP[1]*