Toulouse
JNI 12es Journées Nationales d'Infectiologie

Best of en Infectiologie :
Infections des Voies Respiratoires Basses

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Peut-on Prévoir l'Evolution des Pneumonies ?

La guerre des scores

- Zilberberg M D, CID 2010
- **Arnold FW, Resp Med, 2010**
- Murcia J, J Infect 2010
- Espana PP, J Infect 2010
- Jo S, J Emerg Med, 2010
- Chalmers JD, Thorax 2010
- Chen JH, Thorax 2010
- Loke YK, Thorax 2010

Les biomarqueurs

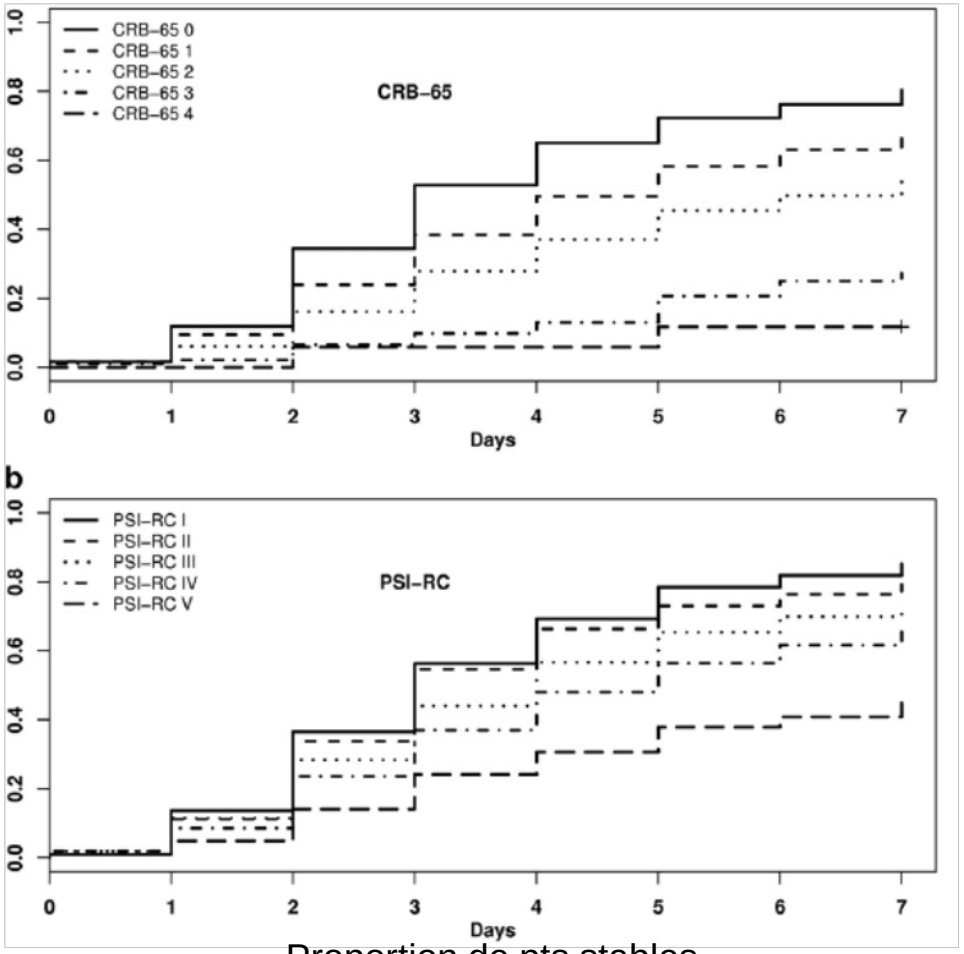
- Ruiz-Gonzales A, Eur J Intern Med 2010
- Krüger S, Am J Respir Crit Care Med 2010
- Lyudt CE, Réanimation, 2010
- Majumdar SR, CID 2011
- Lee JH, J Crit Care 2011
- Salluh JE, J Crit Care 2011
- Moammar MQ, Heart, Lung and Circulation 2010
- Moreno MS, J Infect 2010
- Krüger S, Clin Chim Acta, 2010
- Lee YL, J Crit Care 2010

Predictive Accuracy of the PSI *vs* CRB-65 for Time to Clinical Stability: Results from the CAPO International Cohort Study

PSI (Fine) et CRB-65 (BTS) :
Scores prédictifs de **mortalité**

Délai de stabilisation clinique ?
Mortalité intra Hospitalière ?
Durée de séjour ?

- **Database : 3087 pts, PAC**
- **Établissement des courbes ROC**
  - À partir PSI et CRB-65
  - À J7 d'hospitalisation



Proportion de pts stables

Arnold FW Respiratory medicine 2010;104:1736-43

Predictive Accuracy of the PSI *vs* CRB-65 for Time to Clinical Stability: Results from the CAPO International Cohort Study

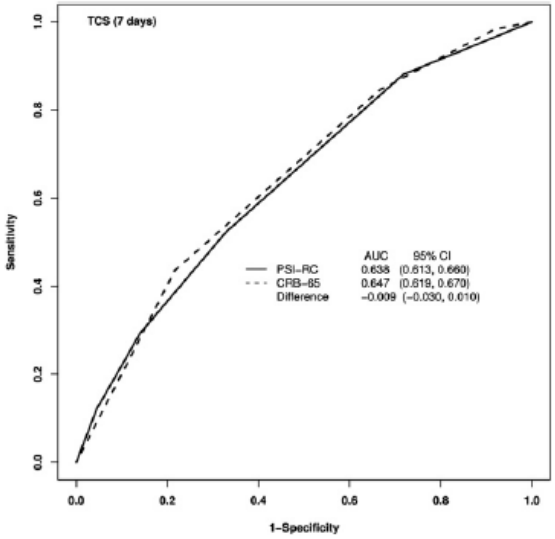


Figure 2 ROC curves for hospitalized patients with community-acquired pneumonia reaching clinical stability within 7 days for each severity score: pneumonia severity index and CRB-65.

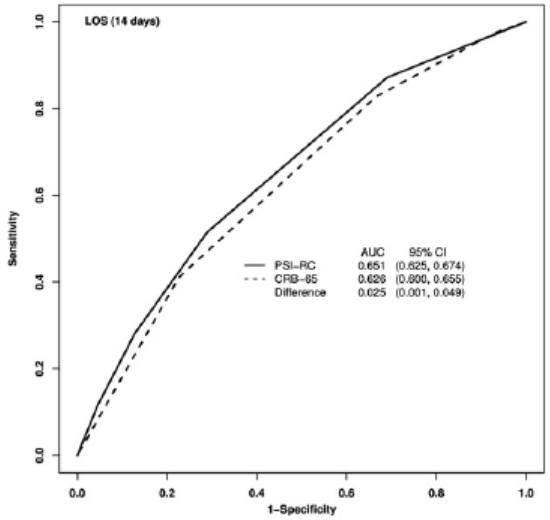


Figure 3 ROC curves for hospitalized patients with community-acquired pneumonia being discharged within 14 days for each severity score: pneumonia severity index and CRB-65.

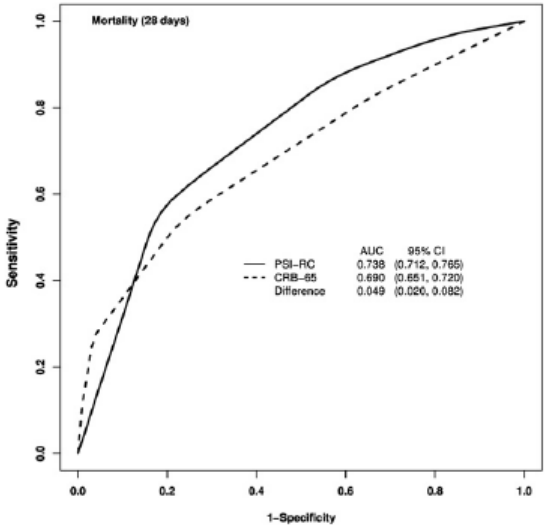


Figure 4 ROC curves for hospitalized patients with community-acquired pneumonia dying within 28 days for each severity score: pneumonia severity index and CRB-65.

	PSI	PSI RC	CRB 65	PSI RC – CRB 65
	AUC 95%CI	AUC 95%CI	AUC 95%CI	Difference 95% CI
TCS within 7d	0,652 (0, 627, 0,674)	0,638 (0,613, 0,660)	0,647 (0,619, 0,670)	0,009 (0,030, 0,010)
Discharge within 14d	0,659 (0,633, 0,685)	0,651 (0,625, 0,674)	0,626 (0,600, 0,655)	0,025 (0,001, 0,049)
In-H 28d mortality	0,756 (0,722, 0,784)	0,738 (0,712, 0,765)	0,69 (0,651, 0,720)	0,049 (0,020, 0,082)

Arnold FW Respiratory Medicine 2010;104:1736-43

Predictive Accuracy of the PSI *vs* CRB-65 for Time to Clinical Stability: Results from the CAPO International Cohort Study

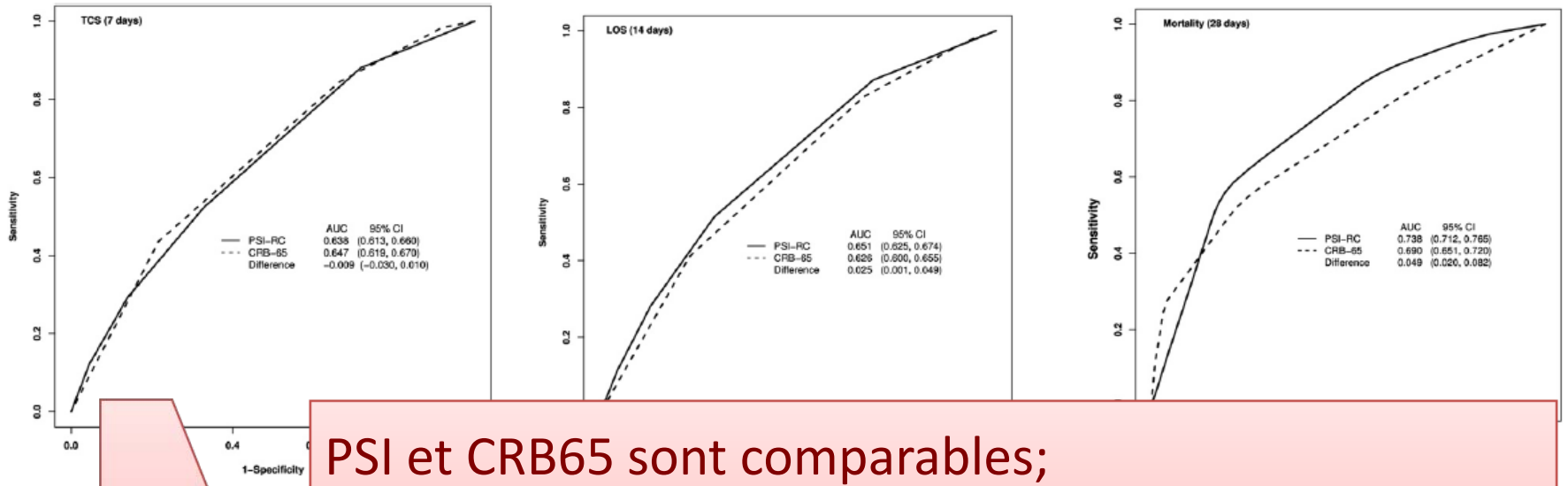


Figure 2 R… hospitalize… nu-
nity-acquired …aching cli… …ity
days for eac… : pneum…
CRB-65.

PSI et CRB65 sont comparables;

Prédictifs pour délai de stabilisation;

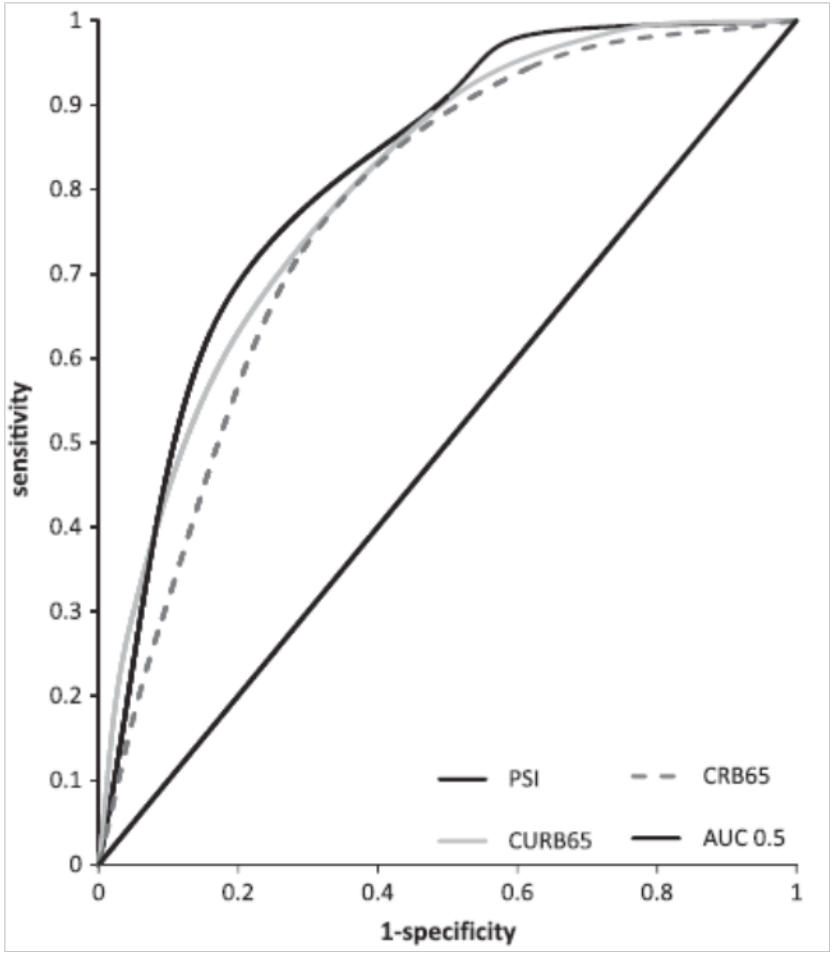
Moins prédictifs pour la durée de séjour;

Moins prédictifs pour la mortalité intra hospitalière.

TCS wi… d				…)
Discharge within 14d	0,659 (0,633, 0,685)	0,651 (0,625, 0,674)	0,626 (0,600, 0,655)	0,025 (0,001, 0,049)
In-H 28d mortality	0,756 (0,722, 0,784)	0,738 (0,712, 0,765)	0,69 (0,651, 0,720)	0,049 (0,020, 0,082)

Arnold FW Respiratory Medicine 2010;104:1736-43

Severity Assessment Tools for Predicting Mortality in Hospitalised Patients with CAP



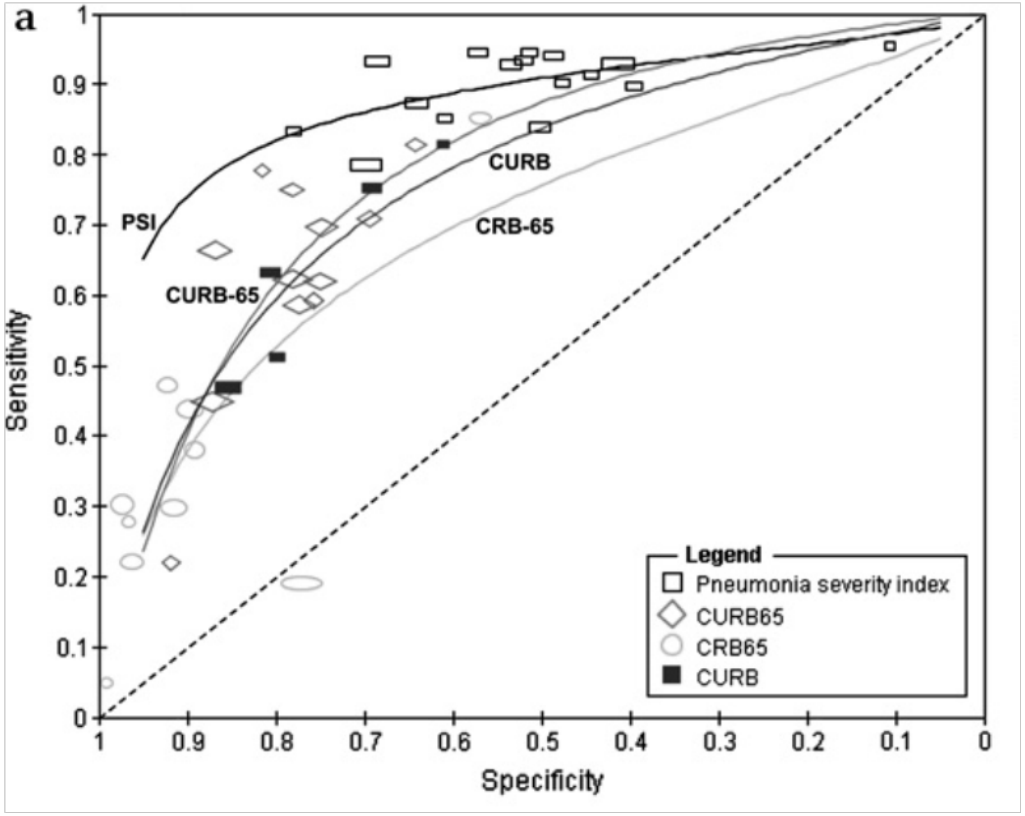
Méta-analyse des scores prédictifs de mortalité CURB65, CRB65 et PSI

- 5102 résumés >> 40 articles retenus
- Comparaison des scores
  - PSI *vs* CURB65, p=0,1,
  - PSI *vs* CRB65, p=0,09,
  - CURB65 *vs* CRB65, p= 0,5
- PSI identifie mieux les pts à faible risque de décès
- CURB65 et CRB65 identifient mieux les pts à risque élevé de décès

Chalmers JD Thorax 2010 ; 65 : 878-883

Value of Severity Scales in Predicting Mortality from CAP: Systematic Review and Meta-Analysis

- Méta-analyse 23 études
- Comparaison PSI *vs* CURB65, CURB, CRB65
- PSI
  - le + sensible
  - le – spécifique
  - Faible taux de faux négatif
  - Identifie le mieux les pts à faible risque de décès
- CURB-65 et variantes
  - + spécifique
  - Identifie le mieux les pts à risque de décès



Loke YK Thorax 2010;65:884-890

Marqueurs Biologiques

Albumin and C-Reactive Protein Have Prognostic Significance in Patients with CAP (I)

- Étude prospective
- 424 pts hospitalisés aux urgences
- Critère principal d'évaluation :
  - survie à J28
- Régression logistique :
  - CRP et albumine : facteurs indépendants de mortalité

Variables	OR (95% CI)	*P*
PA moyenne	1.00 (0,98-1,01)	,506
Hémoglobine	1,01 (0,87-1,17)	,889
Albumine	**0,37 (0,19-0,73)**	**,004**
TP, INR	1,02 (0,39-2,70)	,962
CRP	**1,04 (1,00-1,07)**	**,025**
PSI I-III	Référence	
PSI IV	16,96 (2,4-128,42)	,006
PSI V	36,41 (4,71-281,39)	,001

Mortalité J28

PSI	Albumine		*P*	CRP		*P*
	< 3,3 mg/dL	≥ 3.3 mg/dL		< 14.3 mg/dL	≥ 14.3 mg/dL	
I, II	0/15 (0,0%)	0/57 (0,0%)		0/49 (0,0%)	0/23 (0,0%)	
III	0/23 (0,0%)	1/50 (2,0%)	,495	1/43 (2,3%)	0/30 (0,0%)	,400
IV	16/88 (18,2%)	9/88 (10,2%)	,131	9/100 (9,0%)	16/76 (21,1%)	,023
V	26/64 (40,6%)	6/39 (15,%)	,007	13/59 (22,0%)	19/44 (43,2%)	,022
Total	42/190 (22,1%)	16/234 (6,8%)	< ,001	23/251 (9,2%)	35/173 (20,2%)	,001

Lee JH J Crit Care 2011;26:287-294

Biomarqueurs Facteurs Pronostiques ?

- D-Dimer levels are good predictors of outcome in severe CAP and may augment the predictive ability of scoring systems as APACHE II and SOFA;

Salluh JIF, J Crit Care 2011

- The new biomarkers, MR-proANP, copeptin, CT-proET-1, and MR-proADM are strong predictors of 28 and 180-day mortality from CAP, with the best performance for MR-proADM.

Krüger S AJRCCM 2010

- Oxygen saturations less than 92% are associated with major adverse events in outpatients with pneumonia.

Majumdar SR Clin Infect Dis 2011

- C-Reactive protein levels but not CRP dynamics predict mortality in patients with pneumococcal pneumonia.

Mooiweer E J infect 2011

- Serum and BAL fluid levels of the studied cytokines (IL-1β, IL-6, IL-8, IL-10, TNF-α, C-reactive protein) on admission may provide valuable prognostic information for patients with severe CAP.

Lee YL J Crit Care 2010

Pneumonie = Inflammation = Corticoïdes ???

- **Chen D, Am J Respir Crit Care Med 2011**
- **Snidjers D, Am J Respir Crit Care Med 2010**
- **Salluh JIF, J Crit Care 2011**
- **Salluh JIF, J Crit Care 2011**
- **Meijvis SCA, Lancet 2011**

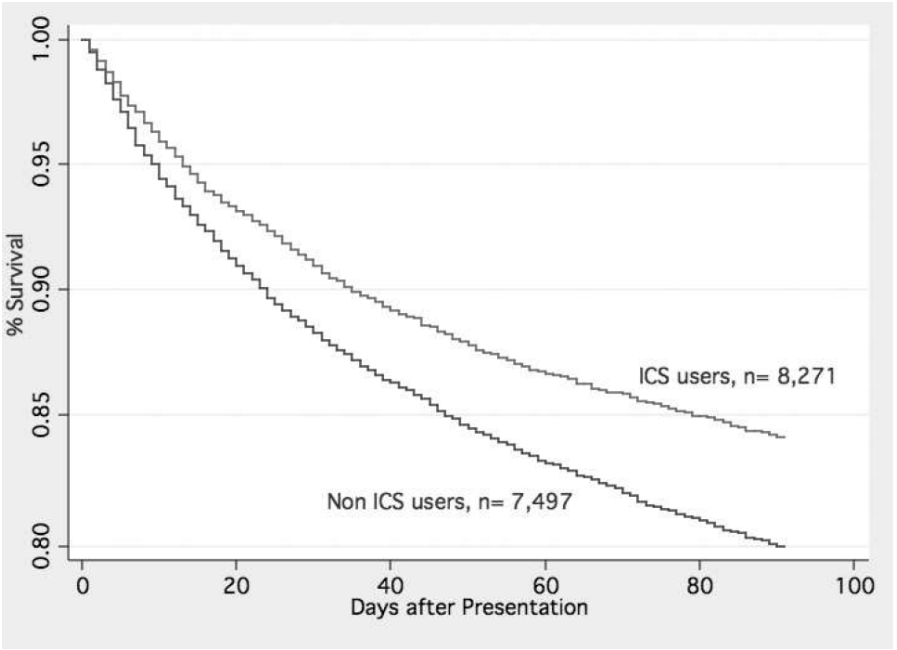
Observational Study of Inhaled Corticosteroids on Outcomes for COPD Patients with Pneumonia

CS pour BPCO : ↗ incidence PAC

Quel impact des CS sur la mortalité ?

Étude rétrospective 15768 pts,
CS vs no CS

- Mortalité 9 j :
  - 17% vs 23%, p<0,001
- Mortalité J30 :
  - OR 0,80, IC95% 0,72-0,89
- Ventilation mécanique :
  - OR 0,83, IC95% 0,72-0,94



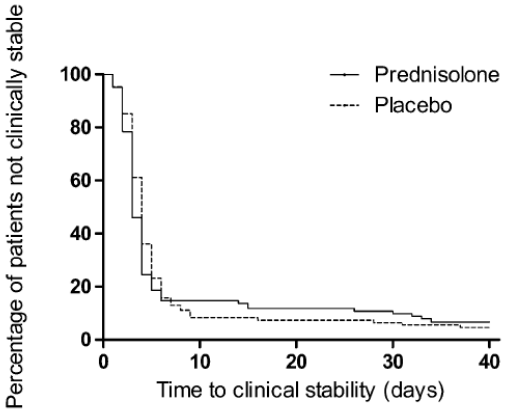
CS inhalés et BPCO : réduction du risque de décès à court terme et de VM au cours d'une hospitalisation pour PAC

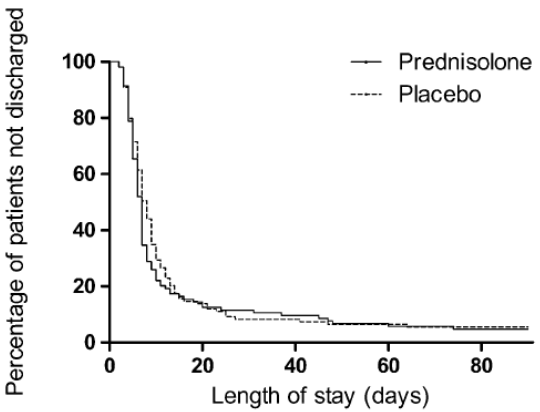
Chen D AJRCCM. Published on April 21, 2011 as doi:10.1164/rccm.201012-2070OC

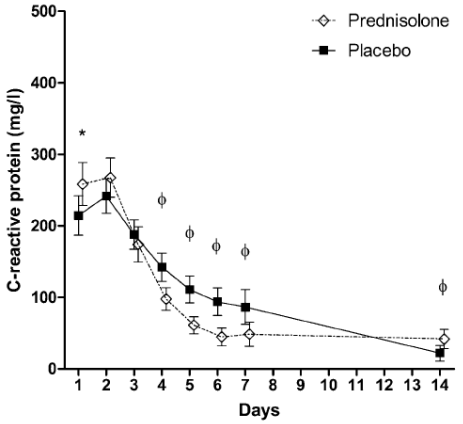
Efficacy of Corticosteroids in CAP
A Randomized Double-Blinded Clinical Trial

- **Randomisation 40 mg prednisolone *vs* placebo**
- **Critères évaluations :**
  - Principal : guérison J7
  - Secondaires : guérison j30, dure séjour, délais stabilisation, defervescence, CRP

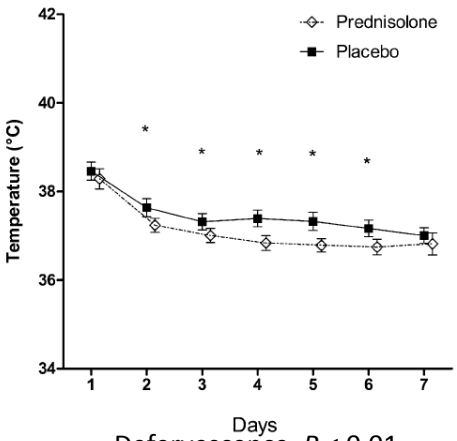
Guérison à J7 : pas de différence.
Échec tardifs plus fréquents si CS (19.% vs 6.4%), *P* = 0.04)
Absence de bénéfice
Traitement non recommandé







CRP, *P* <0,01



Defervescence, *P* < 0,01

Snijders D D AJRCCM 2010; 181:975-982

Impact of Systemic Corticosteroids on the Clinical Course and Outcomes of PTS with **Severe** CAP : A Cohort Study

- Étude de cohorte, deux **USI**, PAC sévères, 111 pts
- CS prescrits (61pts) pour bronchospasme ou choc septique

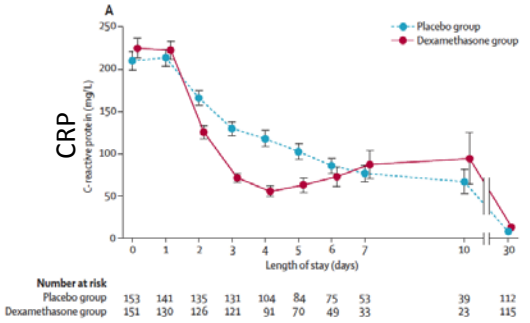
	Corticoïdes systémiques		*P*
	non	**oui**	
Mortalité	32%	29,5%	0,837
Sevrage vasopresseurs pour choc septique	57%	33%	0,53
Complications infectieuses	26%	32%	0,225
Durée totale hospitalisation	21	28	0,003
Durée hospitalisation en réanimation	11	15	0,023

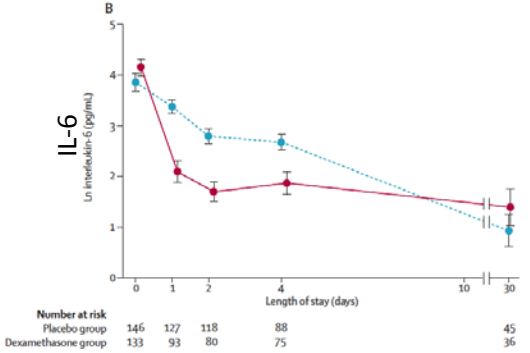
Corticothérapie : Allongement durées hospitalisation
Absence de bénéfice chez les pts avec PAC sévère, VM

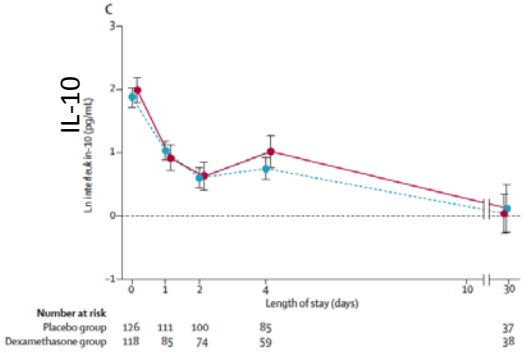
Salluh JIF J Crit Care 2011; 26: 193-200

Dexamethasone and Length of Hospital Stay in PTS with CAP: a Randomised, Double-Blind, Placebo-Controlled Trial

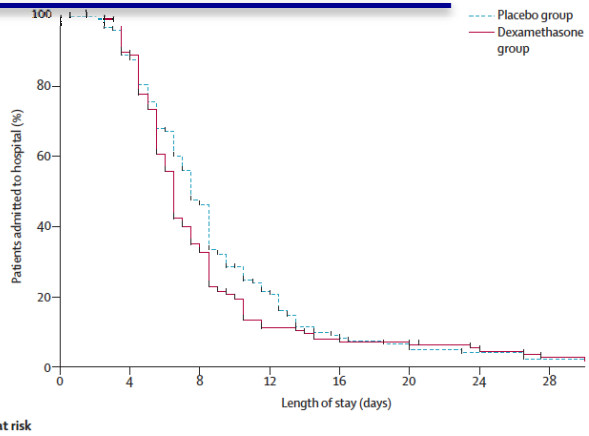
	Dexamethasone group (n=151)	Placebo group (n=153)	p value
Length of stay (days)	**6,5 (5,0–9,0)**	**7,5 (5,3–11,5**	**0,0480**
In-hospital mortality	8 (5%)	8 (5%)	0,98
Time to death (days)	5,5 (2,6–18,9)	8,8 (3,8–12,8)	0,64
30-day mortality	9 (6%)	11 (7%)	0,68
ICU admission	7 (5%)	10 (7%)	0,47
Time to ICU admission (d)	2,5 (1,5–6,5)	1,8 (1,5–2,6)	0,34
Length of stay in ICU (d)	21,5 (14,5–28,5)	15,5 (10,1–28,5)	0,23
Empyema/pleural effusion	7 (5%)	5 (3%)	0,54
Readmission within 30 days from hospital discharge	7 (5%)	7 (5%)	0,98





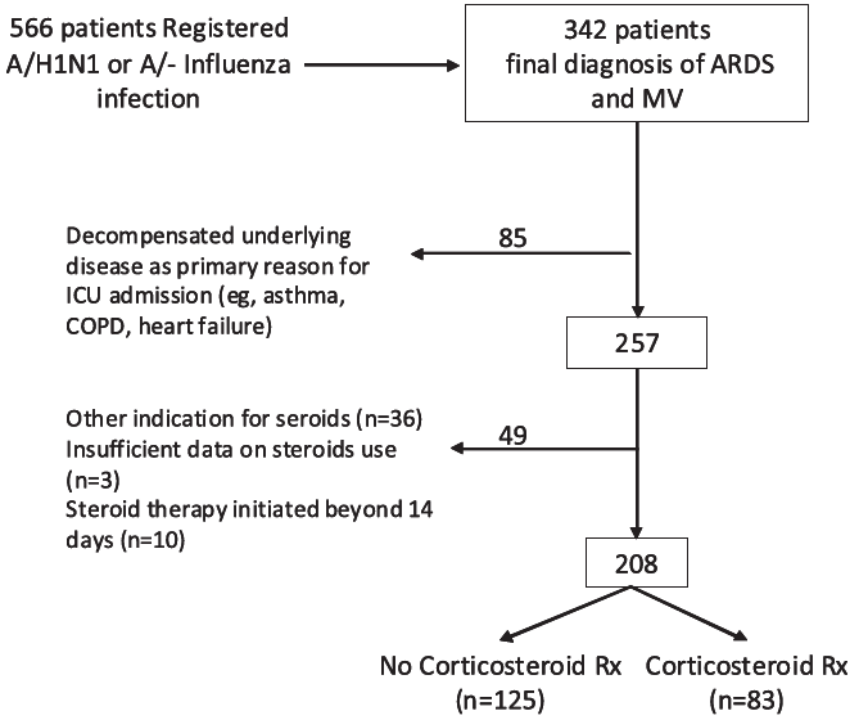


Dexamethasone can reduce length of hospital stay



Meijvis SCA Lancet 2011DOI:10.1016/S0140-6736(11)60607-7

Early Corticosteroids in Severe Influenza A/H1N1 Pneumonia and Acute Respiratory Distress Syndrome



	No Steroïds	Steroïds	*P* value
Death in hospital	**21 (16.8)**	**28 (33.7)**	**0,005**
ICU-acquired infection	44 (35.2)	38 (45.8)	0,52
ICU-acquired pneumonia	**33 (26.4)**	**34 (41.0)**	**0,01**
Duration of MV, d			
All patients (n = 5 208)	13 (8–24)	17 (10–29)	0,07
Survivors only (n = 5 158)	16 (9–24)	17 (12–26)	0,26
Length of ICU stay, d*			
All patients	17 (11–30)	22 (13–39)	0,11
Survivors only	20 (14–33)	25 (14–40)	0,15
Ventilator-free days			
At 28 d	**8 (0–17)**	**0 (0–12)**	**0,01**
At 60 d	**40 (25–49)**	**31 (0–44)**	**0,005**

Corticothérapie débutée dans les 2 première semaines : évolution défavorable
Surtout si précoce (< 3j)
Recommandation négative sur une utilisation en routine dans cette indication

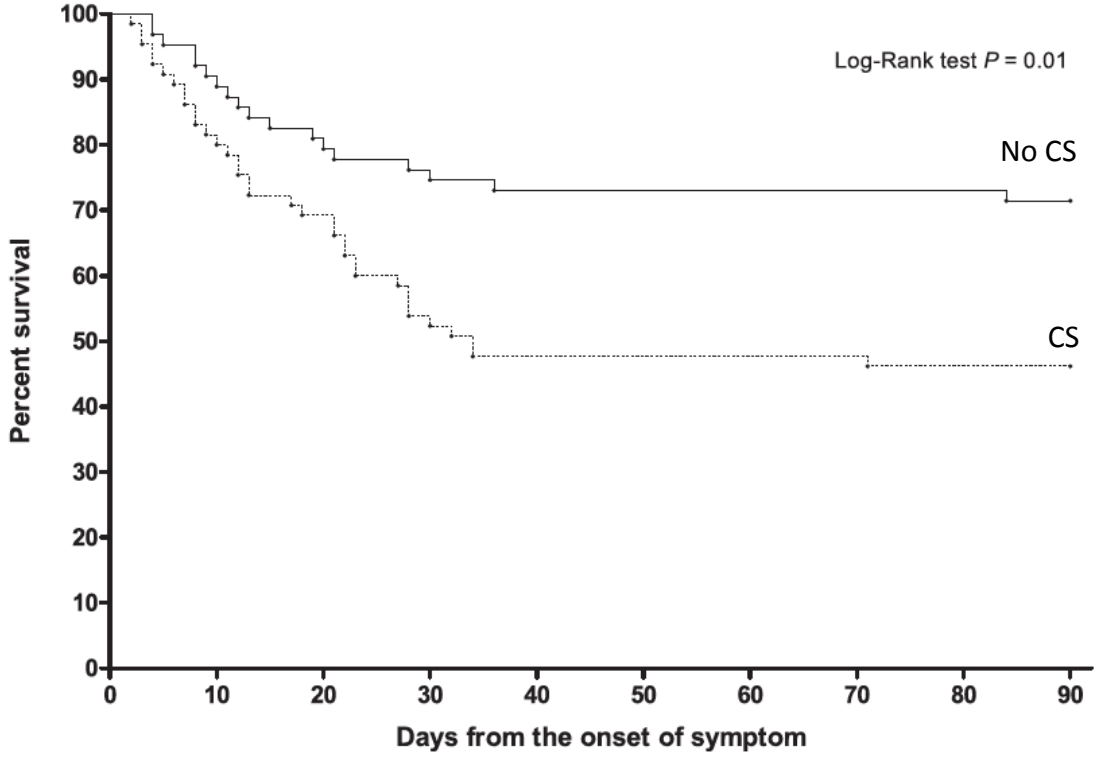
Brun-Buisson C AJRCCM 2011; 183 : 1200-1206

Corticosteroid Treatment in Critically Ill Patients with Pandemic Influenza A/H1N1 2009 Infection

Analytic Strategy Using Propensity Scores

Sung-Han Kim[1], Sang-Bum Hong[2], Sung-Choel Yun[3], Won-Il Choi[4], Jong-Joon Ahn[5], Young Joo Lee[6], Heung-Bum Lee[7], Chae-Man Lim[2], and Younsuck Koh[2]; for the Korean Society of Critical Care Medicine H1N1 Collaborative*

[1]Department of Infectious Diseases, [2]Department of Pulmonary and Critical Care Medicine, and [3]Department of Clinical Epidemiology and Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, Seoul; [4]Keimyung University School of Medicine, Daegu; [5]University of Ulsan Hospital, Ulsan; [6]Ajou University School of Medicine, Suwon; and [7]Chonbuk National University Medical School, Jeonju, Republic of Korea



Adjuvant corticosteroids were significantly associated with higher mortality in critically ill patients with A(H1N1)2009 infection.

Kim SHC AJRCCM 2011; 183 : 1207-1214

Impact of Early Oseltamivir Treatment on Outcome in Critically Ill Patients With 2009 Pandemic Influenza A

- Étude de cohorte observationnelle prospective
- Pts avec défaillance respiratoire USI/réa
- Grippe confirmée RT-PCR
- Oseltamivir PO
- ≤ 2 J vs > 2 j

Impact of early antiviral therapy on mortality in 385 adult ventilated patients with 2009 H1N1 virus infection (multivariate analysis)

Variable	OR	95% CI	P value
Prone ventilation	2.75	1.45 – 5.23	0.001
Number of quadrants infiltrated	1.70	1.28 – 2.25	0.001
APACHE II score (by point)	1.10	1.05 – 1.14	0.001
Early oseltamivir treatment	**0.44**	**0.21 – 0.87**	**0.02**

Rodriguez A J Antimicob Chemother 2011;66:140-1149

Benefit of Early Treatment with Oseltamivir in Hospitalized Pts with Documented A(H1N1)2009 Influenza

- Étude de cohorte rétrospective
- Juillet 2009-janvier 2010
- Pts à risques
- RT PCR + A(H1N1)2009
- Comparaison oseltamivir < 48h vs > 48h

Réduction significative des complications si oseltamivir < 48h

Occurrence of Influenza Complications Multivariable Logistic Regression

Variable	OR	95% CI
Main model (418 pts)		
Late Oseltamivir > 48h after symptom onset	2,37	(1,52 – 3,70)
Sensitivity analyses (only ORs for early oseltamivir shown)		
Including the propensity for early os (n = 418)	2,21	(1,41 – 3,46)
Multiple imputation analysis for missing values (n = 449)	2,33	(1,51 – 3,57)

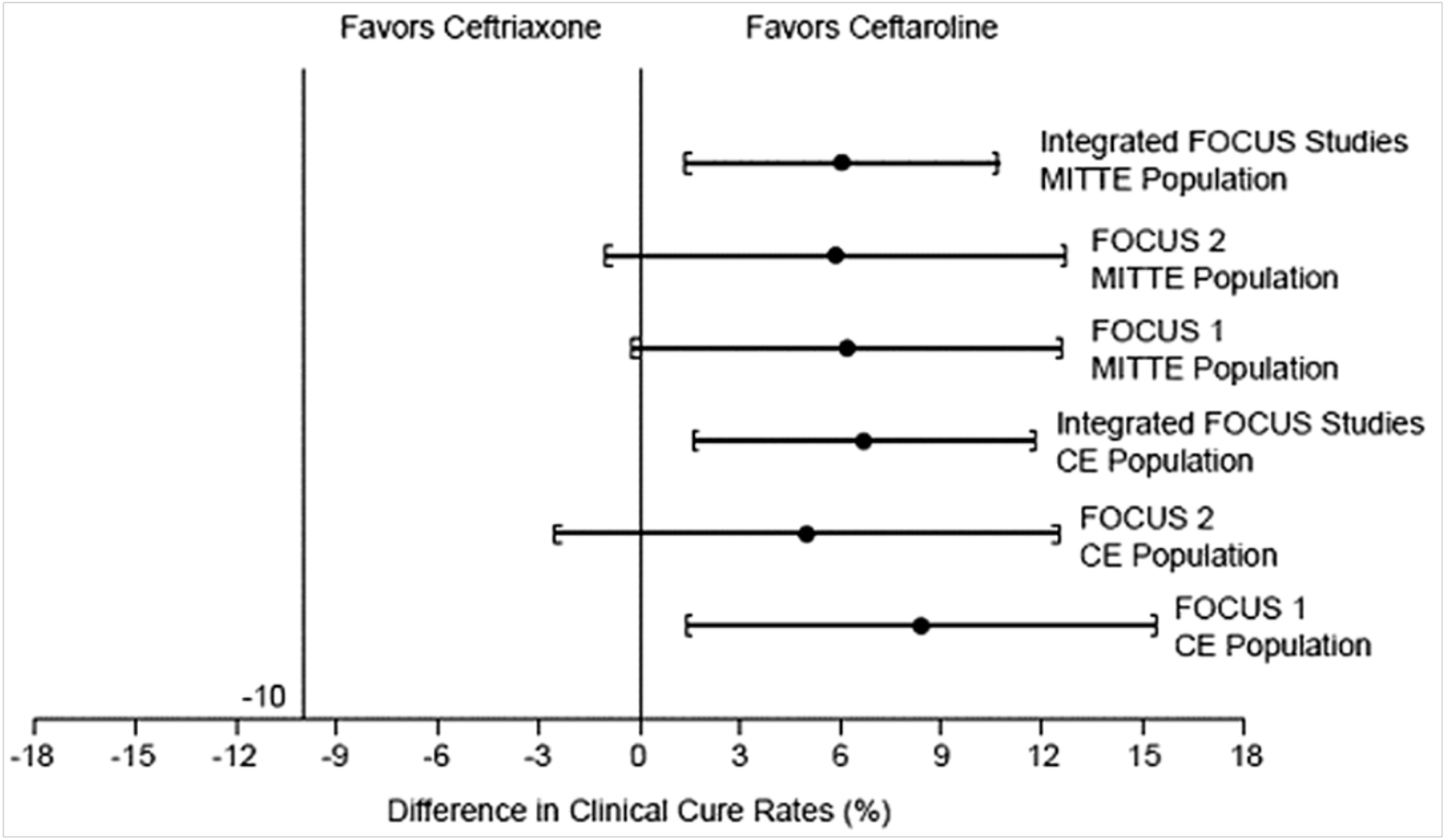
Hiba V J Antimicrob Chemother 2011;66:1150-1155

Efficacy and Safety of Ceftaroline Fosamil *vs* Ceftriaxone in Pts with CAP (I)

- **2 études prospectives randomisées multicentriques FOCUS 1 et FOCUS 2**
- **Non infériorité, delta : - 10**
- **Pts PAC hospitalisés, PSI III ou IV, (non en réanimation)**
  - Ceftaroline 600/12h mg vs ceftriaxone 1g/24h, 5-7 j
  - FOCUS 1 : clarithromycine 500 mg x 2 à J1
- **Critère principal :**
  - Guérison clinique population CE et MITTE, TOC
- **Objectifs secondaires :**
  - Guérison clinique population ME et mMITTE, TOC
  - Guérison clinique EOT
  - Évaluation microbiologique à EOT
  - Succès clinique EOT
  - Réponse clinique et microbiologique à EOT
  - …..

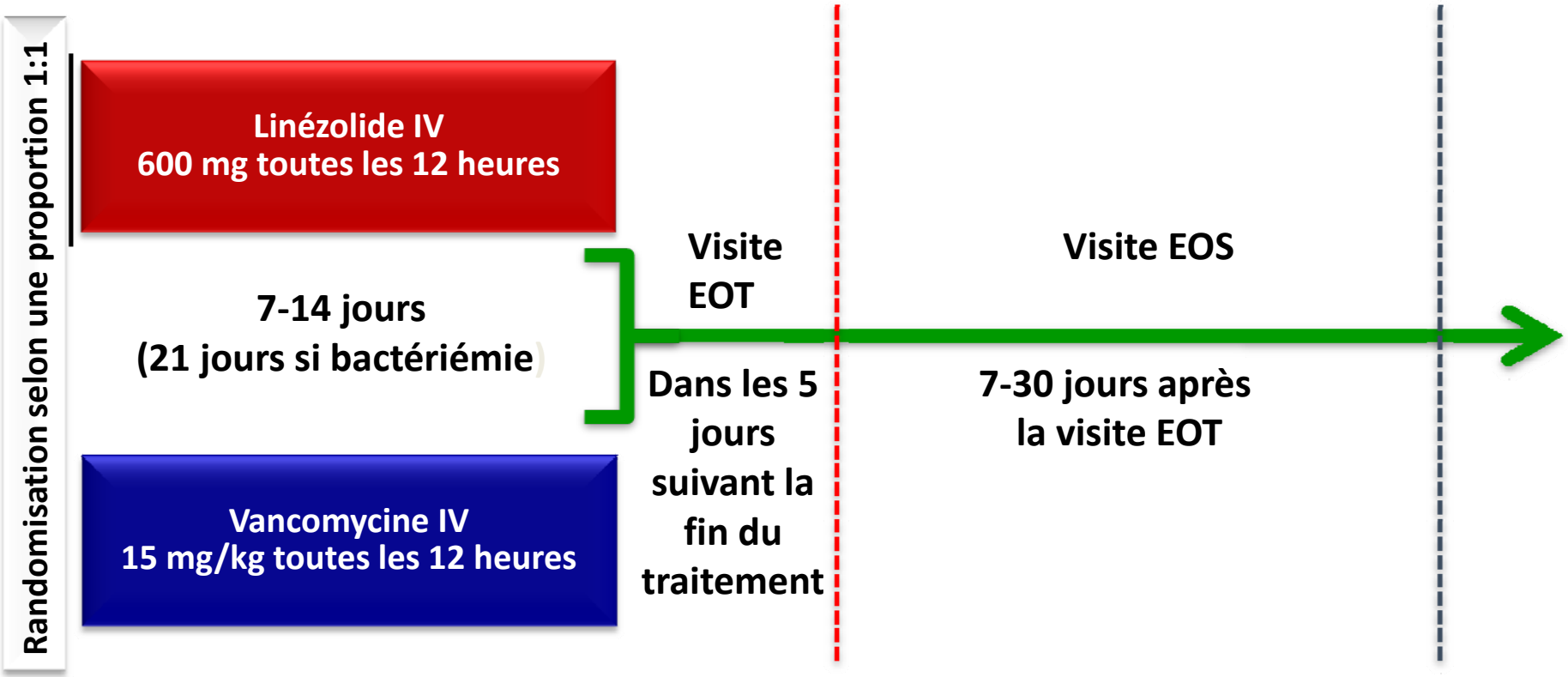
File TM Jr Clin Infect Dis 2010 51:1395-1405

Efficacy and Safety of Ceftaroline Fosamil *vs* Ceftriaxone in Pts with CAP (III)



File TM Jr Clin Infect Dis 2010 51:1395-1405

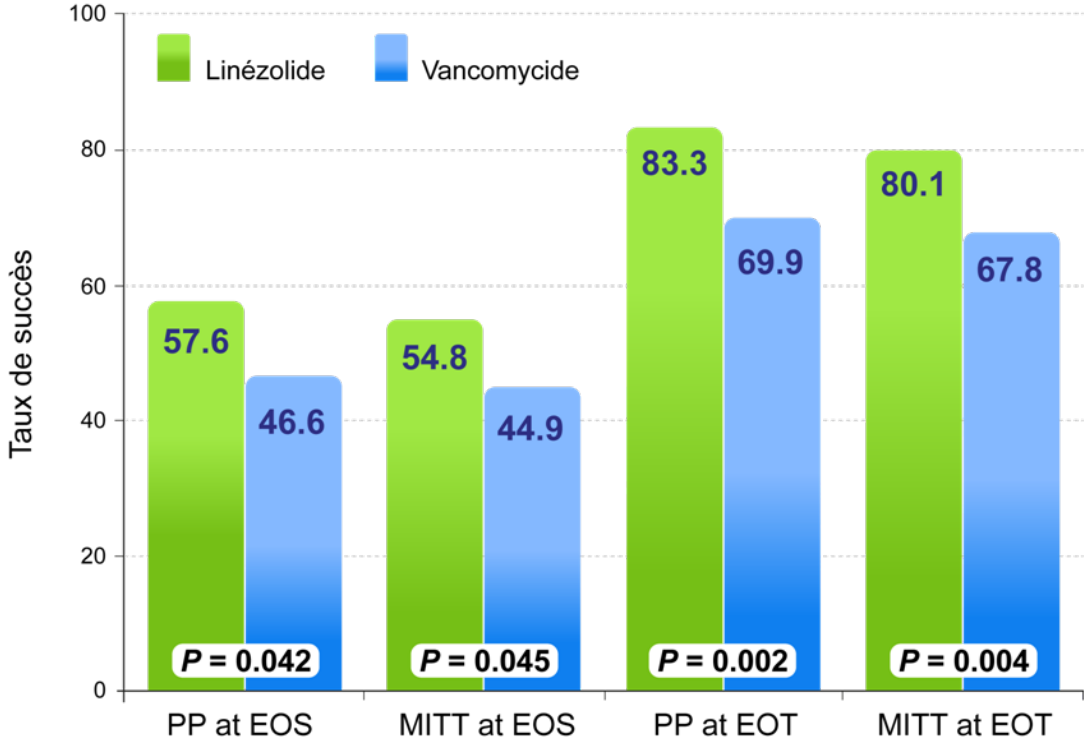
Linézolide vs Vancomycine dans le Traitement des PN Documentées à SARM (ZEPHyR)



- **La dose de vancomycine était ajustée par le pharmacien selon la fonction rénale et les taux résiduels**
- L'administration initiale de céfépime ou d'un autre antibiotique actif sur les Gram négatif (non actif sur le SARM) était systématique

Kunkel M, IDSA, Vancouver, 21-24 oct 2010, non publié

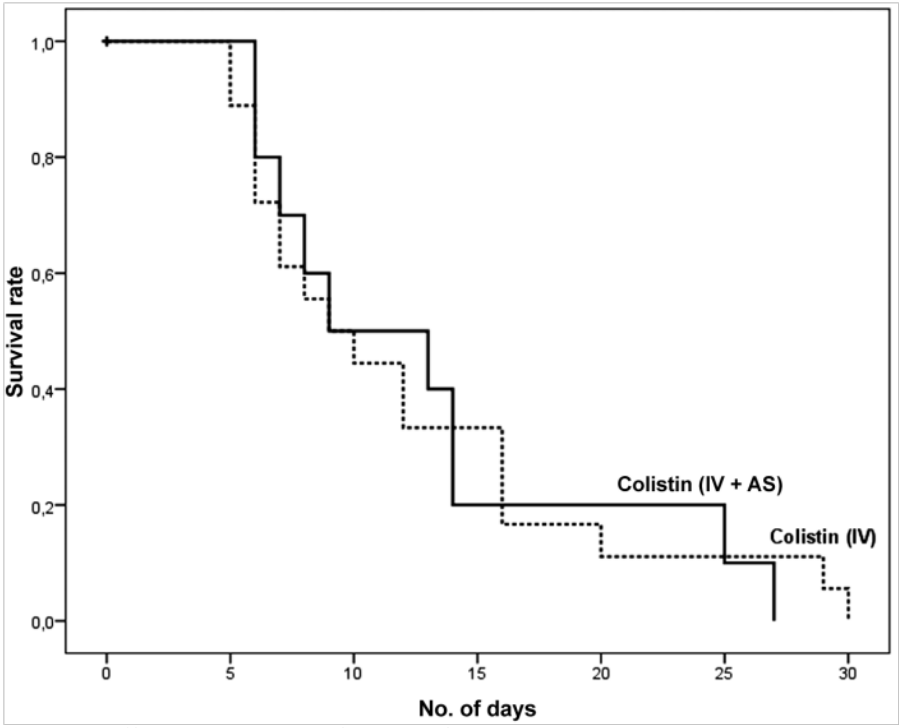
Linézolide vs Vancomycine dans le Traitement des PN Documentées à SARM



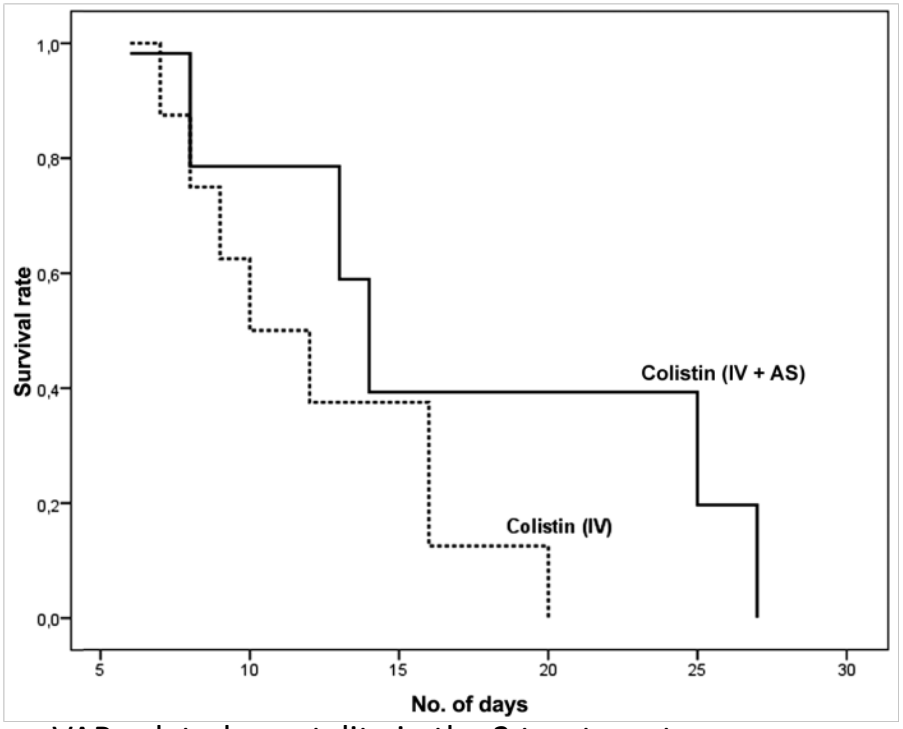
	Linézolide	Vancomycine	*P*	IC à 95 %
Sujets	165 (100)	174 (100)		
Succès / guérison	95 (57,6)	81 (46,6)	0,042	0,5% ; 21,6%
Échec	70 (42,4)	93 (53,4)		

Kunkel M, IDSA, Vancouver, 21-24 oct 2010, non publié

Aerosolized plus IV Colistin *vs* IV Colistin Alone for the Treatment of VAP



All-cause mortality in the 2 treatment groups



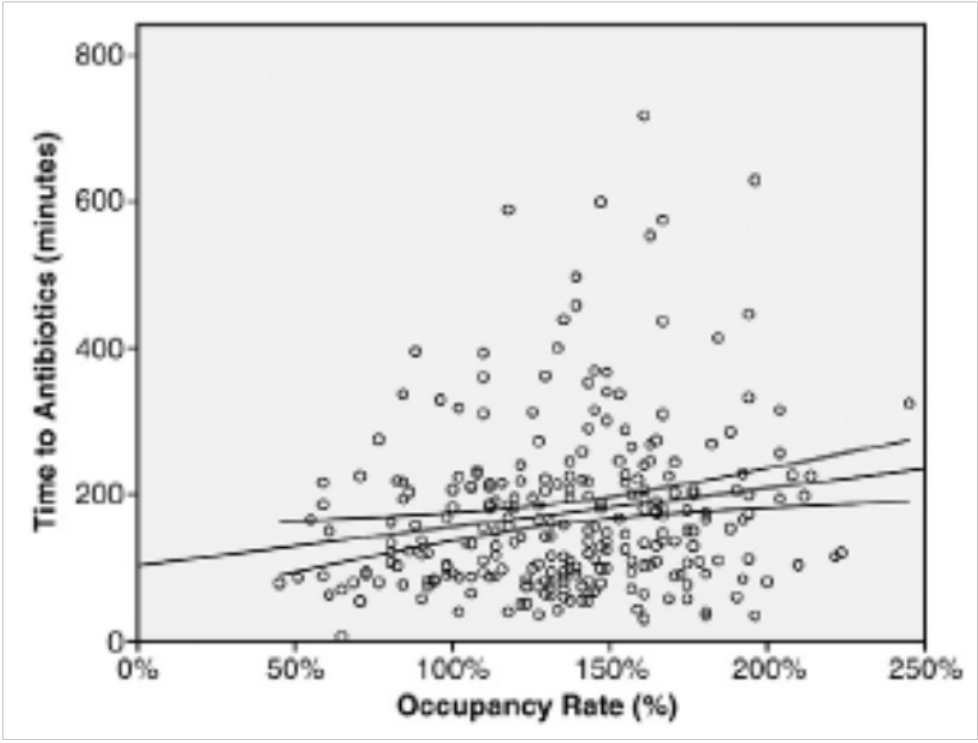
VAP-related mortality in the 2 treatment groups

No significant differences between the 2 groups : clinical cure (*P*=.10), mortality (*P*=.289),
Eradication of pathogens (*P*=.679).
Eight patients (19%) in each treatment group developed reversible renal dysfunction.

Kofteridis DP Clin Infect Dis 2010;51:1238-1244

ED Crowding is Associated with an Increased Time to Pneumonia Treatment

- Etude rétrospective sur 5 mois,
  - **Urgences**
  - **334 pts, 262 dossiers complets**
  - **Taux d'occupation : de 20% à 245%**
  - **81% pts : ABT < 4h**
- Délai médian de tt ABT : 150 mn
- Délai de TT ABT : corrélé au taux d'occupation
  - **Spearman ρ = 0,17, P = ,008**
- Taux d'occupation associé à diminution du risque de recevoir le TT ABT < 4h
  - **OR 0.31; IC95% 0.13-0.75**
- Courbes ROC :
  - **0,62 (95%CI, 0,54-0,70; P = ,009)**



Sikka R Am J Emerg Med 2010;28:809-812

Merci