Une place pour les nouveaux antibiotiques dans le traitement de la pneumonie aigue communautaire ?

M. Wolff

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GREPI 2016

Liens d'intérêt

Type de lien	Compagnies
Expertises ponctuelles	Menarini
Orateur réunion scientifique	Gilead, MSD, Pfizer
« Boards scientifiques »	Basilea, MSD, Sanofi
Partenariat réunions scientifiques (Journée Hôpital Claude Bernard & Journée Scientifique Fédération de Transplantation, Paris 7)	Astellas, MSD, Pfizer, Gilead, GSK, Novartis, Roche, Sanofi (Pasteur)
« Chairman » DMC	MedImmune (AstraZeneca)

Improved survival among ICU-hospitalized patients with community-acquired pneumonia by unidentified organisms: a multicenter case–control study

Eur J Clin Microbiol Infect Dis 2016

J. Rello[1,2] · E. Diaz[2,3] · R. Mañez[4] · J. Sole-Violan[2,5] · J. Valles[2,6] · L. Vidaur[2,7] · R. Zaragoza[8] · S. Gattarello[9] · CAPUCI II Consortium

Variable	2008–2015 (n = 140)	2000–2002 (n = 193)
Previous antibiotic	26 (18.6)	50 (25.6)
Monotherapy	**8 (5.7)**	**44 (22.8)**
Combined therapy	**132 (94.3)**	**149 (77.2)**
Antibiotic initiated 0 to 3 h	**102 (72.9)**	**97 (50.3)**
Antibiotic initiated 4 to 6 h	**25 (17.9)**	**59 (30.6)**
Antibiotic initiated more than 6 h	**13 (9.3)**	**37 (19.2)**
Adequate treatment according to 2007 IDSA/ATS guidelines	**99 (70.7)**	**93 (48.2)**

Facteurs associés à la survie

Variable	Survival (n = 259)	No survival (n = 74)	Univariate analysis: p-value	Multivariate analysis: OR (95 % CI); p-value
Need for vasopressors	**93 (35.9)**	**52 (70.3)**	**<0.01**	0.89 (0.40–1.96); 0.77
Invasive mechanical ventilation	**128 (49.4)**	**67 (90.5)**	**<0.01**	**0.24 (0.10–0.62); <0.01**
Acute kidney injury	**58 (22.7)**	**45 (63.4)**	**<0.01**	**0.21 (0.10–0.44); <0.01**
Rapid radiographic spread	**105 (41.3)**	**41 (57.7)**	**0.02**	0.58 (0.29–1.16); 0.12
Adequate treatment according to 2007 IDSA/ATS guidelines	**164 (63.3)**	**28 (37.8)**	**<0.01**	**2.22 (1.11–4.43); 0.02**
Estimated probability of death[a]	**26.0 (15.0–42.0)**	**46.0 (26.5–61.0)**	**<0.01**	**0.97 (0.95–0.99); <0.01**
Combined therapy	220 (84.9)	61 (82.4)	0.59	
Antibiotic initiated within 3 h	**166 (64.1)**	**33 (44.6)**	**<0.01**	**3.48 (1.70–7.15); <0.01**

Clinical Review & Education

Review

JAMA. 2016;315(6):593-602.

Antibiotic Therapy for Adults Hospitalized With Community-Acquired Pneumonia
A Systematic Review

Jonathan S. Lee, MD; Daniel L. Giesler, MD, PharmD; Walid F. Gellad, MD, MPH; Michael J. Fine, MD, MSc

CONCLUSIONS AND RELEVANCE In adults hospitalized with community-acquired pneumonia, antibiotic therapy consisting of β-lactam plus macrolide combination therapy or fluoroquinolone monotherapy initiated within 4 to 8 hours of hospital arrival was associated with lower adjusted short-term mortality, supported predominantly by low-quality observational studies.

Community-acquired pneumonia

Elena Prina, Otavio T Ranzani, Antoni Torres

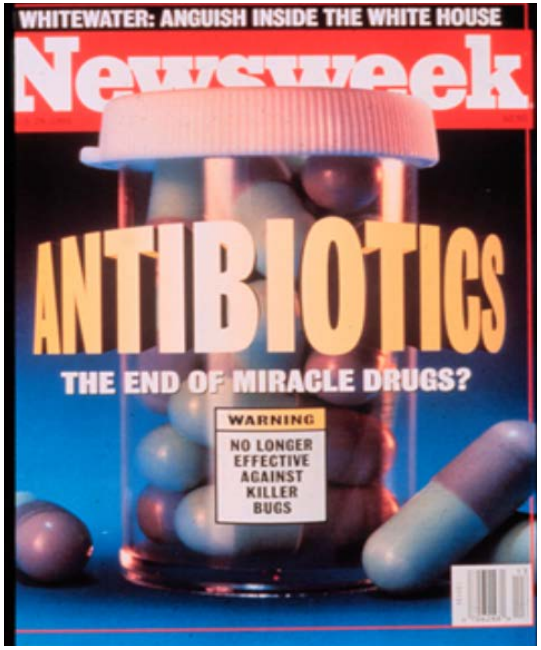
Lancet 2015; 386: 1097–108

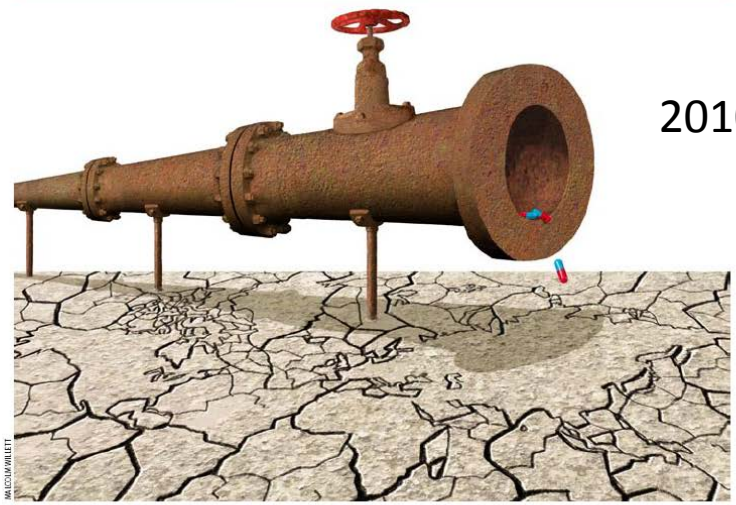
	American (IDSA/ATS)[3]		British (NICE/BTS)[4,6]		European[5]	
	Preferred	Alternative	Preferred	Alternative	Preferred	Alternative
Inpatient not in ICU; moderate severity	β-lactam* plus macrolide	Respiratory fluoroquinolone	Amoxicillin plus macrolide	Respiratory fluoroquinolone†	Aminopenicillin with or without macrolide	Respiratory fluoroquinolone
Inpatient in ICU; high severity	β-lactam‡ plus macrolide	β-lactam‡ plus respiratory fluoroquinolone	β-lactamase stable β-lactams¶ plus macrolide	Respiratory fluoroquinolone†	Third-generation cephalosporin§ plus macrolide	Respiratory fluoroquinolone with or without a third-generation cephalosporin§

Dans ce cadre, quel apport pour des nouvelles molécules ?

Intérêt de nouvelles molécules?

1) La prise en compte de bactéries résistantes
2) Une meilleure efficacité sur des bactéries sensibles
3) Un spectre large permettant une monothérapie
4) Effet anti-inflammatoire





2010

HEALTH SYSTEMS PERSPECTIVES

Stoking the antibiotic pipeline

Très peu de nouveaux antibiotiques en développement

Laxminarayan R *et al.* Lancet Infect Dis. 2013 ;13(12):1057-98

Le pipeline n'est plus à sec!!!!

Les nouvelles molécules (phase 3 ou sur le marché)

Molécules	Gram+	Gram-	IntraC
Ceftolozane-tazobactam*	+/-	+++ (BLSE, *P. aeruginosa*)	-
Ceftazidime-avibactam*	+/-	+++ (tous, certaines EPC)	-
Ceftaroline*	+++ (SARM)	++ (entérobactéries sauf BLSE)	-
Ceftobiprole*	+++ (SARM)	++ (id +/- *P. aeruginosa*)	-
Délafloxacine (FQ)**	+++ (SARM)	+++ (entérobactéries)	+++
Solithromycine (KT)**	+++	+/-	+++
Omadacycline*et **	+++	++	++
Tédizolide (OX)**	+++ (SARM)	-	-
Eravacycline (Cyc) * et **	++	+++ (tous y compris EPC)	?

* Voie IV, ** voie orale

Rethinking the concepts of community-acquired and health-care-associated pneumonia

Lancet Infect Dis 2010; 10: 279–87

Santiago Ewig, Tobias Welte, Jean Chastre, Antoni Torres

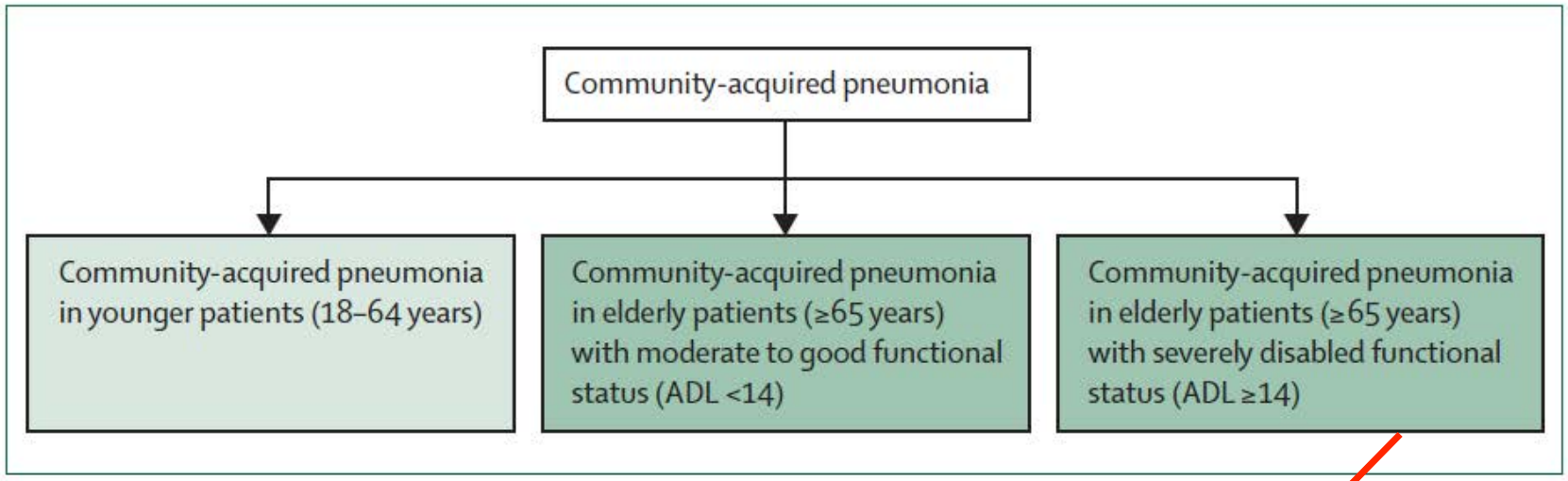
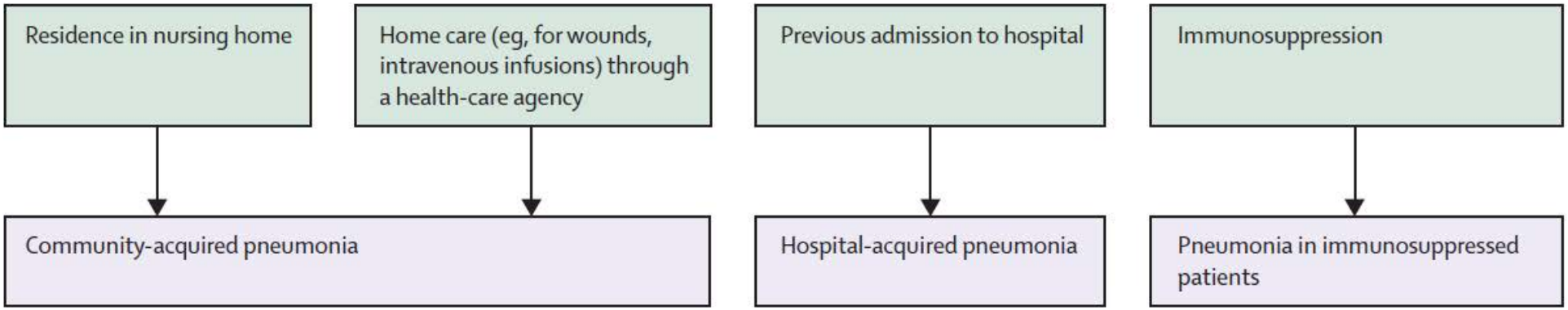


Figure 2: **Suggested subdivision of community-acquired pneumonia according requirements and risk factors modifying the expected microbial spectrum**
ADL=activities of daily living score.

Bactéries résistantes ?

Criteria used to define health-care-associated pneumonia



ORIGINAL ARTICLE INFECTIOUS DISEASES

Low incidence of multidrug-resistant organisms in patients with healthcare-associated pneumonia requiring hospitalization

C. Garcia-Vidal[1], D. Viasus[1], A. Roset[1], J. Adamuz[1], R. Verdaguer[2], J. Dorca[3], F. Gudiol[1] and J. Carratalà[1]

1) *Infectious Disease*, 2) *Microbiology and* 3) *Respiratory Medicine Services, Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), Hospital Universitari de Bellvitge, University of Barcelona, L'Hospitalet de LLobregat, Barcelona, Spain*

Patients avec HCAP groupés par facteurs de risque de BMR

1. Group 1: received any intravenous therapy at home; received wound care or specialized nursing care through a healthcare agency, family, or friends; or had self-administered intravenous medical therapy in the 30 days before pneumonia (patients whose only home therapy was oxygen were excluded).
2. Group 2: attended a hospital or haemodialysis clinic or received intravenous chemotherapy in the 30 days before pneumonia.
3. Group 3: admitted to an acute-care hospital for two or more days in the 90 days before pneumonia.
4. Group 4: resided in a nursing home or long-term-care facility.

Clin Microbiol Infect 2011; **17:** 1659–1665

ORIGINAL ARTICLE INFECTIOUS DISEASES

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TABLE 3. Aetiology by epidemiological group

	CAP	HCAP						
		Group 1[a]		Group 2[a]		Group 3[a]		Group 4[a]
Aetiology	*n* = 1668, no. (%)	*n* = 19, no. (%)	p	*n* = 198, no. (%)	p	*n* = 137, no. (%)	p	*n* = 131, no. (%)	p
Streptococcus pneumoniae	686 (41.1)	8 (42.1)	0.92	80 (40.4)	0.85	51 (37.2)	0.37	49 (37.4)	0.41
Bacteraemic pneumococcal pneumonia	175 (10.9)	1 (5.9)	1	33 (12)	0.66	9 (7)	0.16	12 (9.8)	0.68
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Aspiration pneumonia	91 (5.5)	3 (15.8)	0.08	18 (9.1)	0.03	13 (9.5)	0.05	37 (28.2)	<0.001
Staphylococcus aureus	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	0.37	1 (0.8)	0.36
Atypical pneumonia	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	0.18
Gram-negative bacilli	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	0.31
Bacteraemic Gram-negative bacilli pneumonia	14 (0.8)	0 (0)	1	2 (1)	0.68	2 (1.5)	0.34	2 (1.5)	0.32
Pseudomonas aeruginosa	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	0.67	1 (0.8)	1
Bacteraemic *Pseudomonas aeruginosa* pneumonia	5 (0.3)	0 (0)	1	2 (1)	0.16	1 (0.7)	0.37	0 (0)	1
Other aetiologies	32 (1.9)	0 (0)	1	1 (0.5)	0.24	1 (0.7)	0.50	2 (1.5)	1
Unknown aetiology	602 (36.2)	7 (36.8)	0.95	75 (38.1)	0.60	46 (33.8)	0.58	35 (26.7)	0.02

« Antibiotic-resistant organisms, including MRSA, resistant strains *of Pseudomonas aeruginosa*, and ESBL-producing *Enterobacteriaceae*, were scarce in all groups »

SEULE VRAIE DIFFÉRENCE : PLUS DE PNEUMONIES D'INHALATION CHEZ LES PATIENTS VIVANT EN INSTITUTION

« No differences were found regarding inappropriate initial empirical antibiotic therapy between groups. »

Clin Microbiol Infect 2011; **17:** 1659–1665

Ceftaroline: activité *in vitro*

Gram-positive organisms	Gram-negative organisms
Staphylococcus aureus	*Enterobacter cloacae*
MRSA	*Citrobacter freundii*
MSSA	ESBL-negative *Escherichia coli*
VISA	ESBL-negative *Klebsiella pneumoniae*
VRSA	*Proteus mirabilis*
Coagulase-negative staphylococci	*Providencia rettgeri*
Enterococcus faecalis	*Providencia stuartii*
Listeria monocytogenes	*Serratia marcescens*
Streptococcus agalactiae	*Shigella* spp.
Streptococcus pneumoniae	*Moraxella catarrhalis*
levofloxacin resistant	*Haemophilus influenzae*
penicillin resistant	β-lactamase positive
penicillin intermediate	β-lactamase negative
penicillin susceptible	β-lactamase negative, ampicillin resistant
Streptococcus pyogenes	*Pasteurella multocida*
macrolide resistant	
macrolide susceptible	
Viridans group streptococci	
β-Haemolytic group A streptococci	
β-Haemolytic group B	

Laudano J et al. J Antimicrob Chemother 2011; 66 Suppl 3: iii11–iii18

J Antimicrob Chemother 2016; **71**: 862–870
doi:10.1093/jac/dkv415 Advance Access publication 24 December 2015

Journal of Antimicrobial Chemotherapy

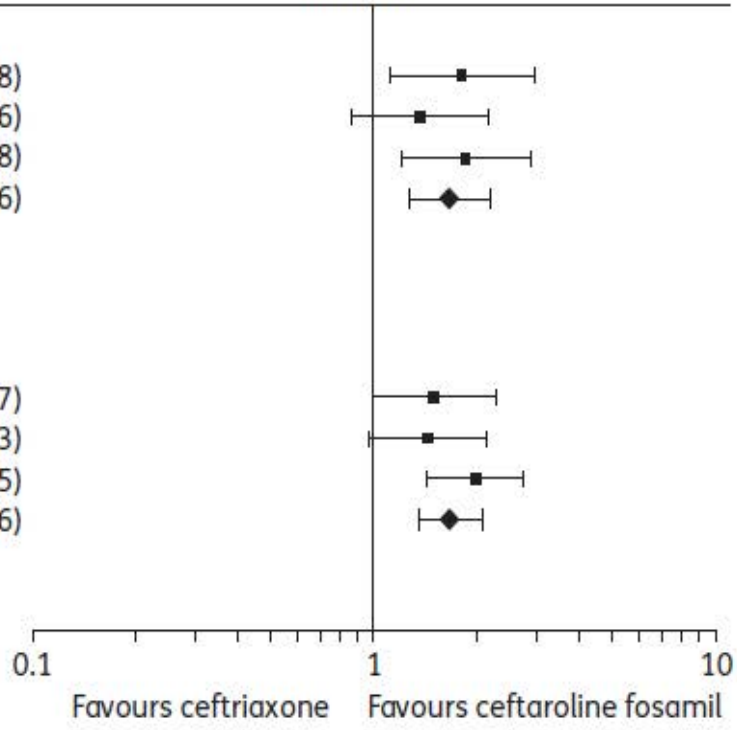
Ceftaroline fosamil versus ceftriaxone for the treatment of community-acquired pneumonia: individual patient data meta-analysis of randomized controlled trials

Maria Taboada[1]*, David Melnick[2]†, Joseph P. Iaconis[3], Fang Sun[4], Nan Shan Zhong[5], Thomas M. File[6,7], Lily Llorens[8]‡, H. David Friedland[8]§ and David Wilson[1]

- 3 études de phase 3 : 1916 patients hospitalisés
- Ceftaroline: 600 mg x 2 *vs* ceftriaxone: 1-2 g/j, 5-7 j
- Critère de jugement: réponse clinique 8-15 j après arrêt du tt, population mITT et CE
- PORT 3 ou 4

Guérison clinique (critère principal)

Study or subgroup	Ceftaroline fosamil Cures	Total	Ceftriaxone Cures	Total	Weight	OR (95% CI)
CE population						
FOCUS 1	194	224	183	234	29.4%	1.80 (1.11, 2.98)
FOCUS 2	193	235	166	215	33.7%	1.36 (0.86, 2.16)
Asia CAP	217	258	178	240	36.9%	1.84 (1.19, 2.88)
Fixed effect					100.0%	1.65 (1.26, 2.16)
Total events	604		527			
Heterogeneity: $\chi^2=1.06$, df = 2 ($P=0.59$); $I^2=0.00\%$						
MITT population						
FOCUS 1	244	291	233	300	27.6%	1.49 (0.99, 2.27)
FOCUS 2	235	289	206	273	28.9%	1.42 (0.95, 2.13)
Asia CAP	305	381	256	382	43.5%	1.98 (1.42, 2.75)
Fixed effect					100.0%	1.66 (1.34, 2.06)
Total events	784		695			
Heterogeneity: $\chi^2=1.92$, df = 2 ($P=0.38$); $I^2=0.00\%$						



	ceftaroline fosamil ($n=211$)	ceftriaxone ($n=209$)
All patients	184/211 (87.2)	166/209 (79.4)
monomicrobial	137/154 (89.0)	120/150 (80.0)
polymicrobial	47/57 (82.5)	46/59 (78.0)
Gram-positive		
S. aureus	22/29 (75.9)	17/31 (54.8)
S. pneumoniae	73/85 (85.9)	54/74 (73.0)
Gram-negative		
E. coli	13/15 (86.7)	14/18 (77.8)
H. influenzae	26/30 (86.7)	23/27 (85.1)
H. parainfluenzae	16/16 (100.0)	19/23 (82.6)
K. pneumoniae	24/27 (88.9)	22/28 (78.6)

Ceftaroline > ceftriaxone ?????

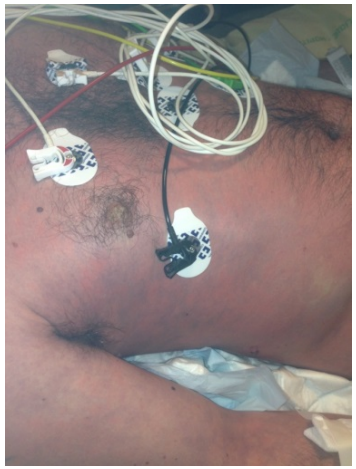
1. Meilleure activité *in vitro* sur les Gram +: CMI_{90} (mg/L)

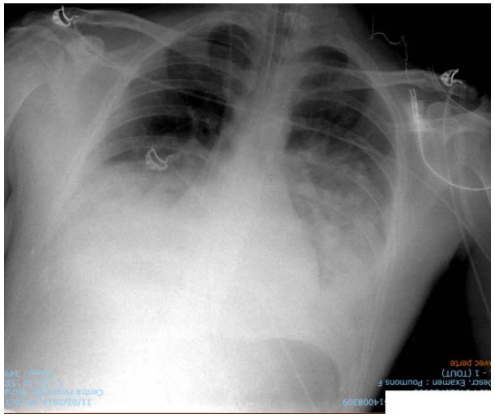
	Ceftaroline	Ceftriaxone
S. pneumoniae	0,03	0,5
S. aureus	0,25	4

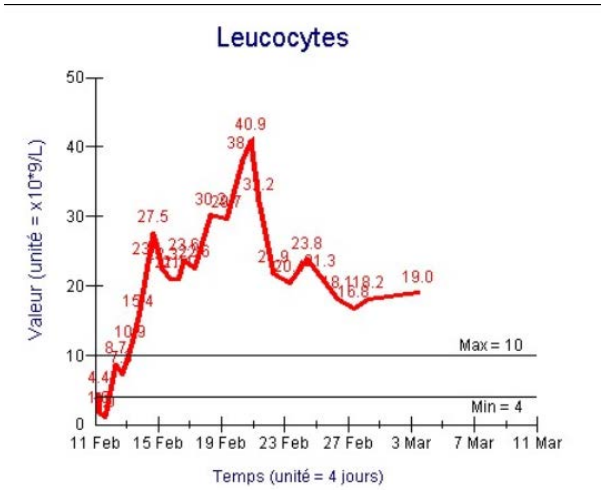
2. Meilleurs paramètres PK-PD ???: plus de forme libre (80% vs 5%), diffusion un peu supérieure….

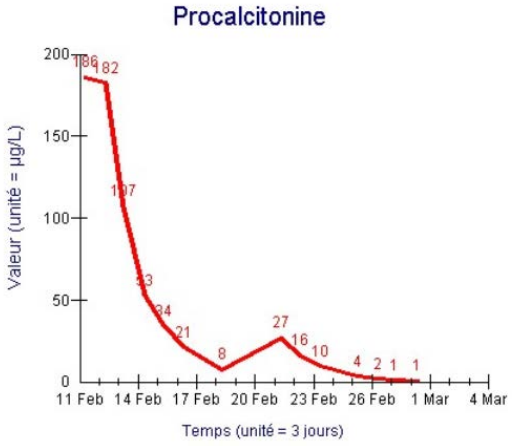
« …. Ceftaroline fosamil should be considered as a replacement of ceftriaxone for the cephalosporin component of empirical antibiotic regimens in adult patients hospitalized with CAP »

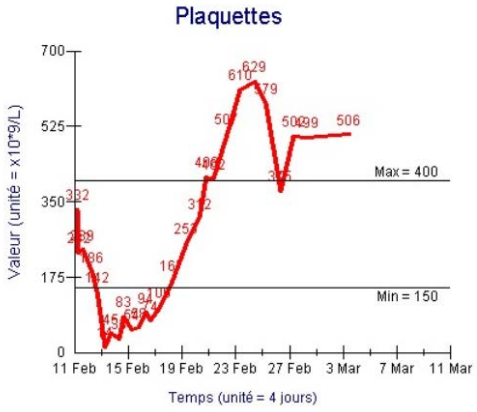
Un homme de 45 ans en insuffisance respiratoire aigue et choc











PDP: direct : rares BGN, nbx CGP en diplo et amas

S

Né(e) le 24/03/1984 Sexe : F
NIP : 3514008309 C

** EXAMEN N. **814072142** *du 11/02/14*
Enregistré le : 11/02/14
Edité le 13/02/14

Réanimation Réa Médicale -1

Bichat -1 Réa Med
Tel : 58122 Fax : 58782

Page 1

PRELEVEMENT RESPIRATOIRE

Nature du prélèvement: **Distal protégé**

Examen direct

Rares hématies
Assez nombreux leucocytes
Quelques cellules
Rares débris cellulaires

Germe(s)

Rares bacilles gram négatif
Nombreux cocci gram positif en diplocoques et amas

Culture

Flore polymicrobienne avec

Très nombreux cocci gram positif
10^6 cocci gram positif en amas

Nature du prelevement:souche isolee n° **81407214**2 a partir d'une souche de pt distal

mecA(encode pour la resistance à la méticilline):Positive

femA spécifique Staphylococcus aureus: **POSITIVE**

Gène luk-PV(encode pour la leucocidine de Panton et Valentine):Positive

Conclusion:

Staphylococcus aureus résistant à la méticilline et portant le gène leucocidine de Panton et Valentine

Examen terminé

ARD
..40.25.80.80
r A. ANDREMONT
N-VEZINET)
BK: 53508 Hygiène: 58516

Médicale -1

l Réa Med
58782

Page 1

hylococcus aureus

Edité le 13/02/14

Page 2

Identification 1

Staphylococcus aureus

SENSIBILITE AUX ANTIBIOTIQUES

		CMI mg/L
Pénicilline G	**Résistant**	
Oxacilline	**Résistant**	
Kanamycine	**Résistant**	
Gentamicine	Sensible	
Tobramycine	Sensible	
Tétracycline	Sensible	
Erythromycine	**Résistant**	
Lincomycine	Sensible	
Pristinamycine	Sensible	
Fosfomycine	Sensible	
Acide fucidique	Sensible	
Rifampicine	Sensible	
Vancomycine	Sensible	1.5
Teicoplanine	Sensible	1
Ofloxacine	**Résistant**	
Lévofloxacine	**Résistant**	
Linézolide	Sensible	2

Examen terminé

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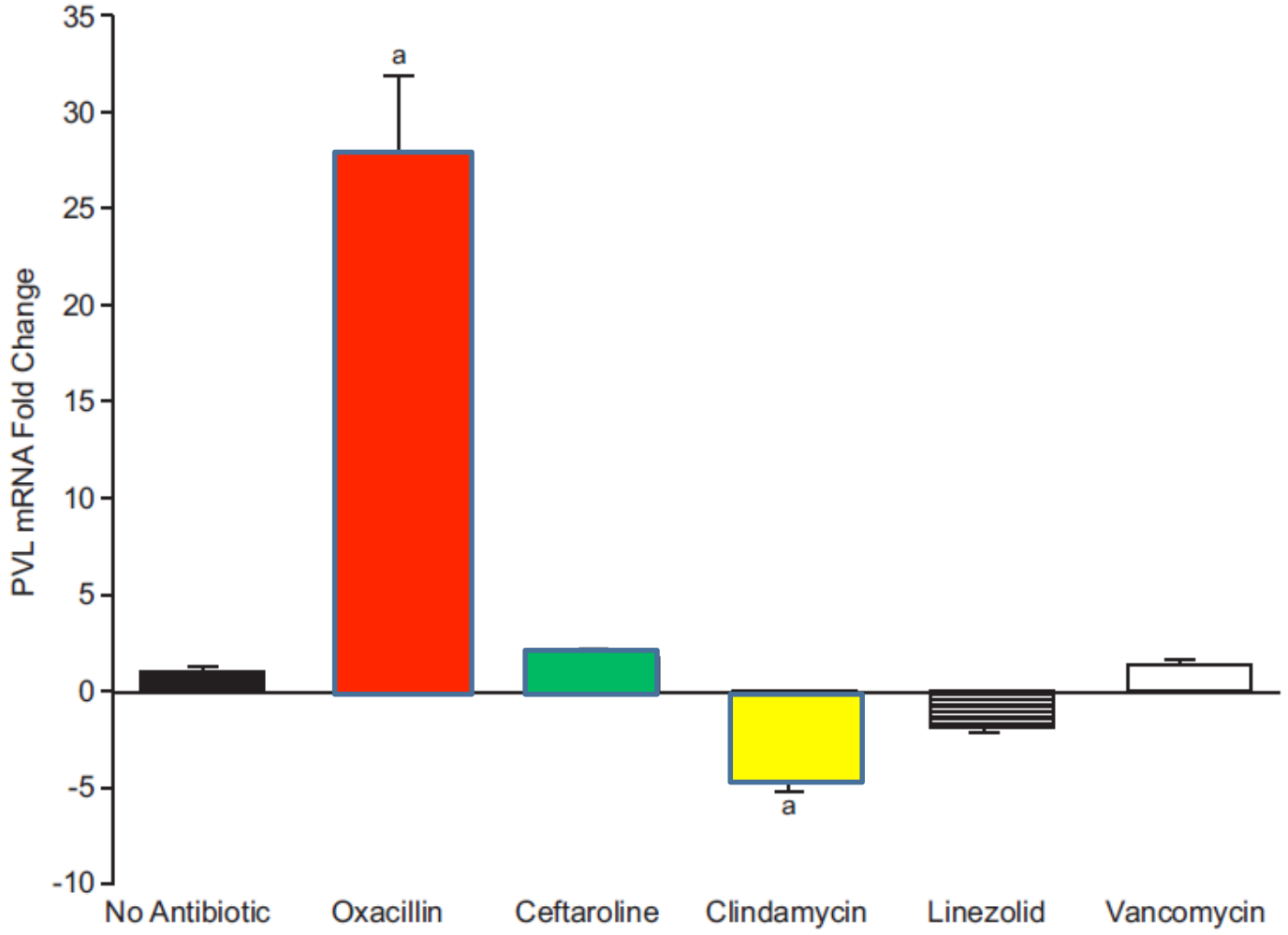
April 2014 Volume 58 Number 4

In Vivo Efficacy of Ceftaroline Fosamil in a Methicillin-Resistant Panton-Valentine Leukocidin-Producing *Staphylococcus aureus* Rabbit Pneumonia Model

Croisier-Bertin D *et al.*



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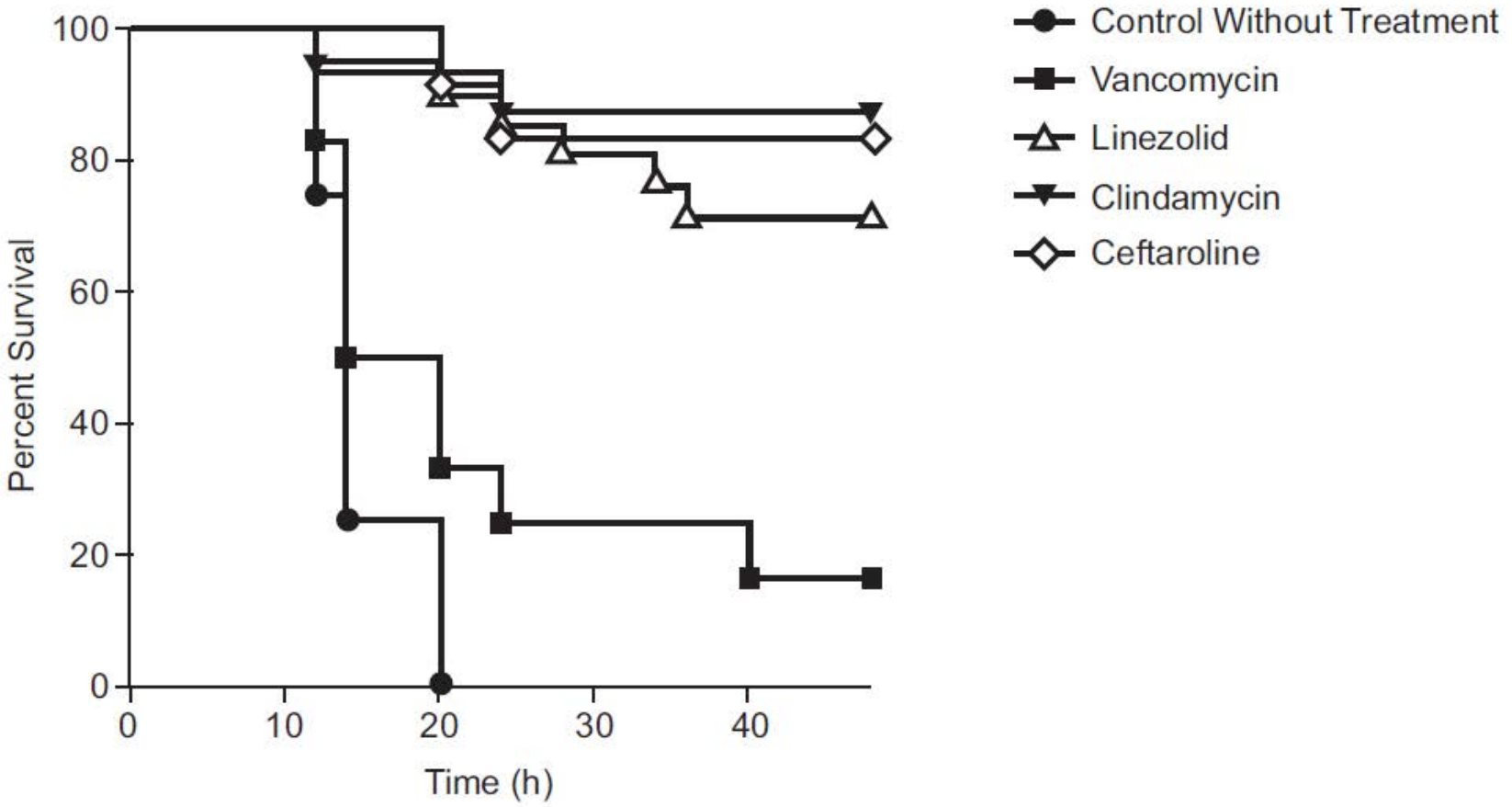
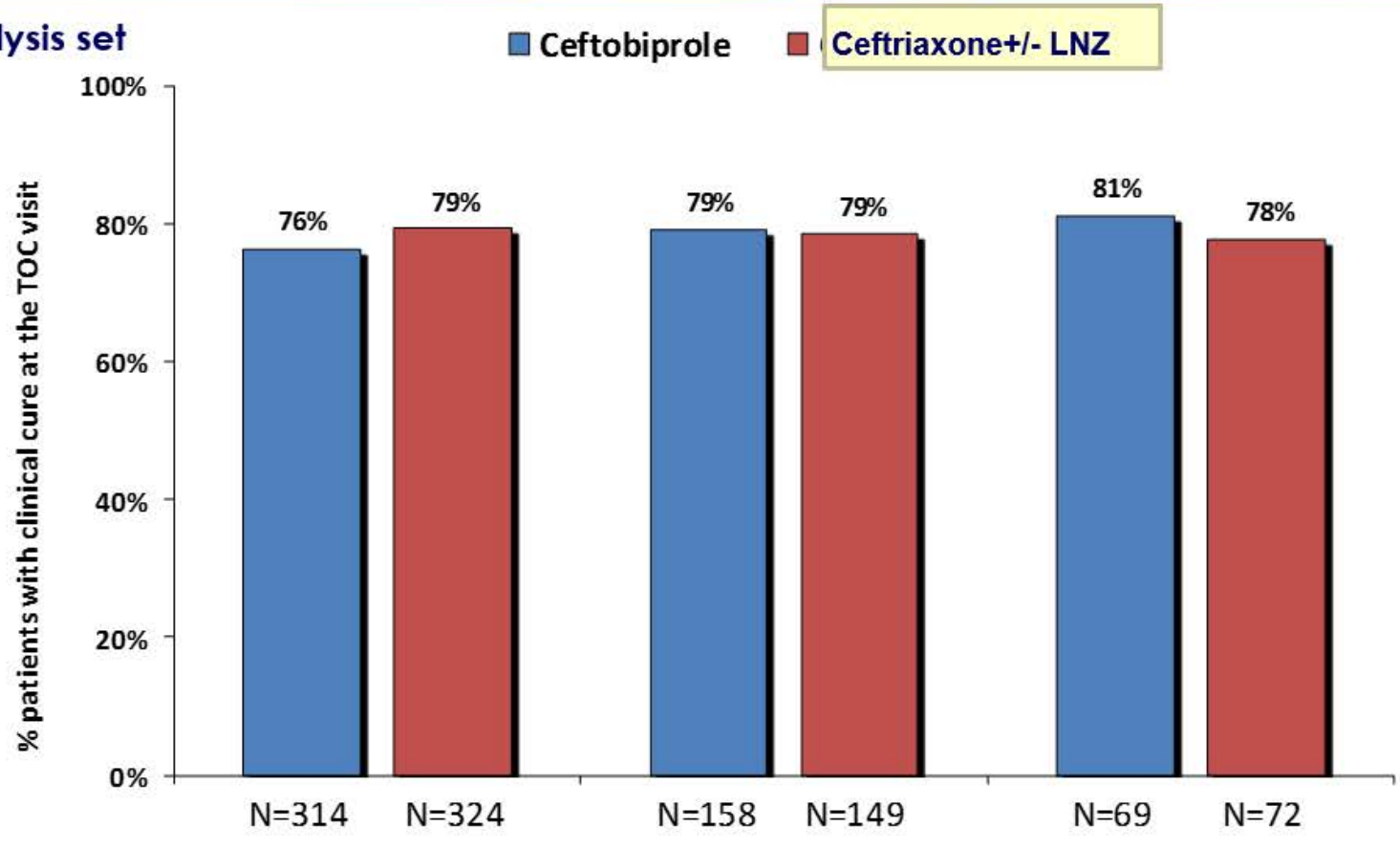
In Vivo Efficacy of Ceftaroline Fosamil in a Methicillin-Resistant Panton-Valentine Leukocidin-Producing *Staphylococcus aureus* Rabbit Pneumonia Model



Croisier-Bertin *et al*.

Clinical cure at TOC (ITT analysis set)

ITT analysis set



Ceftobiprole vs Ceftriaxone ± Linezolid:	All patients	PORT Risk Classes ≥ III	PORT Risk Classes ≥ IV
Difference (95% CI):	**-2.9%** (-9.3; 3.6)	**0.6%** (-8.6; 9.7)	**3.4%** (-9.9; 16.7)

n=4 (ceftobiprole); n=7 patients (comparator) in PORT Risk Class V

Welte, T. *et al.* 2014 ECCMID Poster eP431,

basilea

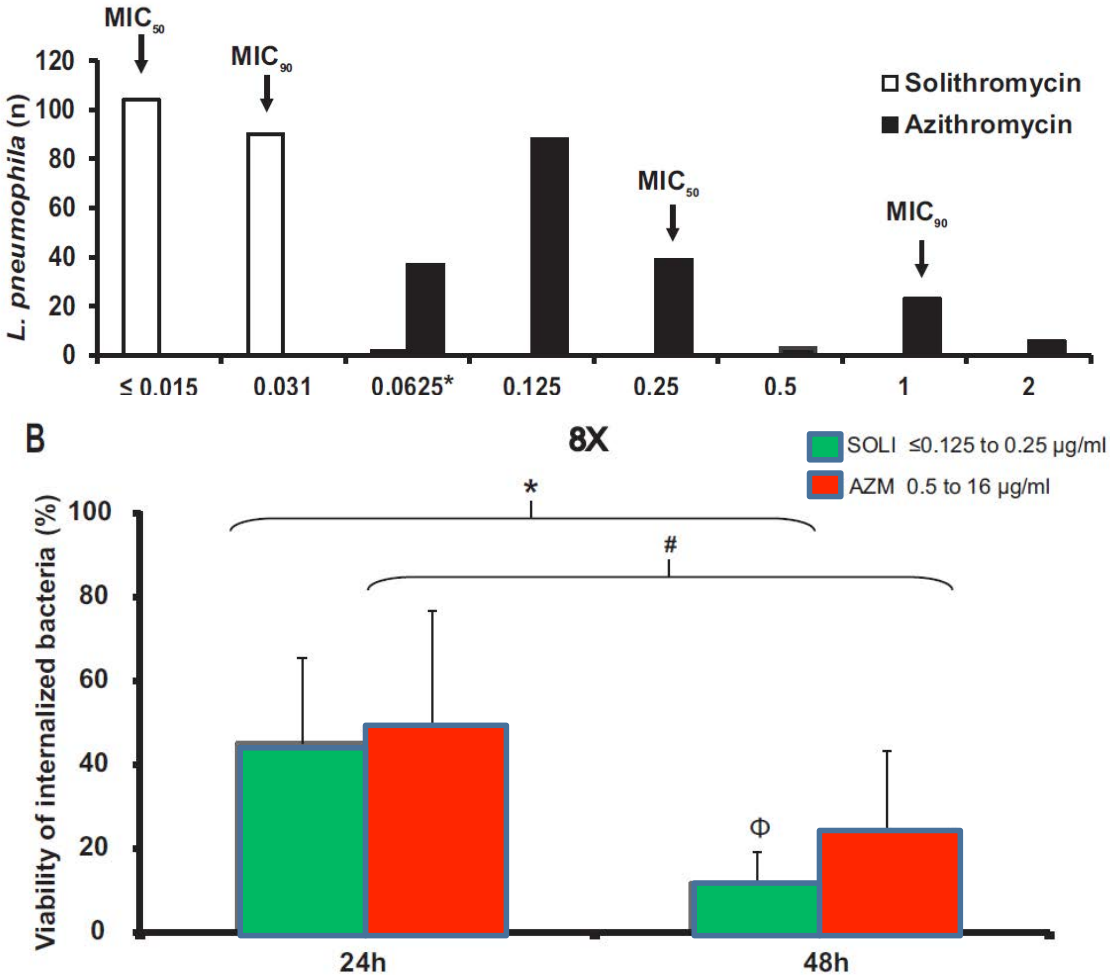
Solithromycine: activité *in vitro*

Bactéries	CMI_{90} (mg/L)
S. pneumoniae	0,12
S. aureus MS	0,06
Streptocoques	0,03
H. influenzae	2
M. catharralis	0,12
L. pneumophila	0,03
M. pneumoniae	0,5

Farell DJ, *et al*. AAC 2014

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

L. pneumophila



Mallegol J, *et al*. AAC 2014

Efficacy and safety of oral solithromycin versus oral moxifloxacin for treatment of community-acquired bacterial pneumonia: a global, double-blind, multicentre, randomised, active-controlled, non-inferiority trial (SOLITAIRE-ORAL)

Lancet Infect Dis 2016; 16: 421–30

Carlos M Barrera, Analia Mykietiuk, Hristo Metev, Mimi Floarea Nitu, Najumuddin Karimjee, Pablo Alexis Doreski, Ismail Mitha, Cristina Mihaela Tanaseanu, Joseph McDermott Molina, Yuri Antonovsky, Dirkie Johanna Van Rensburg, Brian H Rowe, Jose Flores-Figueroa, Barbara Rewerska, Kay Clark, Kara Keedy, Amanda Sheets, Drusilla Scott, Gary Horwith, Anita F Das, Brian Jamieson, Prabhavathi Fernandes, David Oldach, for the SOLITAIRE-ORAL Pneumonia Team

- Solithromycine: 800 mg à J1, 400 mg/j de J2-J5, placebo J6-J7
- Moxifloxacine: 400 mg/j de J1-J7

	Solithromycin group (n=426)	Moxifloxacin group (n=434)
(Continued from previous column)		
PORT score*		
Mean (SD)	71·7 (13·4)	71·2 (13·3)
Median (min–max)	71·0 (48–108)	69·0 (51–112)
PORT risk class*		
I	1 (<1%)	0
II	209 (49%)	223 (51%)
III	168 (39%)	173 (40%)
IV	48 (11%)	38 (9%)
CURB-65 score†		
0	135/416 (32%)	138/429 (32%)
1	175/416 (42%)	166/429 (39%)
2	97/416 (23%)	110/429 (26%)
3	8/416 (2%)	14/429 (3%)
4	1/416 (<1%)	1/429 (<1%)
Met SIRS criteria‡	231 (54%)	262/429 (60%)

Résultats (critère principal)

	Solithromycin group	Moxifloxacin group	Difference (95% CI)
Early clinical response *			
Intention-to-treat population	333/426 (78·2%)	338/434 (77·9%)	0·29% (–5·5 to 6·1)
PORT II score	168/213 (78·9%)	175/217 (80·6%)	–1·77% (–9·8 to 6·3)
PORT III or IV score	165/213 (77·5%)	163/217 (75·1)	2·35% (–6·2 to 10·9)
Age <65 years	211/271 (77·9%)	240/297 (80·8%)	–2·95% (–10·0 to 4·1)
Age 65–74 years	70/93 (75·3%)	54/74 (73·0%)	2·30% (–12·3 to 16·9)
Age ≥75 years	52/62 (83·9%)	44/63 (69·8%)	14·03% (–2·1 to 30·2)
History of COPD or asthma	44/62 (71·0%)	43/64 (67·2%)	3·78% (–13·9 to 21·5)
Clinically evaluable population	326/403 (80·9%)	330/407 (81·1%)	–0·19% (–5·8 to 5·5)

* À 72 heures

Clinical Infectious Diseases

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Clinical Infectious Diseases® 2016;63(8):1007–16

SOLITAIRE-IV: A Randomized, Double-Blind, Multicenter Study Comparing the Efficacy and Safety of Intravenous-to-Oral Solithromycin to Intravenous-to-Oral Moxifloxacin for Treatment of Community-Acquired Bacterial Pneumonia

Thomas M. File Jr,[1] Barbara Rewerska,[2] Violeta Vucinić-Mihailović,[3] Joven Roque V. Gonong,[4] Anita F. Das,[5] Kara Keedy,[6] David Taylor,[6] Amanda Sheets,[6] Prabhavathi Fernandes,[6] David Oldach,[6] and Brian D. Jamieson[6]; for the SOLITAIRE-IV Pneumonia Team

- 863 patients, 147 centres, 22 pays
- Solithromycine (800 mg J1 puis 400 mg/j) *vs* moxifloxacine (400 mg/j) pendant 7 j (IV puis relais oral si malade stable)
- Critère de jugement: réponse clinique précoce (72 h) en ITT
- Population: PORT 3 ou 4

Table 4. Treatment Outcomes: Early Clinical Response and Clinical Success at Short-term Follow-up

Outcome Measure	Solithromycin, % (no./No.)	Moxifloxacin, % (no./No.)	Delta, % (95% CI)
ECR rate			
ITT population	79.3 (344/434)	79.7 (342/429)	−0.46 (−6.1 to 5.2)
ITT, PORT III/IV/V patients	77.8 (253/325)	80.7 (260/322)	−2.90 (−9.4 to 3.6)
Micro-ITT population	80.3 (139/173)	79.1 (121/153)	+1.26 (−8.1 to 10.6)
ECR with vital sign normalization (ITT)	42.6 (185/434)	38.9 (167/429)	+3.70 (−3.1 to 10.5)
Clinical success at SFU visit			
ITT population	84.6 (367/434)	88.6 (380/429)	−4.02 (−8.8 to .8)
ITT, PORT III/IV patients	85.7 (281/328)	88.0 (293/333)	−2.32 (−7.8 to 2.7)[a]

Réponse clinique précoce dans la population microbiologiquement évaluable

Pathogen	ECR, no./No. (%)	
	Solithromycin	Moxifloxacin
Gram-positive bacteria		
Streptococcus pneumoniae	62/79 (79)	64/76 (84)
MDRSP	10/11 (91)	10/14 (71)
Macrolide-resistant	10/12 (83)	10/14 (71)
Staphylococcus aureus	15/21 (71)	13/16 (81)
MRSA	1/1 (100)	2/2 (100)
MSSA	14/20 (70)	11/14 (79)
Gram-negative bacteria		
Haemophilus influenzae	14/18 (78)	17/20 (85)
Moraxella catarrhalis	4/4 (100)	3/3 (100)
Atypical pathogens		
Mycoplasma pneumoniae	34/39 (87)	23/30 (77)
Macrolide-resistant	1/1 (100)	0
Legionella pneumophila	16/18 (89)	11/17 (67)

Effets indésirables: cliniques : pas de

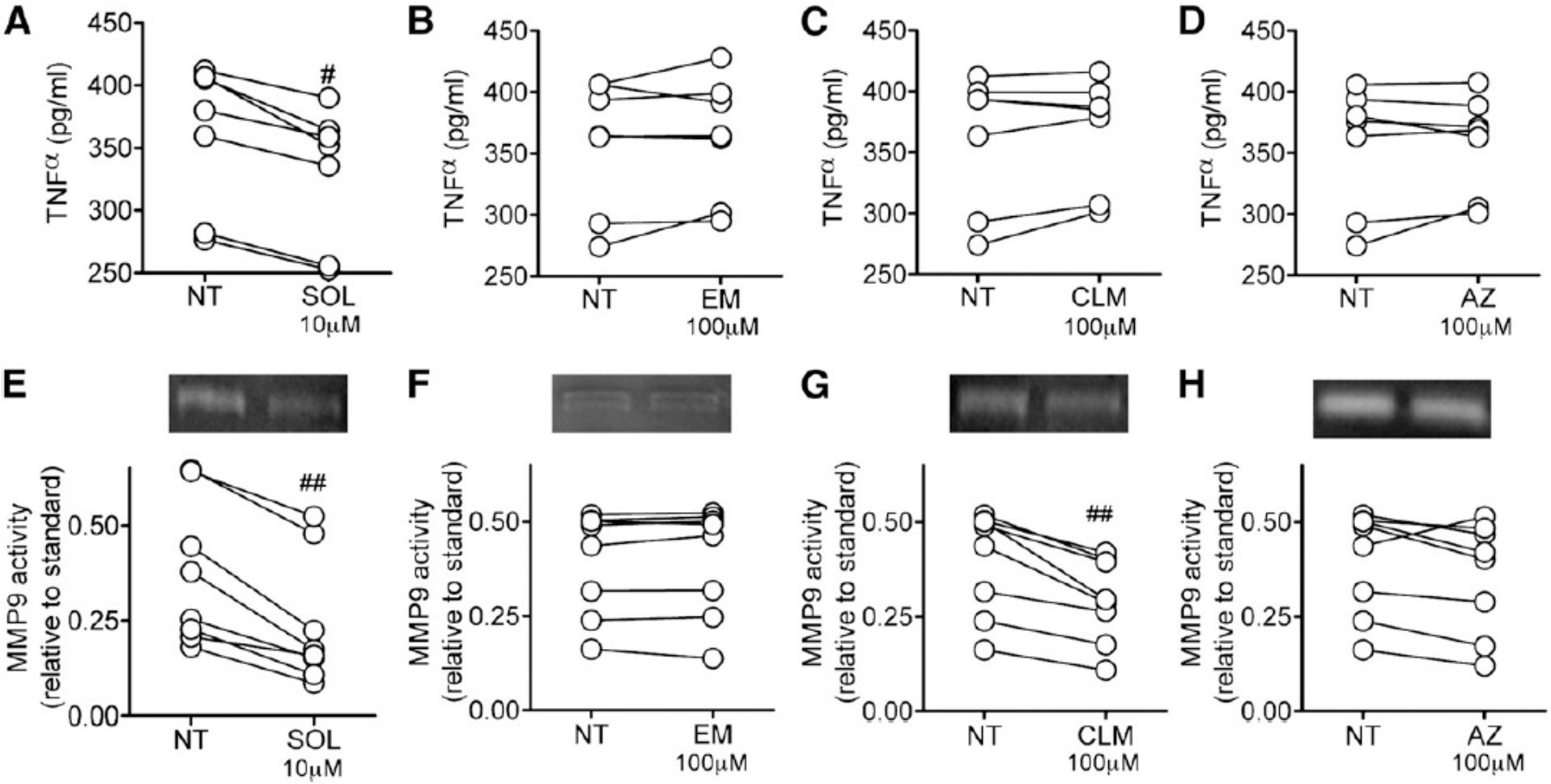
Table 9. Mean Change from Baseline for Selected Laboratory Parameters (Safety Population)

	Mean Change from Baseline (SD)	
Parameter	Solithromycin (n = 432)	Moxifloxacin (n = 426)
ALT, U/L		
Day 4	16.0 (43.33)	5.1 (22.31)
EOT	18.4 (37.19)	6.7 (26.36)
SFU	3.0 (24.62)	1.2 (18.32)
AST, U/L		
Day 4	9.6 (46.26)	0.5 (20.44)
EOT	3.1 (26.14)	−1.8 (19.48)
SFU	−6.0 (22.79)	−4.7 (14.98)
ALP, U/L		
Day 4	5.6 (44.10)	−5.0 (23.26)
EOT	7.0 (54.83)	−6.0 (24.20)
SFU	1.8 (42.25)	−2.8 (26.00)
Total bilirubin, µmol/L		
Day 4	−1.77 (5.108)	−2.41 (5.185)
EOT	−2.02 (5.635)	−2.25 (5.912)
SFU	−1.77 (6.016)	−1.49 (5.731)

A Novel Macrolide Solithromycin Exerts Superior Anti-inflammatory Effect via NF-κB Inhibition[S]

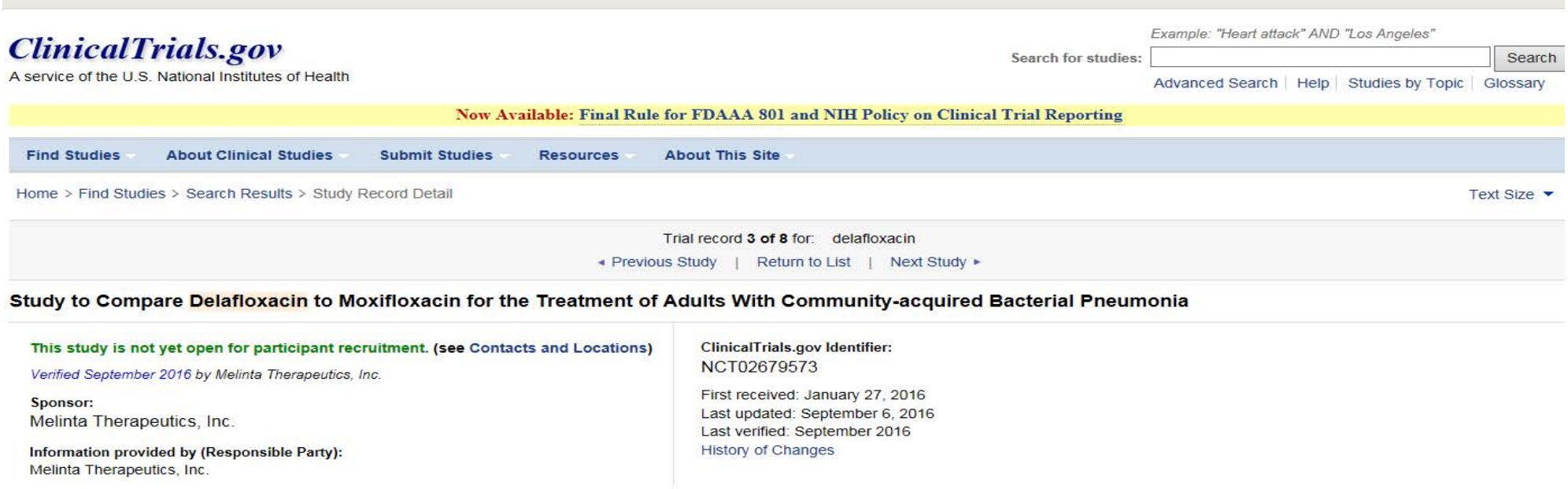
Kobayashi Y, *et al*.

THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS 2013



Effects of macrolides on TNFα release and MMP9 production by PBMC from COPD patients.

La délafloxacine: une perle?



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Trial record 3 of 8 for: delafloxacin
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Study to Compare Delafloxacin to Moxifloxacin for the Treatment of Adults With Community-acquired Bacterial Pneumonia

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified September 2016 by Melinta Therapeutics, Inc.

Sponsor:
Melinta Therapeutics, Inc.

Information provided by (Responsible Party):
Melinta Therapeutics, Inc.

ClinicalTrials.gov Identifier:
NCT02679573

First received: January 27, 2016
Last updated: September 6, 2016
Last verified: September 2016
History of Changes

Délafloxacine: activité *in vitro:* CMI_{90} (mg/l)

	DELA	LEVO	MOXI	CIPRO
S. pneumoniae	0,015	1	0,12	ND
S. aureus FQ S	0,008	0,25	0,1	ND
S. aureus FQ R	1	32	8	ND
H. influenzae	0,002	0,003	0,006	ND
M. catharralis	0,004	0,06	0,06	ND
L. pneumophila	0,5	0,12	ND	ND
M. pneumoniae	0,5	2	ND	ND
K. pneumoniae	0,25	ND	ND	0,03
P. aeruginosa	0,5	ND	ND	0,5

Activité +++ sur *C. difficile*

D'après F. van Bambeke

Future Microbiol. (2015) 10(7), 1111–1123

Activité in vitro de l'omadacycline

- Evaluation de l'activité de omadacycline (nouvelle aminométhylcycline dérivée de la minocycline, actuellement en essais cliniques de phase 3 dans le traitement des ICPM et PAC ; p.o. ou i.v. en 1 fois par jour)
- Souches isolées en 2010-2011 dans 14 pays européens + Israël (45 centres)

CMI_{50} et CMI_{90} (mg/l) omadacycline

Bactéries (nombre de souches)	CMI_{50}	CMI_{90}
S. aureus (5533)	0,12	0,25
SARM (1539)	0,12	0,25
SCN (1256)	0,12	1
E. faecalis (1196)	0,12	0,25
E. faecium (692)	0,06	0,12
S. pneumoniae (2233)	0,06	0,06
Streptocoques β-hémolytiques (1313)	0,06	0,12
E. coli (3757)	0,5	2
K. pneumoniae (1250)	2	8
A. baumannii (502)	2	4

➔ **Large spectre antibactérien anti-Gram + et Gram -**

Flamm R, ECCMID 2016, Abs. P1317

Conclusions

1. Eu égard à l'absence de problèmes majeurs de résistance, les pneumonies communautaires ne sont pas un champ privilégié pour les nouvelles molécules
2. L'efficacité, la simplicité d'administration de certaines d'entre elles (kétolides, fluoroquinolones) et leur bonne tolérance devraient permettre de les intégrer dans les schémas thérapeutiques