



Le infezioni comunitarie “Life-threatening”

Polmonite comunitaria grave e cefalosporine di V generazione

Mario Venditti

Dipartimento di Sanità Pubblica e Malattie Infettive,
Università «Sapienza»
Policlinico Umberto I, Roma

My disclosures (last two years)

■ Advisor/consultant

- MSD, Angelini, Menarini, Infectofarm,
Mundipharma

■ Speaker/chairman

- Pfizer, MSD, Gilead, Angelini, Correvio,
Menarini

Polmonite comunitaria grave secondo linee guida ATS/IDSA 2019

Almeno
1 criterio
maggiore
o ≥ 3 criteri
minori

CRITERI MAGGIORI

- Shock settico con necessità di vasopressori
- Insufficienza respiratoria che richiede ventilazione meccanica

CRITERI MINORI

- FR \geq 30 atti/min
- P/F \leq 250
- Infiltrati polmonari multilobari
- Confusione/disorientamento
- Uremia (BUN \geq 20 mg/dl)
- Leucopenia (GB < 4000/ μ L)
- Trombocitopenia (PLT < 100000/ μ L)
- Ipotermia ($T < 36^{\circ}\text{C}$)
- Ipotensione che richiede riempimento volemico

Expanded CURB-65: a new score system predicts severity of CAP with superior efficiency

Liu J , Xu F , Zhou H , Wu X , Shi L , Lu R, Farcomeni A , Venditti M , Dong X, & Falcone M *Sci Rep.* 2016 Mar 18;6:22911.

Derivation cohort:1640 pts (Zhejiang University); validation cohort: 1164 pts (Sapienza University – Rome).

Se 0-2 = paziente dimissibile

Se 3-4 = valutazione ricovero

Se 5-6 = necessità di ricovero ospedaliero

Confusione	+ 1
Urea (BUN) >19mg/dl	+ 1
FR ≥ 30atti/min	+ 1
PA Sistolica <90mmHg p PA Diastolica ≤ 60mmHg	+ 1
Età ≥ 65 anni	+ 1
LDH >230U/L	+ 1
Albumina < 3,5 gr/dl	+ 1
Piastrine < 100000/mmc	+ 1

PES Score , PES Pathogens (Pseudomonas aeruginosa, ESBL Enterobacteriaceae, or MRSA) in Severe Community- Acquired Pneumonia

Ceccato et al *Ann Am Thorac Soc.* 2021

Se ≤3 = basso rischio

Se 4-5 = valutazione terapia antibiotica a spettro allargato

Se >5= alto rischio

Età > 65 anni	+ 1
Sesso maschile	+ 2
Precedente utilizzo di antibiotici	+ 2
Malattia respiratoria cronica	+ 2
Insufficienza renale cronica	+ 2
Alterazione della coscienza o evidenza di aspirazione	+ 2
Febbre o brividi	- 1

ARUC Score per l'identificazione precoce di pazienti con CAP da MDR

Falcone M et al *Plos one*, 2015

Se $< 0,5$ = basso rischio

Se $> 0,5$ = valutazione trattamento antibiotico a spettro allargato

Se ≥ 3 = alto rischio

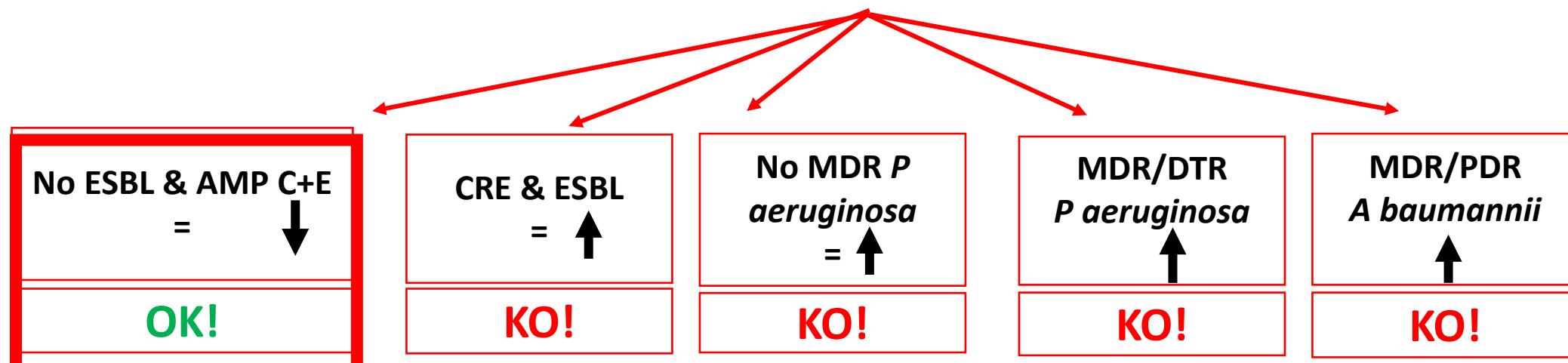
HCAP (healthcare-associated pneumonia) ovvero almeno uno tra : - ricovero negli ultimi 3 mesi, - dialisi, - terapia antibiotica endovenosa negli ultimi 30 giorni, - residenza in case di cura o LTF (long term facility)	+ 1
Infiltrati polmonari bilaterali	+0,5
Versamento pleurico	+ 0,5
P/F < 300	+ 1,5

Antibiotics recently introduced in therapy armamentarium: FDA and/or EU approvals

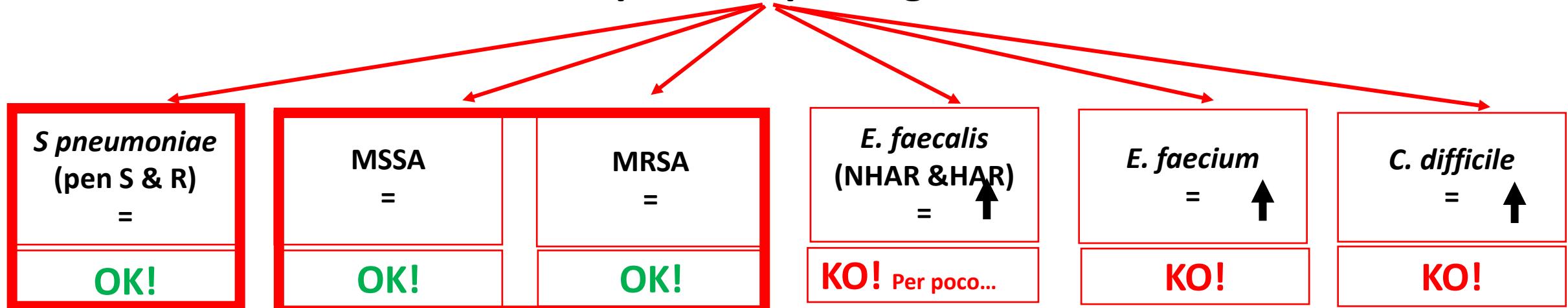
- **Ceftaroline:** cSSSIs (or ABSSSIs), CAP
- **Ceftobiprole:** CAP, HAP, not VAP
- **Ceftolozane tazobactam:** cUTIs, clAIs*, HAP & VAP
- **Ceftazidime avibactam:** cUTIs & pyelonephritis, clAIs*, HAP & VAP
- **Meropenem vaborbactam:** cUTIs, infections caused by KPC+CRE
- **Cefiderocol:** cUTIs, HAP & VAP

Significant Gram negative pathogens and gram positive bacteria : epidemiology trends scenarios and potential role of ceftaroline

Gram negative pathogens



Gram positive pathogens



Ceftaroline fosamil: Clinical Experience

FOCUS 1

- Randomized, double-blind, multicenter phase III trial
- 1:1 Randomization to ceftaroline (600 x 2v) or ceftriaxone (1gr)
- Ceftaroline demonstrated considerably high clinical cure rates in patients with moderate-severe CAP (86% vs. 78%).

Focus 2

- Randomized, double-blind, multicenter phase III trial
- 1:1 Randomization to ceftaroline (600 x 2v) or ceftriaxone (1gr)
- Ceftaroline demonstrated considerably high clinical cure rates in patients with moderate-severe CAP (82% vs. 77%).

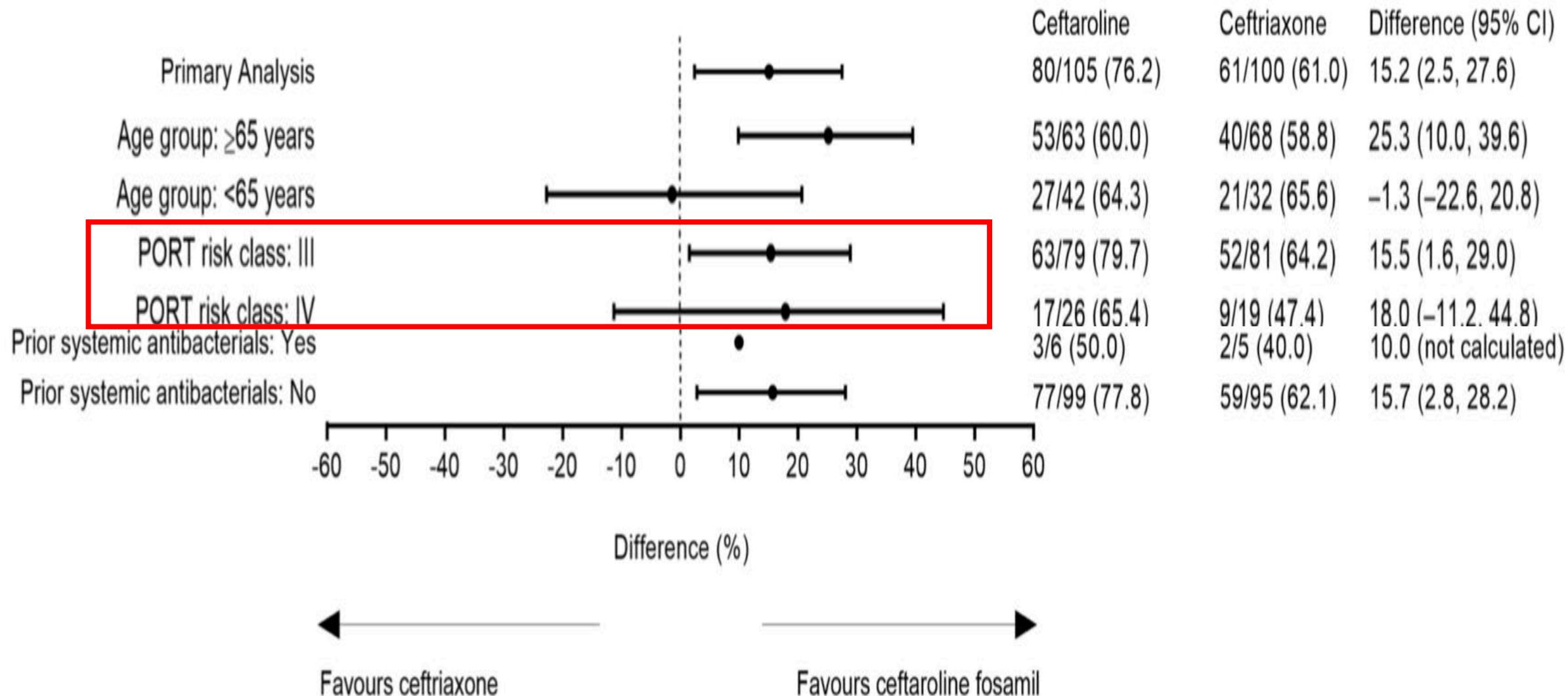
Asia- CAP

- Prospective, randomized, multicenter, double-blind, phase III study in ASIA
- 1:1 Randomization to ceftaroline (600 x 2v) or ceftriaxone (2gr)

- Ceftaroline was superior to ceftriaxone 2gr in the treatment of patients with moderate-severe CAP.

Subgroup analysis of clinical cure rates at the TOC visit (ASIA CAP study)

Zhuo et al *Infection and Drug Resistance*, 2022



Impact on in-hospital mortality of ceftaroline versus standard of care in CAP: a propensity-matched analysis

Cilloniz et al *European Journal of Clinical Microbiology & Infectious Diseases* (2022) 41:271–279

- Hospitalized patients with CAP were grouped according to the empiric regimen (ceftaroline versus standard therapy, almost universally ceftriaxone) and analyzed using a propensity score matching (PSM) method to reduce confounding factors.
- Out of the 6981 patients enrolled, 5640 met the inclusion criteria, and 89 of these received ceftaroline. After PSM, 78 patients were considered in the ceftaroline group (cases) and 78 in the standard group (controls).
- Ceftaroline was mainly prescribed in cases with severe pneumonia (67% vs. 32 in original 5640 controls $p<0.001$ and vs 56% in PSM controls, $p = 0.215$) with high suspicion of *S. aureus* infection (9% in cases vs. 0% in PSM controls, $p = 0.026$).
- Compared to PSM controls, cases had a longer length of hospital stay (13 days vs. 10 days, $p = 0.007$), while an increased risk of in-hospital mortality ($p = 0.003$) was observed in the PSM control group (21%) compared to the case group (13%).
- Conclusion: The empiric use of ceftaroline in hospitalized patients with severe CAP was associated with a decreased risk of in-hospital mortality.

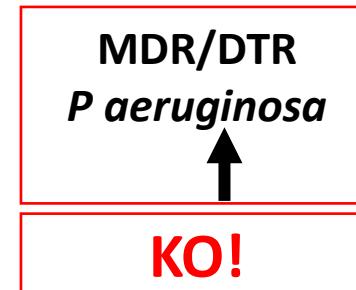
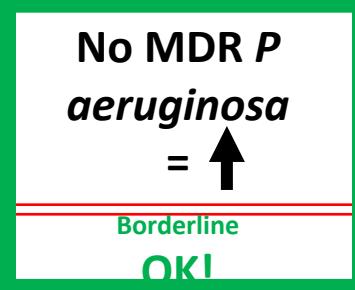
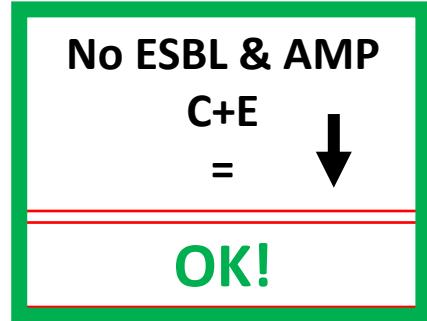
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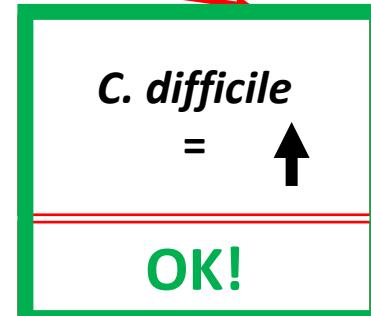
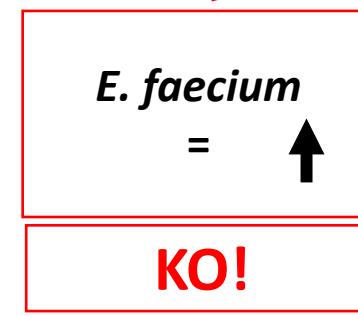
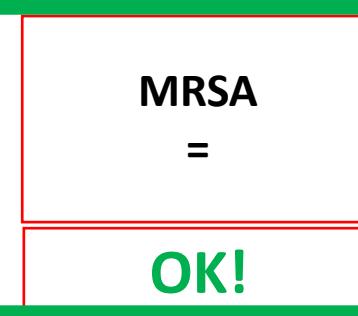
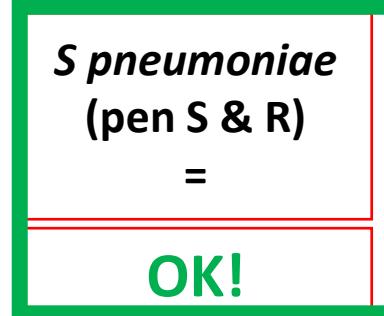
Significant Gram negative pathogens and gram positive bacteria : epidemiology trends scenarios and potential role of ceftobiprole

Gram negative pathogens

Epidemiology trend: = ↓ ↑



Gram positive pathogens

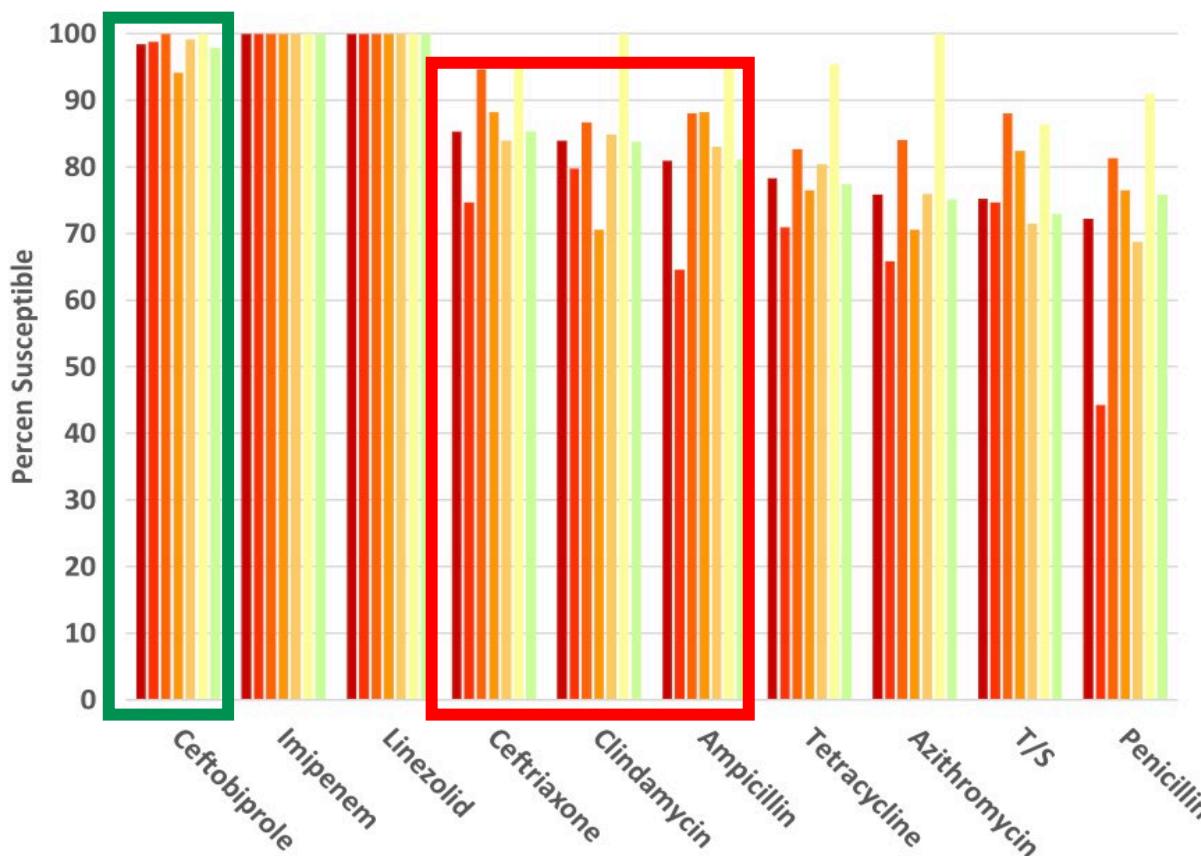


Susceptibility of ceftobiprole against Gram-positive clinical isolates from 2019 from different European territories

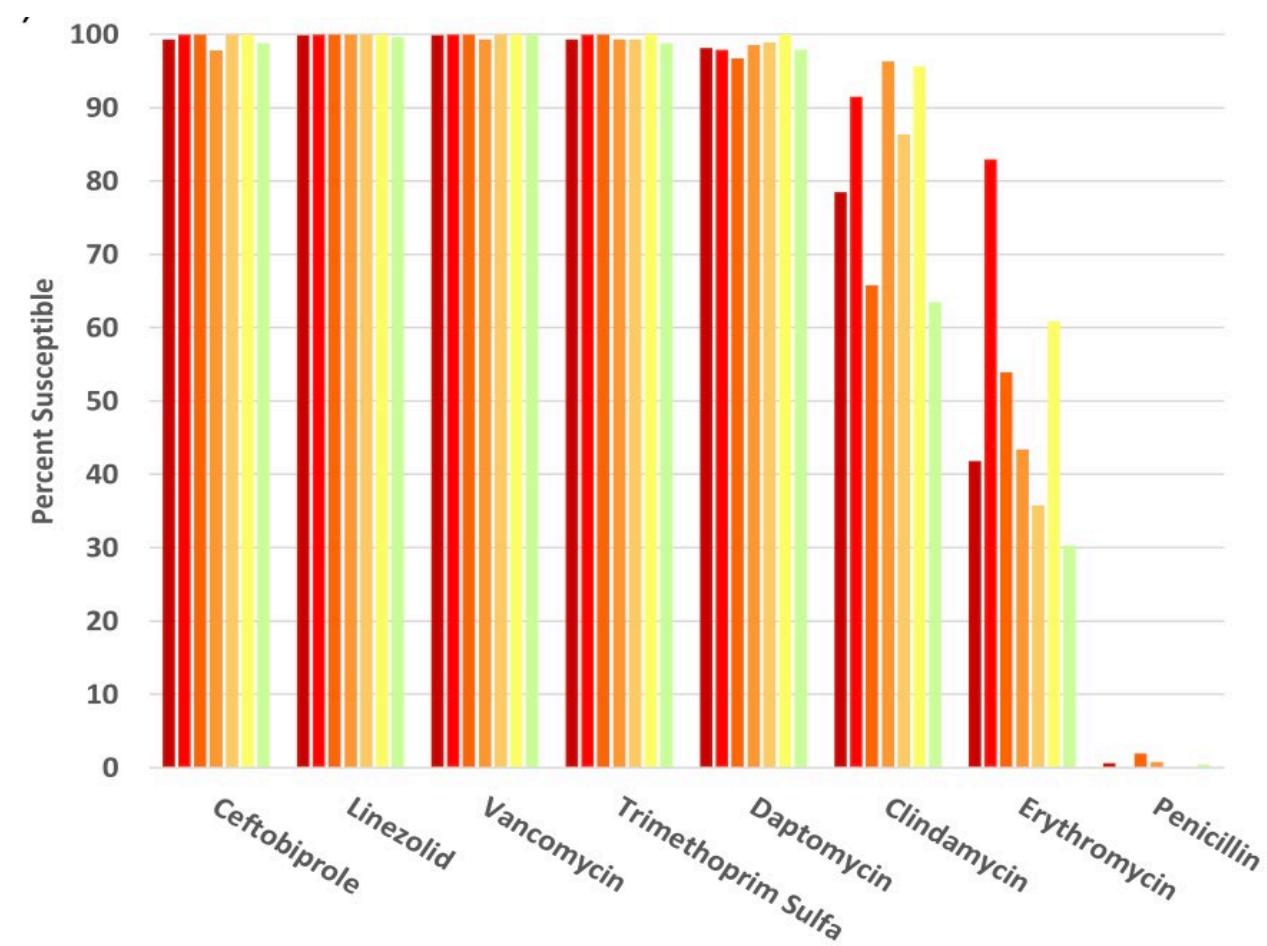
Hawser et al *Journal of Global Antimicrobial Resistance* 29 (2022) 393–397

■ Europe ■ France ■ Germany ■ Italy ■ Spain ■ United Kingdom ■ Other countries

S. pneumoniae



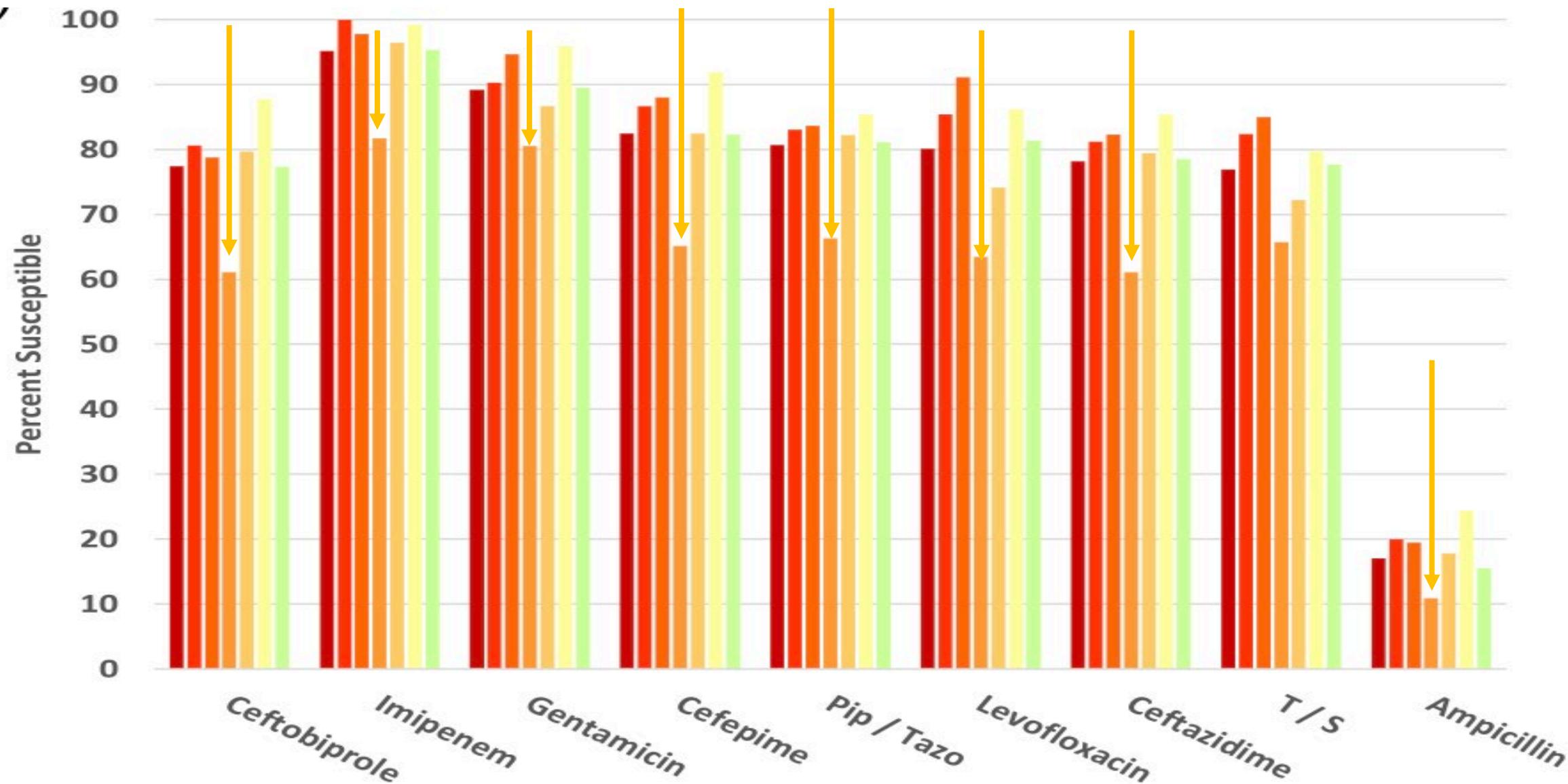
MRSA



Susceptibility of ceftobiprole vs Enterobacterales clinical isolates from 2019 from different European territories

Hawser et al *Journal of Global Antimicrobial Resistance* 29 (2022) 393–397

■ Europe ■ France ■ Germany ■ Italy ■ Spain ■ United Kingdom ■ Other countries



Susceptibility of ceftobiprole vs gramnegative clinical isolates from 2019 from different European territories

Hawser et al *Journal of Global Antimicrobial Resistance* 29 (2022) 393–397

	% Res	MIC₅₀	MIC₉₀
Enterobacterales^a (n = 1790)			
Ceftobiprole	22.6	0.06	>64
Ampicillin	83.0	>64	>64
Cefepime	13.4	0.06	>8
Ceftazidime	18.4	0.25	>8
Gentamicin	10.8	0.5	8
Imipenem	3.6	0.25	2
Levofloxacin	16.8	0.06	>4
Pip/Tazo	15.8	2	>32
T/S	22.7	≤0.12	>4
P. aeruginosa (n = 544)			
Ceftobiprole	-	2	16
Cefepime	19.3	4	32
Ceftazidime	23.2	4	>32
Colistin	1.1	1	2
Gentamicin	-	2	16
Imipenem	24.3	2	16
Levofloxacin	34.6	0.5	16
Piperacillin	27.9	8	>32
Pip/Tazo	21.5	4	>32

MICs for the four *C. difficile* test strains

Nerandzic et al AAC, 2011

Antibiotic	MIC ($\mu\text{g/ml}$) ^a			
	ATCC 43599	VA 11	VA 17	VA 20
Piperacillin-tazobactam	2	2	8	8
Ertapenem	4	8	8	8
Ceftobiprole	1	1	2	1
Ceftobiprole medocaril	1	2	2	2
Ceftazidime	128	>256	64	64
Ceftriaxone	8	128	64	64
Cefotaxime	16	128	64	64
Cefoxitin	128	>256	>256	>256
Clindamycin	>256	>256	>256	>256

A randomised, double-blind trial comparing ceftobiprole with ceftriaxone with or without linezolid for the treatment of patients with CAP requiring hospitalisation

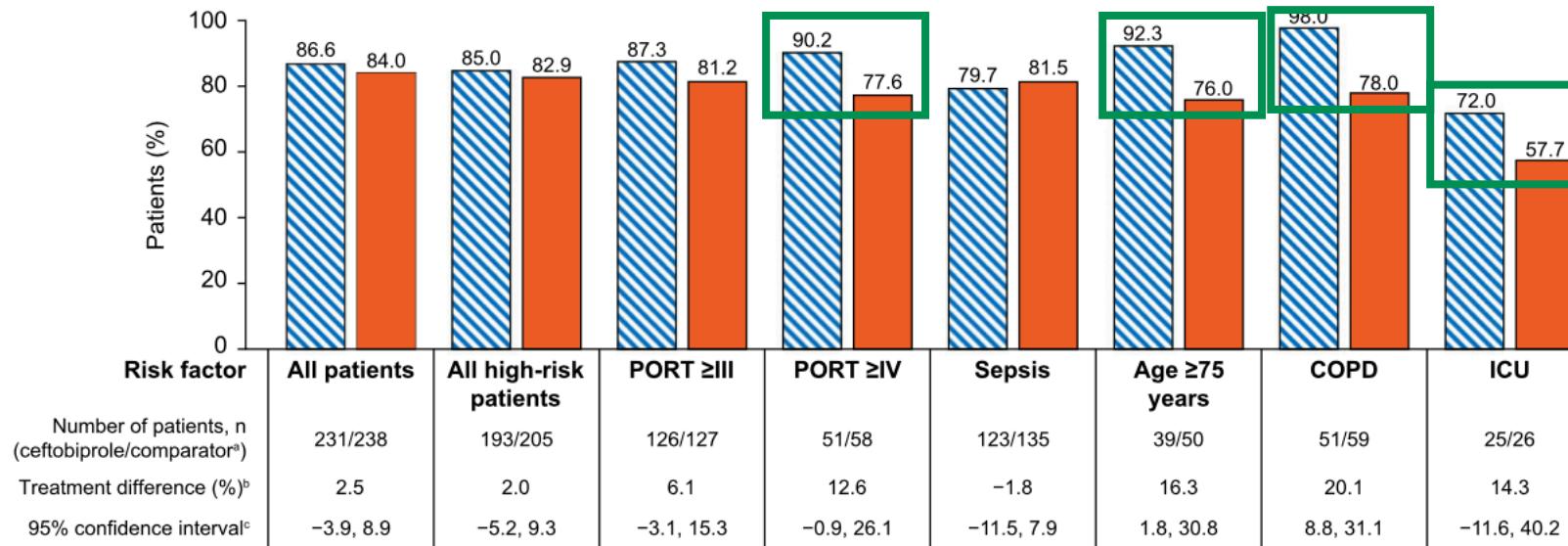
Nicholson et al IJAA, 2012

	Ceftobiprole n (%)	Ceftriaxone n (%)
Advanced age		
<65 years	120/141 (85.1)	121/141 (85.8)
≥65 years	80/90 (88.9)	87/97 (89.7)
<75 years	164/192 (85.4)	165/188 (87.8)
≥75 years	36/39 (92.3)	43/50 (86.0)
PSI score		
<91	154/180 (85.6)	159/180 (88.3)
≥91	46/51 (90.2)	49/58 (84.5)
PORT score		
I	10/12 (83.3)	7/7 (100)
II	81/93 (87.1)	100/113 (88.5)
III	63/75 (84.0)	52/59 (88.1)
IV	43/48 (89.6)	44/52 (84.6)
V	3/3 (100)	5/6 (83.3)
Presence of SIRS		
No	96/108 (88.9)	91/103 (88.3)
Yes	104/123 (84.6)	117/135 (86.7)
CAP complicated by bacteraemia		
No	194/224 (86.6)	196/224 (87.5)
Yes	6/7 (85.7)	12/14 (85.7)
Yes	6/7 (85.7)	12/14 (85.7)

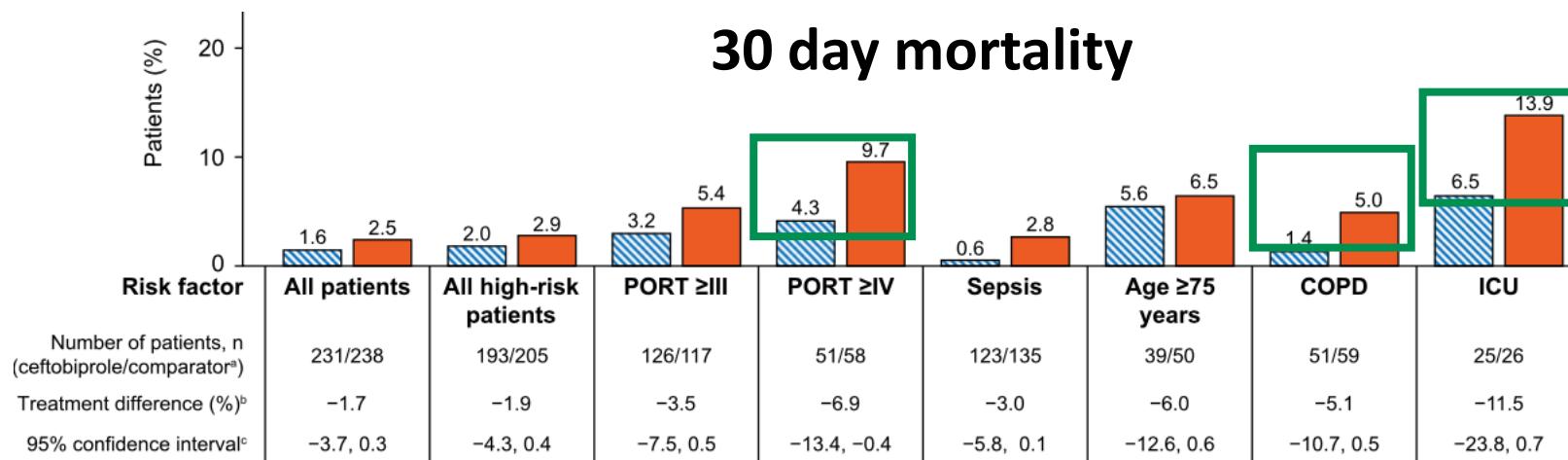
Subanalysis of randomised, double-blind trial comparing ceftobiprole with ceftriaxone with linezolid for pts with CAP requiring hospitalisation

Nicholson et al IJAA, 2012; Scheeren et al. *BMC Infectious Diseases* (2019) 19:195

Early improvement



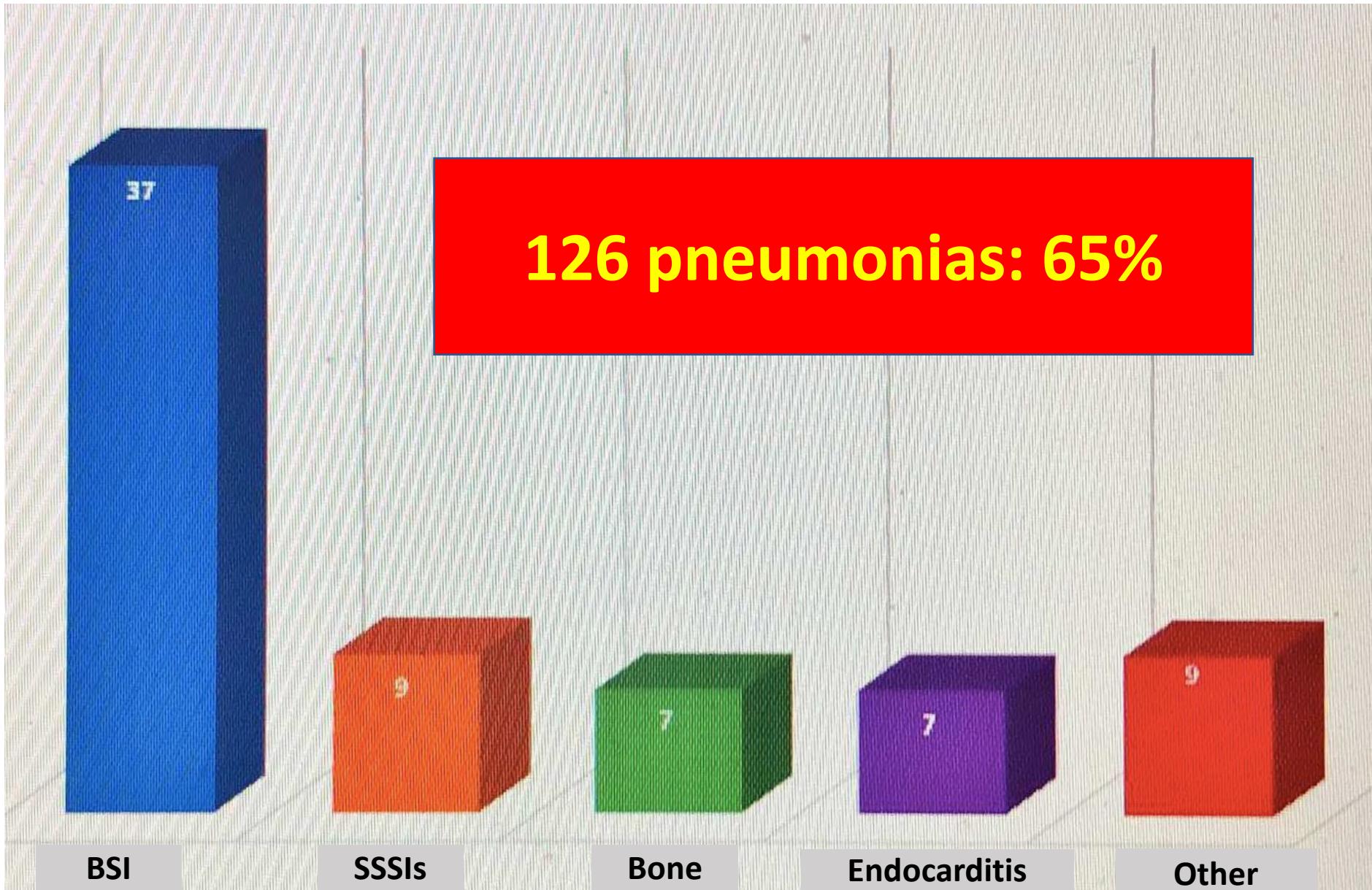
30 day mortality



Effect of ceftobiprole therapy in real life

(195 infections , data collected retrospectively in 133 cases and prospectively in 62 cases)

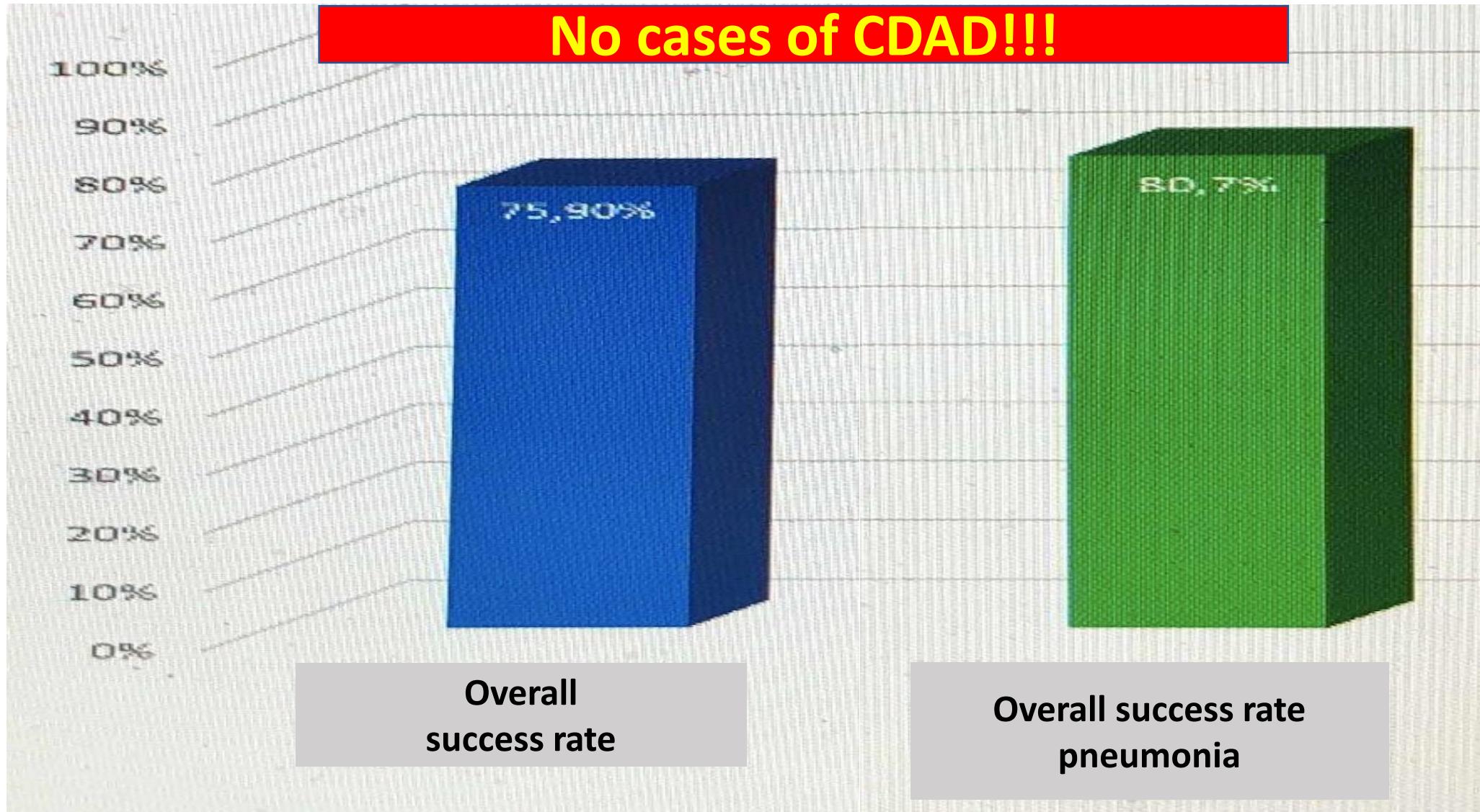
Gentile I et al unpublished data (communication at ACCP, 2021)



Effect of ceftobiprole therapy in real life

(195 infections , data collected retrospectively in 133 cases and prospectively in 62 cases)

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Ceftaroline and ceftobiprole....
What about
***Staphylococcus aureus* CAP?**

Se FdR per MDR chiamare infettivologo ed eseguire TN per MRSA

GRAVE**

(eseguire BAL appena possibile)

NO

Fattori di rischio BAR
[Tabella3-4]

SI

MEM +VAN/LZD

Esito Tampone nasale MRSA

-

Sospendere
VAN/LZD

+

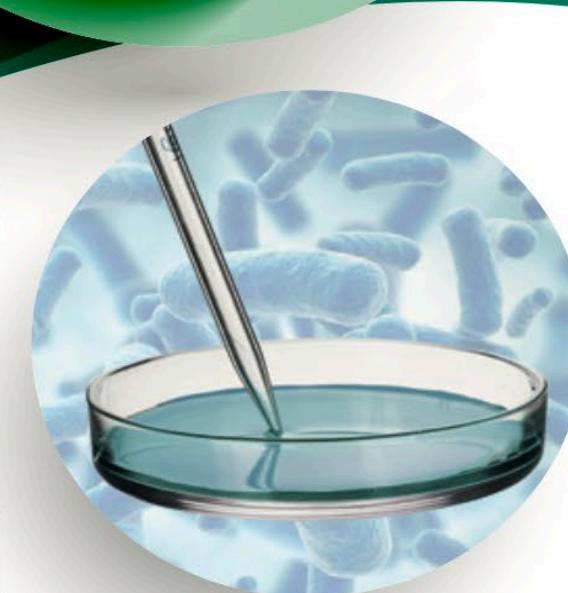
VAN/LZD ± MEM o
eventuale BPR/CPT sec
valutazione infettivologica

Sul BAL eseguire oltre esame culturale e ATB fenotipico anche pannello sindromico di FAST MICRO per virus respiratori, patogeni batterici e determinanti di antibiotico-resistenza per avviare entro 3 ore una semi-targeted therapy

Uso dei nuovi (e vecchi) antibiotici: una proposta pragmatica di place in therapy nei pazienti critici

10 - 11 novembre 2022

NH Venezia Laguna Palace Hotel
Mestre (Venezia)



chiusa la parente



Apri la parente

