



ACCP 2023

Meeting on  
Antimicrobial  
Chemotherapy  
in Clinical Practice (ACCP)

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# Quanta paura dobbiamo avere di *Klebsiella pneumoniae*?

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# Antibiotic resistance patterns among uropathogens in female outpatients affected by uncomplicated cystitis: Focus on fosfomicin.

*Cai T et al, Int J Antimicrob Ag 2023 Nov; 62:106974*

Urinary samples were collected from three high-volume laboratories from Jan 2015 to Dec 2020. The pattern of resistance to fosfomicin was analysed by using the Vitek II automated system. A total of 7289 urinary samples were collected and **8321 strains** were analysed during the study period.

## Isolated strain prevalente

		<b>Fosfo R Escherichia coli</b>	<b>12.2%</b>
Escherichia coli	6585	<b>Fosfo R Klebsiella spp.</b>	<b>16.2%</b>
Klebsiella spp.	1241		
Enterococcus faecalis	236		
Enterococcus faecium	43	<b>ESBL Escherichia coli</b>	<b>27.1%</b>
Pseudomonas spp.	156	<b>ESBL Klebsiella spp.</b>	<b>44.3%</b>
Enterobacter spp.	54		
<b>ESBL producing</b>	<b>2338 (35.5%)</b>		

Bloodstream infections due to Gram-negative bacteria in patients with hematologic malignancies: updated epidemiology and risk factors for MDR strains in an Italian perspective survey. *Trecarichi EM, et al. Int J Antimicrob Agents. 2023. Jun;61(6):106806.*

A total of 834 GNB were recovered in 811 BSI episodes from Jan 2016 to Dec 2018

The overall 30-day mortality rate was 16.3% (132/811).

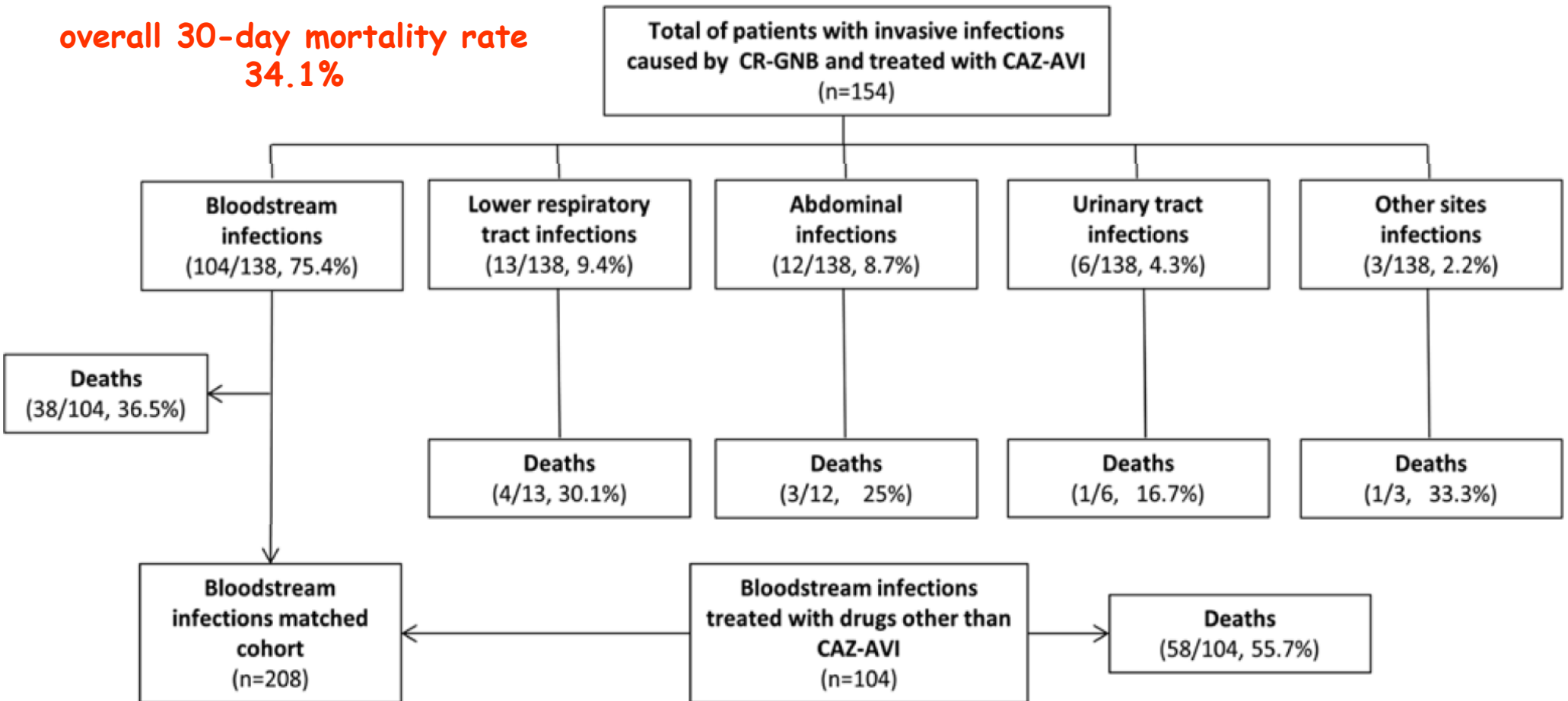
**Mortality rate** was significantly higher in patients who had a BSI caused by an MDR GNB than in those who had a non-MDR GNB BSI (88/256), **34.4%** vs. 44/555, 7.9%;  $P < 0.001$ ),

# Efficacy of Ceftazidime-Avibactam salvage therapy in patients with infections caused by KPC-producing *K. pneumoniae* Tumbarello M et al. Clin Infect Dis. 2019;68:355-364

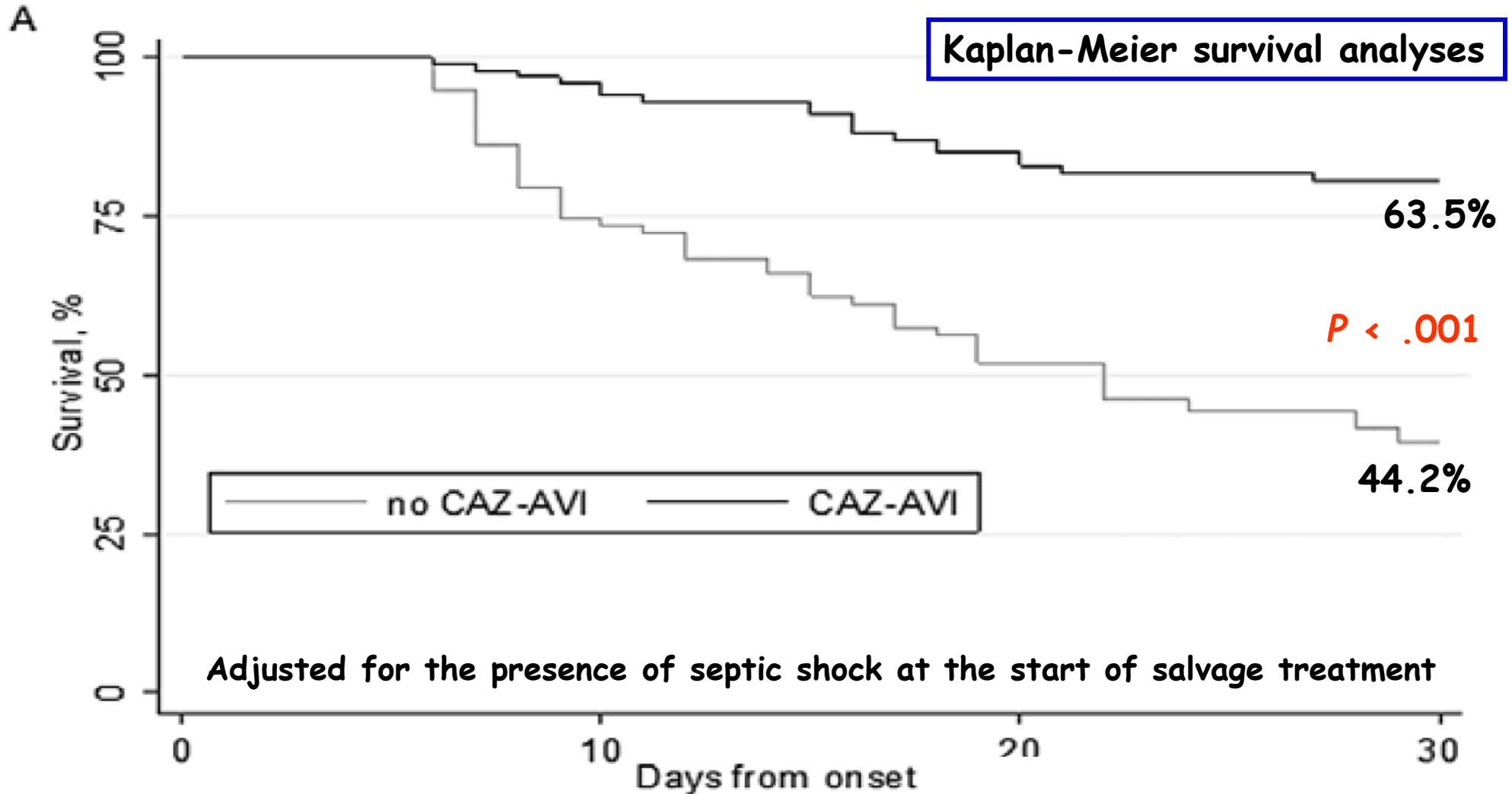
## Flowchart of patients' inclusion process

Case-control matching was based on the number of days from BSI onset to the initiation of salvage therapy and Pitt bacteremia scores.

overall 30-day mortality rate  
34.1%

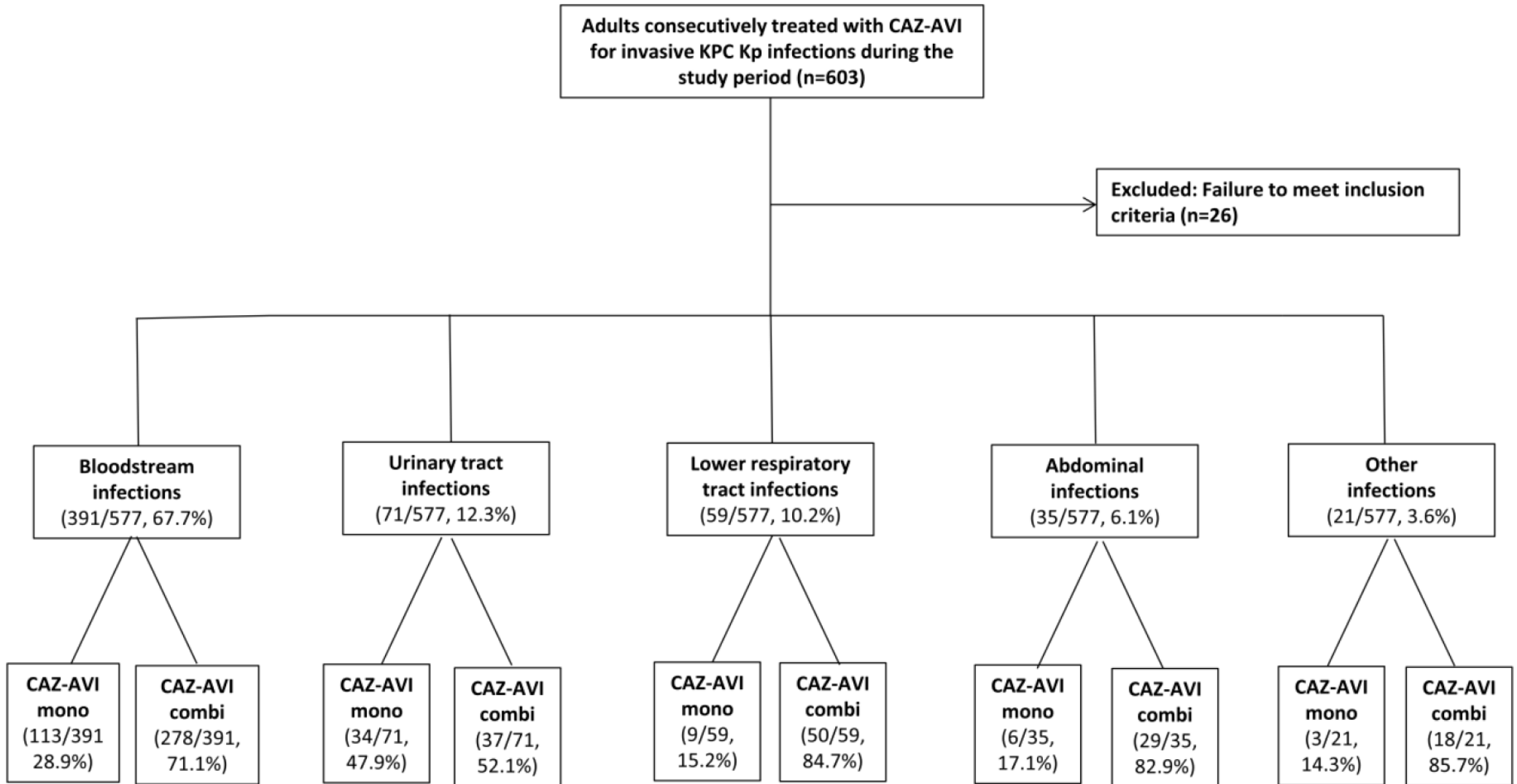


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# Ceftazidime-avibactam use for KPC-Kp infections: a retrospective observational multicenter study

Tumbarello M et al Clin Infect Dis. 2021;73:1664-1676



# Ceftazidime-avibactam use for KPC-Kp infections: a retrospective observational multicenter study

Tumbarello M et al Clin Infect Dis. 2021;73:1664-1676

Multivariate analysis of factors associated with 30-day mortality.

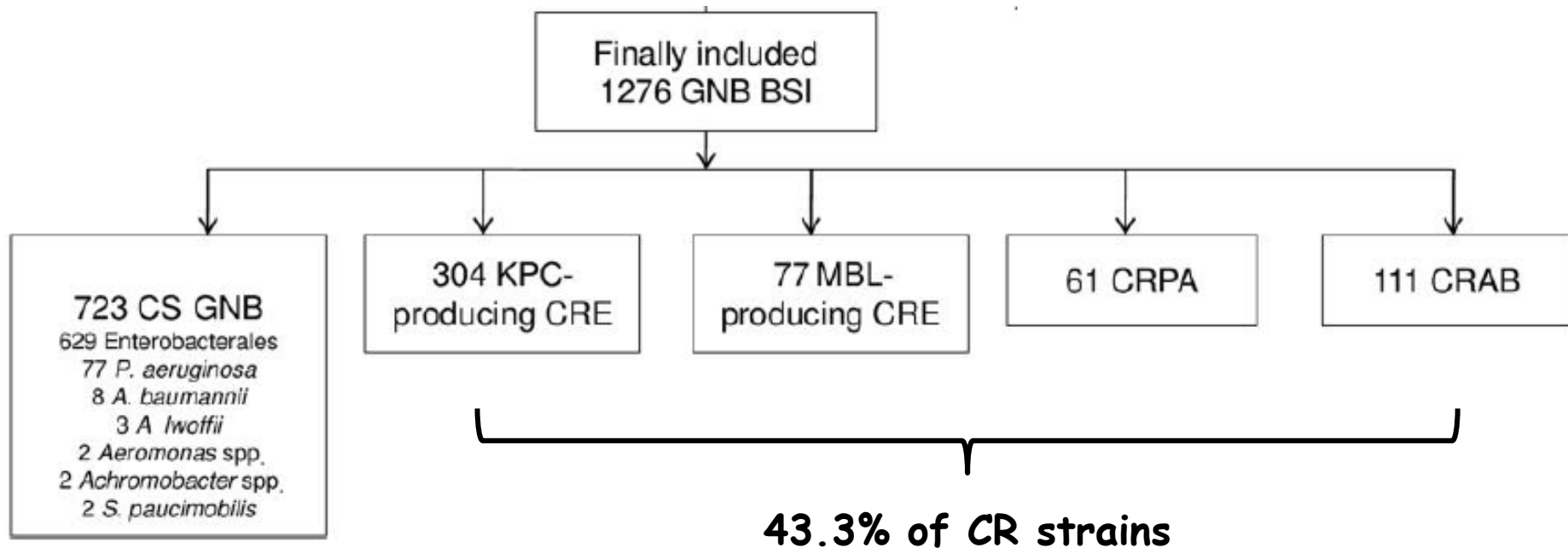
Adjusted for the propensity score matching for combination therapy?

Variables	P value	NO	P value	YES
		OR (95% CI)		OR (95% CI)
INCREMENT score >8	0.01	2.06 (1.18-3.59)	0.005	2.23 (1.27-3.91)
Septic shock at onset	0.002	2.72 (1.45-5.09)	0.003	2.59 (1.37-4.89)
Neutropenia	<0.001	6.37 (2.42-16.74)	<0.001	6.86 (2.55-18.42)
LRT infection	0.04	1.90 (1.03-3.53)	0.008	2.48 (1.26-4.86)
➡ CAZ-AVI by CI	0.003	0.52 (0.34-0.79)	0.006	0.54 (0.34-0.83)
➡ CAZ AVI dose adjustment for renal function	0.001	2.39 (1.42-4.03)	0.010	2.01 (1.15-3.48)

# Mortality Attributable to Bloodstream Infections Caused by Different Carbapenem-Resistant Gram-Negative Bacilli: Results From a Nationwide Study in Italy (ALARICO Network).

Falcone M et al Clin Infect Dis 2023; 76(12):2059-69

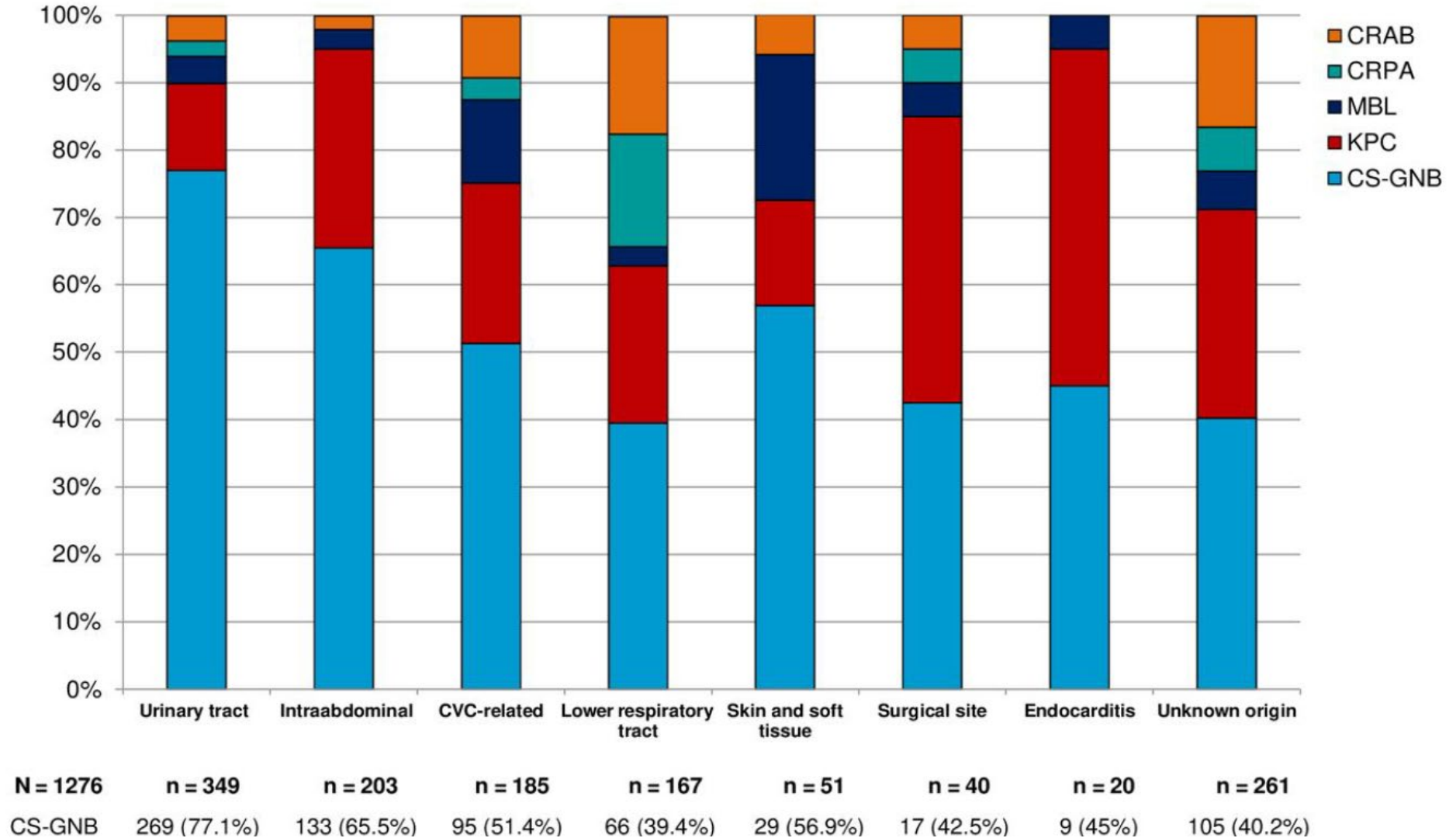
Prospective multicentric study including patients with GNB-BSI from 19 Italian hospitals (Jun 2018-Jan 2020). Patients were followed to 30 days. Primary outcomes were 30-day mortality and attributable mortality. A total of 1276 pts with monomicrobial GNB BSI were included.





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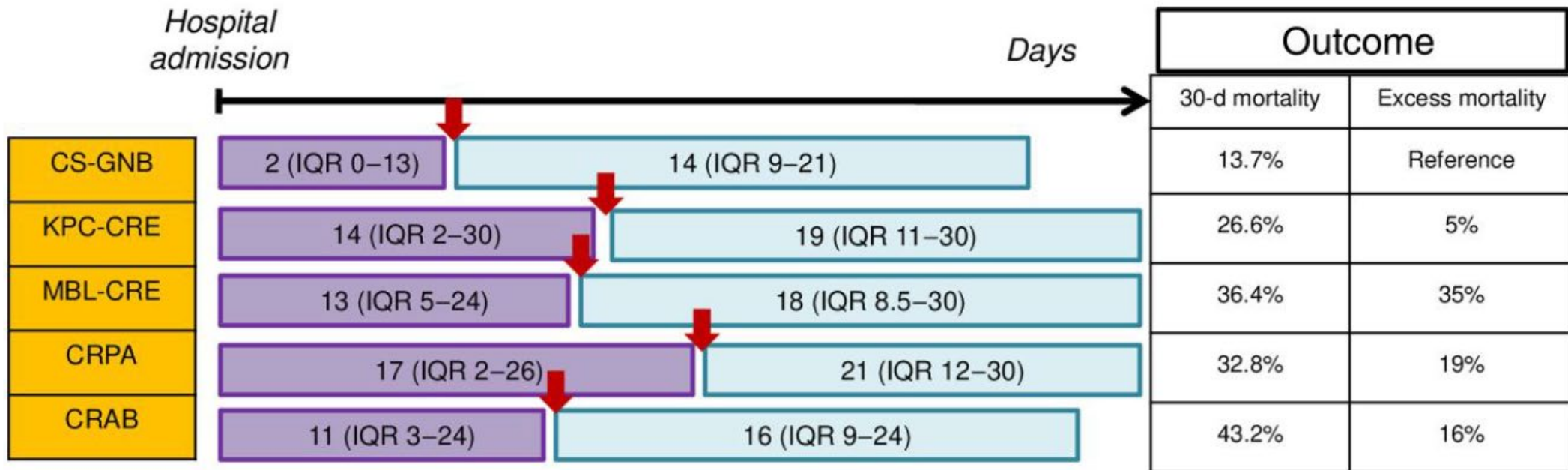
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# Mortality Attributable to Bloodstream Infections Caused by Different Carbapenem-Resistant Gram-Negative Bacilli: Results From a Nationwide Study in Italy (ALARICO Network).

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Timeline of patient events in relation to the hospital admission, exposures, and outcomes



**Mortality in KPC-producing *Klebsiella pneumoniae* bloodstream infections: a changing landscape. Giacobbe DR et al, J Antimicrob Chemother 2023; 78(10):2505-2514**

Overall, 426 patients, collected between Jan and Aug 2020 were included: 107/426 (25%) had carbapenem-resistant *K. pneumoniae* BSI and 319/426 (75%) had carbapenem-susceptible *K. pneumoniae* BSI

In multivariable analyses, variables showing an unfavourable association with mortality after correction for multiple testing were,

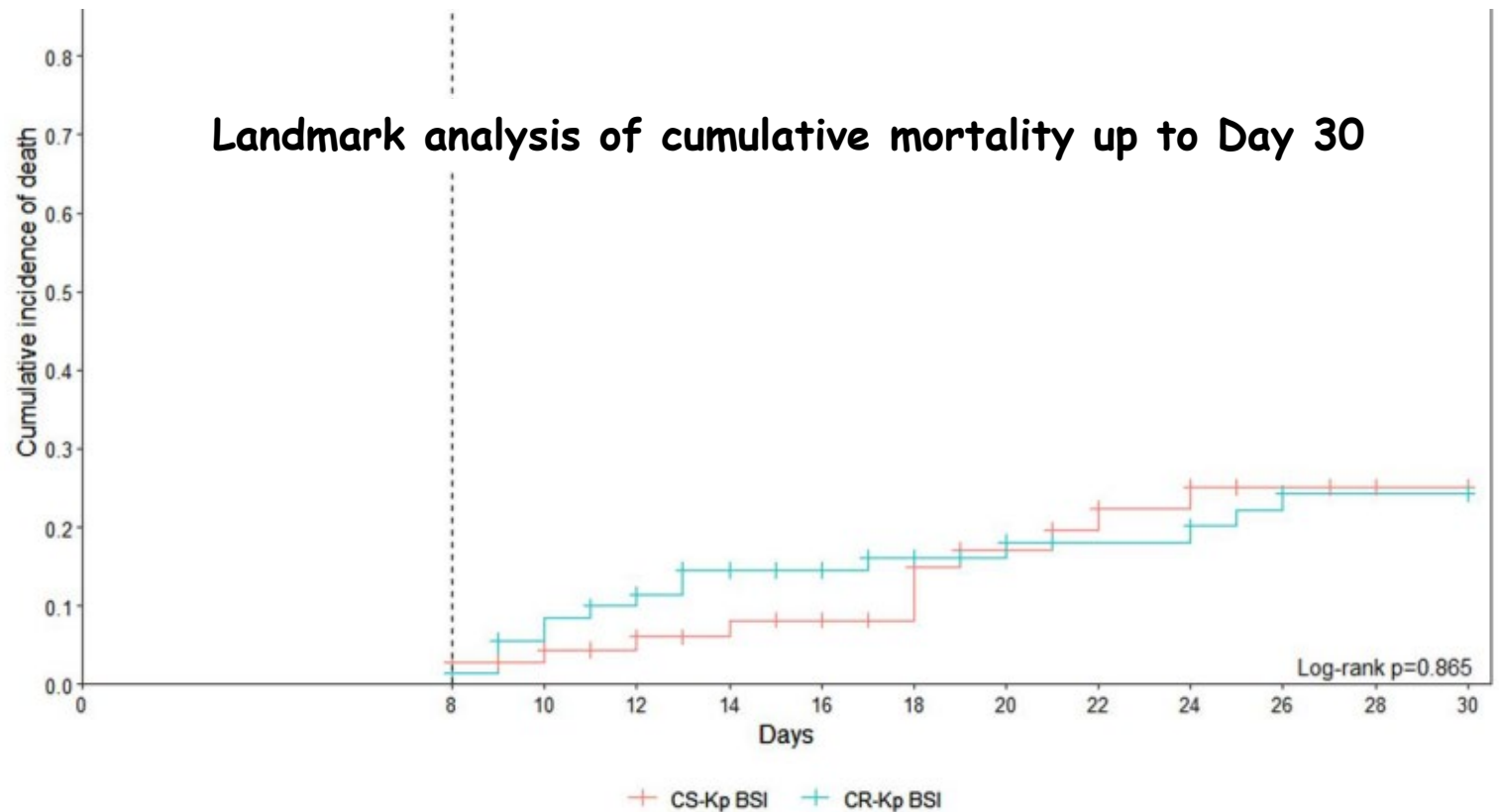
- age-adjusted Charlson comorbidity index (HR 1.20; 95% CI 1.10-1.31,  $P < 0.001$ )
- Pitt score (HR 1.33; 95% CI 1.15-1.55,  $P < 0.001$ ),

**BUT NOT**

- carbapenem resistance (HR 1.28, 95% CI 0.74-2.22,  $P = 0.410$ ).

## Mortality in KPC-producing *Klebsiella pneumoniae* bloodstream infections: a changing landscape. *Giacobbe DR et al, J Antimicrob Chemother 2023; 78(10):2505-2514*

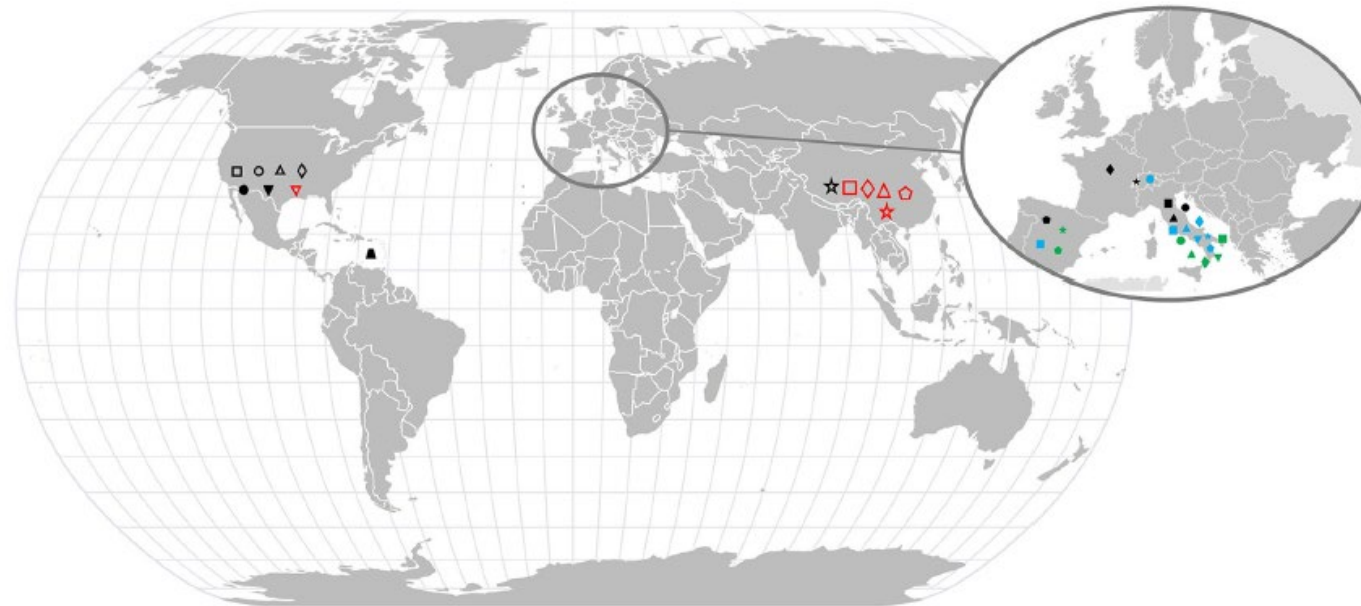
In a propensity score-matched analysis, there was no difference in mortality between patients appropriately treated with ceftazidime/avibactam for CR-Kp BSI and patients appropriately treated with other agents (mainly meropenem monotherapy or piperacillin/tazobactam monotherapy) for CS-Kp BSI (HR 1.07; 95% CI 0.50-2.29, P = 0.866).





# *Klebsiella pneumoniae* Carbapenemase Variants Resistant to Ceftazidime-Avibactam: an Evolutionary Overview

Claire Amaris Hobson,<sup>a</sup> Gautier Pierrat,<sup>a</sup> Olivier Tenailon,<sup>a</sup> Stéphane Bonacorsi,<sup>a,b</sup> Béatrice Bercot,<sup>a,c</sup> Ella Jaouen,<sup>a</sup> Hervé Jacquier,<sup>a,c</sup> André Birgy<sup>a,b</sup>



**Variants from KPC-2**

- |          |           |
|----------|-----------|
| □ KPC-14 | □ KPC-52  |
| ○ KPC-25 | ○ KPC-57  |
| △ KPC-33 | △ KPC-71  |
| ◇ KPC-35 | ◇ KPC-78  |
| ▽ KPC-44 | ▽ KPC-82  |
| ★ KPC-51 | ★ KPC-90  |
|          | ○ KPC-123 |

**Variants from KPC-3**

- |          |          |          |
|----------|----------|----------|
| ▲ KPC-8  | ■ KPC-49 | ■ KPC-66 |
| ● KPC-29 | ● KPC-50 | ● KPC-67 |
| ▲ KPC-31 | ▲ KPC-53 | ▲ KPC-68 |
| ▲ KPC-36 | ◆ KPC-62 | ◆ KPC-69 |
| ◆ KPC-39 | ▼ KPC-63 | ▼ KPC-70 |
| ▼ KPC-40 | ★ KPC-64 | ★ KPC-94 |
| ★ KPC-41 | ● KPC-65 | ● KPC-95 |
| ● KPC-48 |          |          |

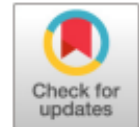


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MECHANISMS OF RESISTANCE

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# Ceftazidime-Avibactam Resistance Associated with Increased *bla*<sub>KPC-3</sub> Gene Copy Number Mediated by pKpQIL Plasmid Derivatives in Sequence Type 258 *Klebsiella pneumoniae*

Marco Coppi,<sup>a</sup>  Vincenzo Di Pilato,<sup>a\*</sup> Francesco Monaco,<sup>b</sup>  Tommaso Gianj,<sup>a</sup> Pier Giulio Conaldi,<sup>b,c</sup> Gian Maria Rossolini<sup>a,d</sup>

## **Clonal dissemination of *Klebsiella pneumoniae* resistant to cefiderocol, ceftazidime/avibactam, meropenem/vaborbactam and imipenem/relebactam co-producing KPC and OXA-181 carbapenemase**

**Federica Bovo<sup>1†</sup>, Stefano Amadesi <sup>1†</sup>, Marta Palombo<sup>1</sup>, Tiziana Lazzarotto<sup>1,2</sup>, Simone Ambretti<sup>1,2</sup>  
and Paolo Gaibani <sup>1\*</sup>**

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**NON VERGOGNAMOCI DI AVERE PAURA:  
SOLO COSI' NASCE IL CORAGGIO**

