Comparison of meropenem-vaborbactam *vs* ceftazidime-avibactam in the treatment of KPC-producing *Klebsiella pneumoniae* infections

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BACKGROUND

KPC is the most prevalent carbapenemase among *Enterobacterales* in the European Union[1]. International guidelines recommend Ceftazidime/avibactam (CAZ/AVI) and meropenem/vaborbactam (MER/VAB); however, data comparing these treatments are lacking.

METHODS

A multicentric retrospective cohort study was conducted on patients treated with CAZ/AVI or MER/VAB for microbiologically documented KPC-producing K. pneumoniae infections between 2018 and 2024, enrolled in the ongoing SUSANA (Surveillance of Safety and Outcome of New Antibiotics) cohort. Collected data included demographics, treatment regimens, infection sites, pathogens, adverse events and clinical outcomes at the end of treatment. Kaplan-Meier curves were used to compare 28-day survival between groups and hazard ratio (HR, 95% confidence interval, CI) to evaluate the impact of associated factors.

RESULTS

One-hundred thirty patients were enrolled(104 in CAZ/AVI, 26 in MER/VAB). Median age was 66 years in CAZ/AVI and 69 in MER/VAB. Median Charlson Comorbidity Index was 5 in both groups. The most represented site of infection was the lower respiratory tract. Concomitant bacteremia was present in 61 (58.7%) patients in the CAZ/AVI group and in 16 (61.5%) patients in the MER/VAB **[Table1].** The evaluated outcomes yielded comparable results between the two groups). No differences were found by site of infection **[Table2]**.

	CAZ/AVI (N=104)	MER/VAB (N=26)	p-value
Male sex, n (%)	66 (63.5%)	16 (61.5%)	0.372
Median age, years (IQR)	66 (58-78)	69 (59-78)	0.431
Comorbidities, n (%)			
Diabetes	24 (23.1%)	5 (19.2%)	0.861
Localized or metastatic solid cancer	20 (19.2%)	6 (23.1%)	0.905
Peripheral Vascular Disease	22 (21.1%)	10 (38.5%)	0.091
Moderate to Severe Chronic Kidney Disease	20 (19.2%)	9 (34.6%)	0.115
History of Stroke	14 (13.5%)	3 (11.5%)	0.743
History of Myocardial Infarction	17 (16.3%)	3 (11.5%)	0.463
COPD	15 (14.4%)	6 (23.1 %)	0.336
Congestive Heart Failure	15 (14.4%)	7 (26.9%)	0.154
Liver Disease	13 (12.5%)	0 (0.0%)	0.153
Dementia	9 (8.7%)	1 (3.9%)	0.380
Hemiplegia	9 (8.7%)	3 (11.5%)	0.706
Connective Tissue Disease	7 (6.7%)	2 (7.7%)	0.913
Peptic Ulcer Disease	5 (4.8%)	1 (3.8%)	0.791
Leukemia	3 (2.9%)	3 (11.5%)	0.069
Lymphoma	1 (1.0%)	0 (0.0%)	0.611
AIDS	1 (1.0%)	0 (0.0%)	0.609
Median CCI, (IQR)	5 (3-7)	5 (4-7)	0.414
Hospitalization in the previous 12 months, n (%)	57 (54.8%)	14 (53.8%)	0.992
Resident in a nursing home	4 (3.9%)	0 (0.0%)	0.328
Immunosuppressed state, n (%)	18 (17.3%)	10 (38.5%)	0.039
Intermittent dialysis	7 (6.7%)	0 (0.0%)	0.177

Table 1: Patient Characteristics in CAZ/AVI and MER/VAB Groups.
Legend: IQR: Interquartile Range; **COPD:** Chronic Obstructive Pulmonary Disease; **AIDS:** Acquired Immunodeficiency Syndrome; **CCI:** Charlson Comorbidity Index; **ICU**: Intensive Care Unit; **CVVH:** Continuous venovenous haemofiltration

	CAZ/AVI (N=104)	MER/VAB (N=26)	p-value
Infection site, n (%)			
Lower respiratory tract	38 (36.5%)	9 (34.6%)	0.86
Genitourinary	32 (30.8%)	5 (19.2%)	0.24
Abdominal	15 (14.4%)	6 (23.1%)	0.28
Cardiovascular	15 (14.4%)	1 (3.8%)	0.19
Skin and soft tissue	6 (5.8%)	3 (11.5%)	0.30
Unidentified site	7 (6.7%)	0 (0.0%)	0.34
Central venous catheter-related	0 (0.0%)	3 (11.5%)	0.007
With bacteremia, n (%)	61 (58.7%)	16 (61.5%)	0.62
Septic shock, n (%)	13 (12.5%)	5 (19.2%)	0.47
ICU Admission, n (%)	38 (36.5%)	4 (15.4%)	0.04
CVVH treatment during hospitalization	6 (5.8%)	1 (3.9%)	0.70
Clinical outcomes			
Overall, n (%)			0.72
Clinical cure	65 (62.5%)	17 (65.4%)	
In-hospital mortality	25 (24.0%)	7 (26.9%)	
Relapse	14 (13.5%)	2 (7.7%)	
Lower respiratory tract, n (%)			0.92
Clinical cure	23 (60.5%)	6 (66.7%)	
In-hospital mortality	13 (30.2%)	5 (35.7%)	
Relapse	4 (9.3%)	1 (7.1%)	
Genitourinary tract, n (%)			0.28
Clinical cure	24 (75.0%)	2 (40.0%)	
In-hospital mortality	5 (15.6%)	2 (40.0%)	
Relapse	3 (9.4%)	1 (20.0%)	
Abdominal, n (%)			0.52
Clinical cure	8 (53.3%)	3 (50%)	
In-hospital mortality	2 (13.3%)	2 (33.3%)	
Relapse	5 (33.3%)	1 (16.6%)	

Table 2: Infection characteristics, rates of clinical cure, in-hospital mortality and relapse in CAZ/AVI and MER/VAB Groups.
Legend: ICU: Intensive care unit; **CVVH:** Continuous venovenous haemofiltration

Kaplan-Meier survival curves **(Figure 1)** showed no significant difference in overall 28-day survival (22.1% *vs* 26.9%, log-rank p=0.62) between the two groups. A multivariate model including ICU, immunosuppressed state and treatment group confirmed that no significant difference existed in terms of efficacy (adjusted HR for MER/VAB vs CAZ/AVI 1.74 0.71-4.30, p=0.31). Adverse events were rare in both cohorts: among the CAZ/AVI group 6 events (4.62%) were reported, which included neuralgia, platelet count decrease, urticaria *vs* 1 (0.77%) in the MER/VAB group (pancytopenia).

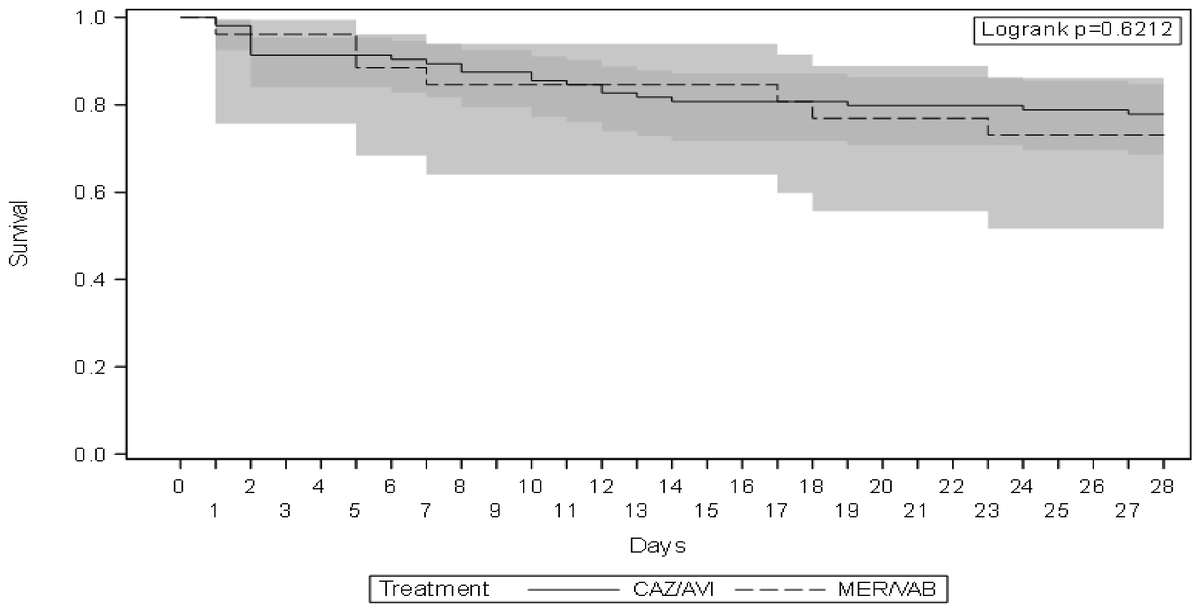

Figure 1. Kaplan-Meier surival analysis comparing Ceftazidime/avibactam group and Meropenem/Vaborbactam

CAZ/AVI and MER/VAB are effective treatments for KPC K. pneumoniae infections, showing similar clinical outcomes

References: 1. Grundmann H et Al.; European Survey of Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) Working Group. Occurrence of carbapenemase-producing Klebsiella pneumoniae and Escherichia coli in the European survey of carbapenemase-producing Enterobacteriaceae (EuSCAPE): a prospective, multinational study. Lancet Infect Dis. 2017 Feb. doi: 10.1016/S1473-3099(16)30257-2

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