Meropenem Vaborbactam in Patients with Carbapenem-resistant Enterobacteriaceae Gram-Negative Bloodstream Infection: a Case Series

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Background

- Antimicrobial resistance in Gram-negative bacteria, particularly carbapenem-resistant Enterobacteriaceae (CRE), is one of the most critical challenges in infectious diseases.
- Meropenem with vaborbactam (MVB) is a novel beta-lactamase inhibitor combined with meropenem, a well-established antipseudomonal carbapenem that has activity against CRE.
- MVB received Food and Drug Administration (FDA) approval for the treatment of complicated urinary tract infections (cUTI) and acute pyelonephritis (AP) caused by susceptible organisms in August, 2017. However, evidence regarding MVB use in non-FDA approved indications, particularly bacteremia is rather limited.
- The objective of this analysis was to evaluate the clinical and safety outcomes for patients treated with MVB for CRE bacteremia.

Methods

- Multi-site at the Detroit Medical Center, retrospective cohort study from August, 2018 to March, 2019.
- Inclusion criteria: Age ≥ 18 years, treated with MVB for ≥ 24 hours.
- CRE was defined according to the Center for Disease Control and Prevention.
- Clinical success was defined as survival, resolution of signs and symptoms of infection and absence of recurrence at 30 days following the onset of infection.
- Microbiological success was defined as absence of isolation of initial pathogen following 7 days of MVB treatment.
- Baseline clinical and infection characteristics were evaluated for patients who received MVB as the primary agent against CRE
- All analysis performed using SPSS Statistics, IBM SPSS software, version 25.0 (IBM Corp., Armonk, NY).

Results

Table 1. Description of cases

Case	Age / sex	Pathogen	Prior antibiotics	Source	Total days	IV antibiotics with MVB	Micro-biological Success in days	Resolution of signs and symptoms	30 day Survival	Any Survival	30-day recurrence or readmission	Clinical Success	Susceptibilities (MIC)
1	63 M	• *Enterobacter cloacae*	No	Primary Bacteremia	5	No	Yes 1 day	Improvement Deescalated to oral therapy	Yes	Yes	Readmission but no recurrence	Yes	• Enterobacter: MER: 0.5 (S), IMI (S); 1, ERT (R): 2
2	27 M	• *Escherichia coli* • *Klebsiella pneumoniae*	No	Primary Bacteremia	5	No	Yes 1 day	Improvement	Yes	Yes	No	Yes	• Escherichia coli: MER(S): 0.125, • Klebsiella pneumoniae: MER(S): 0.125
3	61 M	• *Escherichia coli* • *Klebsiella Pneumoniae*	No	UTI	1	No	NA	Improvement	Yes	Yes	Readmission but no recurrence	Yes	• Escherichia coli: MER(S): 0.125, IMI (S); 0.25, ERT (S): 0.25 • Klebsiella pneumoniae: MER(R): 8, ERT (R): 1, CEFTAZ (S): 2, MVB (S): 0.032
4	43 M	• *Klebsiella pneumoniae*	Yes	Unknown	4	No	Yes 2 days	Improvement	Yes	No	No	Yes	• Klebsiella pneumoniae: MER (I): 2, CEFAZ (S): 0.5, MVB (S): 0.06
5	25 M	• *Klebsiella pneumoniae*	No	Intravenous catheter	17	No	Yes 4 days	Improvement	Yes	Yes	No	Yes	• Klebsiella pneumoniae: MER (S): 0.125, IMI (S); 0.25, ERT (I): 1 CEFAZ (S): 4, MVB (S): 0.032

MIC: minimum inhibitory concentration. MVB: meropenem-vabrobactam, CEFAZ: Ceftazidime / tazobactam, MER: meropenem, IMI: imipenem, ERT: ertapenem, MIC; minimum inhibitory concentration; UTI, urinary tract infection.

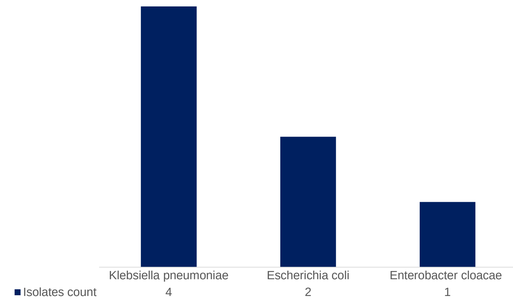
Table 2. Baseline Criteria

Characteristics, n (%)	
Demographics and Comorbid Conditions, n (%)	
Mean age (yr)	**43 (25 – 63)**
No. of male participants (%)	**5 (100%)**
African American	**5 (100%)**
Comorbid conditions	
Chronic renal disease	**2 (40%)**
Lung disease; asthma or COPD	**3 (60%)**
Diabetes	**1 (10%)**
Liver disease	**1 (10%)**
Heart failure	**1 (20%)**
Chronic dialysis	**1 (10%)**
Immunosuppression	**1 (20%)**
Clinical Characteristics, median (IQR)	
APACHE II score	**20 (6.5-29.5)**
MDR Risk factor, n (%)	
Prior hospitalization >48 in preceding 90 days	**1 (20%)**
Prior antibiotics ≥ 24 in preceding 90 days	**1 (20%)**
Prior infection with resistant organism	**3 (60%)**

COPD: Chronic obstructive pulmonary disease. APACHE II, acute physiology and chronic health evaluation. MDR: Multidrug resistant.

IQR: interquartile range

Figure 1. Targeted pathogens



Results

Figure 2. Clinical Outcomes

Conclusions

- Clinical success was achieved in 100% of evaluable patients treated with MVB for bacteremia.
- MVB appeared to be safe, well tolerated and improved patients' outcomes.
- Studies with longer follow up, more patients, various indications and other non CRE infections are required to assess the role of MVB in comparison to other anti-CRE agents.

References

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Disclosures

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