POSTER# 710

BUDGET IMPACT AND COST-EFFECTIVENESS OF MEROPENEM-VABORBACTAM (M-V) COMPARED WITH CEFTAZIDIME-AVIBACTAM (C-A) IN US HOSPITALS

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ABSTRACT

Introduction: Carbapenem-resistant Enterobacteriaceae (CRE) infections continue to spread worldwide and are considered an urgent antimicrobial resistance threat. CRE infections may cost US hospitals approximately $275 million annually (nearly $30,000 per patient). Meropenem-vaborbactam (M-V) is a carbapenem/beta-lactamase inhibitor combination designed to have enhanced in vitro activity against select carbapenemase-producing Enterobacteriaceae, and is a potential new option for the treatment of severe gram-negative infections, including CRE. Here, we examine the budget impact and cost-effectiveness of M-V as compared to ceftazidime-avibactam (C-A) to aid decision making.

Methods: Two decision analytic models, a budget impact model and cost-effectiveness model, were developed from the perspective of a US hospital to examine the budget impact and cost-effectiveness of M-V for the management of hospitalized patients with suspected or confirmed CRE. Data was derived from clinical studies and published literature. Key clinical inputs included clinically-cured infection, mortality at 28 days, and incidence of renal failure. Key economic inputs included cost of drug, hospitalization length of stay (LOS) (both general ward and intensive care unit (ICU) days), treatment failure and acute renal failure; unit costs were sourced from the literature.

Results: In a hospital hypothetically treating 30 patients per year, total annual costs associated with M-V were estimated to be $898,221 vs. $968,810 with C-A, for a total cost savings of $70,589 per year associated with use of M-V. M-V was dominant (more effective, less costly) compared to C-A; these results were robust to sensitivity analysis. Cost-effectiveness and budget impact differences were largely driven by improved clinical cure and mortality rates associated with M-V. While data from both TANGO I and II suggest a potential ICU LOS reduction, overall LOS in the model was conservatively assumed equal across treatment arms. Incorporating this benefit would have therefore resulted in more favorable cost-effectiveness estimates and lower total costs for M-V.

Conclusion: The models' results indicate that M-V is likely to be associated with a favorable budget impact and high cost-effectiveness for the treatment of CRE infections.

INTRODUCTION

- Although estimates vary widely, the economic cost of antibacterial resistance in the United States could be as high as $20 billion and $35 billion a year in excess direct healthcare costs and lost productivity costs, respectively.[1]
- Specific to CRE, one recently published model estimates that an infection incidence of 2.93 per 100,000 population in the US (9,418 infections annually) would cost society $553 million (95% credibility range [CR]: $303-1,593 million), third party payers $147 million (95% CR: $129-172 million), and hospitals $275 million (95% CR: $217-334 million).[2]
  - Bartsch and colleagues estimate the cost of a single CRE infection to be $29,157 (95% CR: $22,993-$35,503) from a hospital perspective ; similar to estimates reported in other published literature.
- A single-pathogen analysis by Spellberg and Rex indicates that antibiotics aimed at treating highly resistant pathogens are likely to remain cost-effective at prices of $10,000 per course, with an overall cost-effectiveness value of $1,908 per life-year saved.[3]
  - In sensitivity analyses, even at pricing as high as up to $30,000 per course, the cost per quality-adjusted life-year (QALY) remained below $50,000, a commonly cited cost-effectiveness benchmark.
- At standard dosing for eGFR rates ≥50 mL/min/1.73m2 (VABOMERE 4 grams [meropenem 2 grams and vaborbactam 2 grams] every 8 hours by intravenous infusion over 3 hours) and wholesale acquisition costs (WAC) ($165/vial), a course of meropenem-vaborbactam may cost approximately $7,920 for a median duration of 8 days of therapy (range $4,950-$13,860 for 5-14 days of therapy).
  - This suggests that treatment with meropenem-vaborbactam for serious gram-negative infections including CRE is likely to be highly cost-effective.
- Here, we examine the economic impact of meropenem-vaborbactam versus ceftazidime-avibactam for the treatment of patients with CRE,

METHODS

- 2 models were developed from the perspective of a US hospital to examine the economic impact of meropenem-vaborbactam in the management of hospitalized patients with suspected or confirmed CRE (Figure 1).
  - Clinically-cured is defined as complete resolution or significant improvement of the baseline signs and symptoms, and the model assumes no further antimicrobial treatment is warranted.
  - Patients who do not respond adequately to the assigned antibiotic and are not clinically-cured are assumed to switch to a mixture of second-line antibiotics to treat their ongoing infection, and incur a lump-sum cost that reflects the downstream management costs. The management costs of those who die are included in the treatment failure cost outputs.
  - Treatment failure is assumed to be assessed after a specified number of days (3 days for the base case), and meropenem-vaborbactam and ceftazidime-avibactam treatments are then stopped. The average duration of treatment for the base case is therefore assumed to be shorter for treatment failure than for the clinically-cured cases.
- Hospitalization cost inputs include the costs incurred by hospitalized patients with CRE infections in the general ward and intensive care unit (ICU), and exclude the costs for antibiotics prescribed for CRE and any additional management costs to treat major adverse event (AEs).
  - For each of the antibiotic treatments, the administration cost for IV infusion is assumed to be accounted for under the hospitalization cost.
  - The costs associated with other concomitant medications are captured within the hospitalization cost.

FIGURE 1: MODEL STRUCTURE

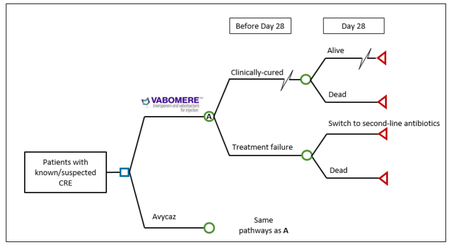


TABLE 1: KEY MODEL INPUTS

	Meropenem-vaborbactam	Ceftazidime-avibactam	Source
Clinical inputs			
Clinical cure rate	64.3%	59.0%	4, 5
Mortality at 28 days	17.9%	24.0%	4, 5
Rate of acute renal failure	2.2%	10.0%	4, 5
LOS – general ward	7.26 days	7.26 days	6
LOS - ICU	2.65 days	3.16 days	6, 7
Economic and health resource utilization inputs			
Cost per day of therapy	$990	$898*	8
Mean days of treatment for patients who are clinically cured	8.4	8.4	4
Mean days of treatment for patients who fail treatment	3.0	3.0	9
Hospital cost per day – general ward	$1,382	$1,382	6
Hospital cost per day – ICU	$3,551	$3,551	6
Cost of treatment failure	$10,312	$10,312	10
Cost of acute renal failure	$9,001	$9,001	11

*Avycaz price at the time the analysis was conducted; price increases will drive results further in favor of Vabomere

RESULTS

Budget Impact

- In a hospital treating 30 patients per year, total annual costs associated with meropenem-vaborbactam were estimated to be $898,221 vs. $968,810 with ceftazidime-avibactam, for a total cost savings of $70,589 per year (Figure 2).
- On a per patient basis, costs were $29,941 per patient treated with meropenem-vaborbactam vs. $32,294 with ceftazidime-avibactam (estimated difference of $2,353 per patient).
- Cost differences were largely driven by increased clinical cure rates associated with meropenem-vaborbactam vs. ceftazidime-avibactam (64.3% vs. 59.0% , respectively), resulting in reduced incidence and associated costs of treatment failure ($10,312 per treatment failure).
- Incidence of key clinical outcomes is summarized in Figure 3. The numbers needed to treat (NNT) per clinically-cured infection and death avoided were 19 and 16, respectively.

Cost Effectiveness

- At a cost of $990.00 per day, meropenem-vaborbactam was dominant (less costly, more effective) compared to ceftazidime-avibactam.
- Total per-patient costs were estimated to be approximately $31,978 with meropenem-vaborbactam and $32,513 with ceftazidime-avibactam; well in line with published estimates of per-patient costs associated with CRE
- Cost-effectiveness and cost differences were largely driven by improved clinical cure and mortality rates associated with meropenem-vaborbactam.

Limitations

- Analyses are conducted from the US hospital perspective. The model considers initial hospital costs and mortality within 30 days of therapy but does not capture outpatient or longer term costs accrued post-discharge.
- The potential impact of a delay in starting the appropriate antibiotic treatment on costs or mortality is not captured at this time.
- The efficacy of each antibiotic is captured through the proportion of patients assessed as clinically-cured and 28-day mortality. Differences in the time to clinically-cured infection are not considered.
- There may be differences between the real world management practices and assumptions made in the model, such as clinical monitoring, antibiotic dose adjustment, or treatment duration.
- The model is limited by the lack of head-to-head trial data for meropenem-vaborbactam and ceftazidime-avibactam. Published data from a retrospective, single arm, single institution study is used (n=37). After comparing the study populations, it was determined that the similarities among the populations allowed for direct comparison and represent the best currently available data; both studies examine patients across similar infection types with confirmed CRE infections.
- Costs of renal failure are sourced from the published literature and based on a general hospitalized population.
- Actual costs in CRE patients will vary by institution.

FIGURE 2: TOTAL ANNUAL BUDGET IMPACT, MEROPENEM-VABORBACTAM (VABOMERE™) VS. CEFTAZIDIME-AVIBACTAM (AVYCAZ©) IN A HYPOTHETICAL HOSPITAL TREATING 30 PATIENTS PER YEAR

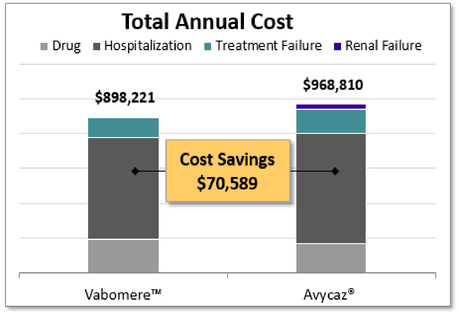
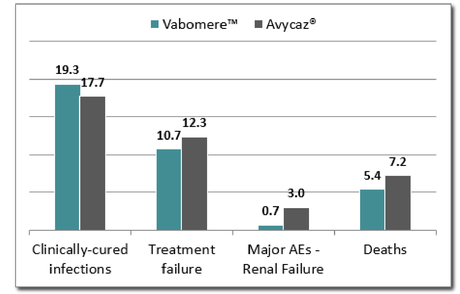


FIGURE 3: INCIDENCE OF KEY CLINICAL OUTCOMES, MEROPENEM-VABORBACTAM (VABOMERE™) VS. CEFTAZIDIME-AVIBACTAM (AVYCAZ©)



CONCLUSION

- These model results indicate that M-V is likely to be associated with a favorable budget impact and high cost-effectiveness for the treatment of CRE infections.
- The specific economic value of meropenem-vaborbactam will vary at the institutional level based on current antimicrobial stewardship practices, treatment patterns, and institutional prevalence and resistance patterns associated with CRE.

REFERENCES

1. CDC. Antibiotic Resistance Threats in the United States, 2013. http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf.
2. Bartsch SM, et al. Potential Economic Burden of Carbapenem-ResistantEnterobacteriaceae (CRE) in the United States. Clin Microbiol Infect. 2016 Sep 15. pii: S1198-743X(
3. Spellberg B, Rex JH. The value of single-pathogen antibacterial agents. Nat Rev Drug Discov. 2013 Dec;12(12):963.16)30389-5.
4. Data on file
5. Shields R, et.al. CID 2016; 63(12):1615-8.
6. Data on File. Premier Perspective database analysis (2009-2012) of CRE patients based on ICD-9 codes for cUTI, Bacteremia and Pneumonia
7. ICU LOS for CRE patients calculated from the Premier Perspective Database was reduced by 16.2%, consistent with Shorr A. et al, 2017: Shorr A, et al. Hospital and ICU Length of Stay (LOS) with Meropenem-Vaborbactam (M-V) versus Piperacillin-Tazobactam (P-T) in Complicated Urinary Tract Infections (cUTI), including Acute Pyelonephritis (AP) in TANGO I. Presented at ASM Microbe — June 1-5, 2017, New Orleans, LA
8. PriceRx Accessed 11/1/17.
9. Assumption based on expert opinion
10. Zilberberg MD, Nathanson BH, Sulham K. et al. Carbapenem resistance, inappropriate empiric treatment and outcomes among patients hospitalized with Enterobacteriaceae urinary tract infection, pneumonia and sepsis. BMC Infectious Diseases (2017) 17:279
11. Silver SA, Long J, Zheng Y, et al. Cost of acute kidney injury in hospitalized patients. J. Hosp. Med. 2017 February;12(2)70-76. Costs were reported in 2012 dollars ($7933) and converted to 2017$ based on the Medical services CPI (https://www.bls.gov/cpi/cpi_dr.htm#2008).