# Cost-Effectiveness of Ceftazidime-Avibactam for Patients with Hospital-Acquired Pneumonia Caused by Multi-Drug Resistant Enterobacteriaceae or Pseudomonas in China

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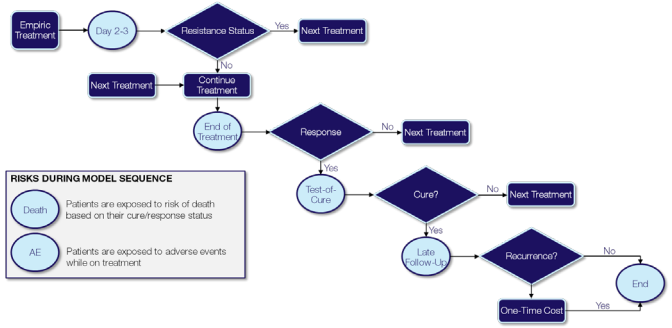
## OBJECTIVE

- To estimate the cost-effectiveness of ceftazidime-avibactam (CAZ-AVI) for the treatment of hospital-acquired pneumonia (HAP) including ventilator-associated pneumonia (VAP) caused by multi-drug resistant enterobacteriaceae (MDRE) or MDR pseudomonas aeruginosa (MDRPA) in China.

## METHODS

- A previously published patient-level simulation model was localized to China to estimate the cost-effectiveness of first-line CAZ-AVI compared to meropenem from a healthcare perspective.
- Patients flowed through the model which evaluates resistance status, response, and adverse events (AEs), which can all lead to a treatment switch (Figure 1).
- Second-line therapy of colistin plus high dose carbapenem (meropenem) was used for both arms.

### Figure 1. Patient Flow Diagram




- Resistance rates were 0.7% (CAZ-AVI) and 7.6% (meropenem) for MDRE, and 10.7% (CAZ-AVI) and 35.5% (meropenem) for MDRPA. Resistance for second-line colistin + high-dose carbapenem was assumed to be the same as colistin and was 0.90% for MDRPA and 34.8% for MDRE. These values were sourced from Sader et al. 2018.
- Effectiveness rates for CAZ-AVI and meropenem were based on a randomized, double-blind, phase 3 clinical trial (Table 1). Effectiveness for second-line colistin + high dose carbapenem was informed via KOL opinion.
- Adverse event rates were 8.64% for CAZ-AVI (REPROVE), 6.45% for meropenem (REPROVE, and 6.45% for colistin + high-dose carbapenem (assumed same as meropenem).

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### Table 1. Effectiveness Inputs

| ANTIBIOTIC REGIMEN | MDRE | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *K. PNEUMONIA (N=376)* | | *E. COLI (N=441)* | | *E. CLOACAE (N=146)* | | WEIGHTED AVERAGE[1] | |
| | EOT | TOC | EOT | TOC | EOT | TOC | EOT | TOC |
| *First-Line* | | | | | | | | |
| CAZ-AVI[2] | 86.9% | 89.1% | 90.7% | 92.4% | 92.9% | 78.3% | 89.5% | 89.0% |
| Meropenem[2] | 87.6% | 89.2% | 92.7% | 85.8% | 87.5% | 88.9% | 89.9% | 87.6% |
| *Second-Line Regimen* | | | | | | | | |
| Colistin + HD CBP[3] | 58.0% | 100% | 58.0% | 100% | 58.0% | 100% | 58.0% | 100% |

| ANTIBIOTIC REGIMEN | MDRPA *P. AERUGINOSA* | |
|---|---|---|
| | EOT | TOC |
| *First-Line* | | |
| CAZ-AVI[2] | 84.4% | 76.1% |
| Meropenem[2] | 88.9% | 86.8% |
| *Second-Line Regimen* | | |
| Colistin + HD CBP[3] | 58.0% | 100% |

Notes: HD = High-Dose; CBP = Carbapenem; EOT = End-of-Treatment; TOC = Test-of-Cure; Effectiveness weighted according to pathogen prevalence in Sader et al. 2018.
Sources: [1]Sader et al. 2018; [2]REPROVE; [3]KOL Opinion/Assumption

- All cost data, including drugs, AEs, and hospitalization were localized to China (Table 2).
- Treatment duration was based on the clinical trials and EMA product labels and was 10.5 days for CAZ-AVI, 12.0 days for meropenem, and 9.5 days for colistin + high-dose carbapenem.
- Mortality was included as the probability of death given the appropriate first-line treatment is used (14.02%) and relative risks

### Table 2. Cost & HCRU Inputs

| VARIABLE | VALUE |
|---|---|
| Drug Costs (Per Course) | |
| CAZ-AVI | ¥43,974 |
| Meropenem | ¥11,228 |
| Colistin + HD CBP | ¥101,378 |
| Number of Days in Hospital[1] | |
| Cure | ¥16.40 |
| Failure | ¥19.10 |
| Proportion of Hospitalized Days in ICU[2] | |
| Cure | ¥43.90 |
| Failure | ¥56.02 |
| Hospitalization Cost (Per Day)[3] | |
| General Ward | ¥234 |
| ICU | ¥4,820 |
| Adverse Event Cost (Per Event)[4] | ¥16,692 |

Sources: [1]Based on clinical trial data; [2]REPROVE Payer Analysis (Global Model); [3]World Health Organization; [4]Global Model and Converted Using Purchasing Power Parity from Italy to China.

for inappropriate treatment without a resistant pathogen (1.88) and with a resistant pathogen (2.26) (Wilke et al. 2011).

- Utility values were 0.92 for patients achieving a clinical cure (Song et al. 2012) and 0.61 for patients without response (Delate et al. 2001).
- Costs and benefits were discounted at 5% over the five-year time horizon.

## RESULTS

- At a cost-effectiveness threshold of three-times GDP per capita, CAZ-AVI was cost-effective compared to meropenem for HAP/VAP caused by both MDRE and MDRPA with ICERs of ¥147,500 (2.1x GDP per capita) and ¥30,496 (<1x GDP per capita), respectively.

### Table 4. Model Results

| OUTCOME | MDRE | | | MDRPA | | |
|---|---|---|---|---|---|---|
| | CAZ-AVI | MPN | INC | CAZ-AVI | MPN | INC |
| **Costs** | | | | | | |
| Treatment | ¥88,079 | ¥71,954 | ¥16,125 | ¥182,118 | ¥178,873 | ¥3,245 |
| Hospitalization | ¥46,830 | ¥49,627 | -¥2,796 | ¥60,724 | ¥59,212 | ¥1,511 |
| Adverse Events | ¥1,498 | ¥1,127 | ¥371 | ¥1,609 | ¥1,159 | ¥450 |
| Total Costs | ¥136,407 | ¥122,708 | ¥13,699 | ¥244,451 | ¥239,244 | ¥5,207 |
| **Health Outcome** | | | | | | |
| *Clinical Cure* | | | | | | |
| At First Line | 66.66% | 61.14% | 5.52% | 48.4% | 42.3% | 6.1% |
| Overall | 66.88% | 61.54% | 5.34% | 49.1% | 43.3% | 5.8% |
| Life Years | 3.73 | 3.70 | 0.04 | 3.64 | 3.50 | 0.14 |
| QALYs | 3.25 | 3.16 | 0.09 | 2.94 | 2.77 | 0.17 |
| | | **ICER** | **¥147,500** | | | **¥30,496** |
| | **3x GDP Per Capita Multiple** | | **2.1x** | | | **0.14x** |

Source: GDP Per Capita = National Bureau of Statistics 2020. Available at: http://www.stats.gov.cn/tjsj/zxfb/202002/t20200228_1728913.html

- Specifically, CAZ-AVI had ¥13,699 and 0.09 additional total costs and QALYs, respectively, within MDRE; ¥5,207 and 0.17 additional total costs and QALYs, respectively, within MDRPA. Length of stay was reduced by 0.65 days and 1.37 in the CAZ-AVI arms of the MDRE and MDRPA analyses, respectively.
- Despite similar effectiveness rates, the overall rate of clinical cure was 5.34% and 5.8% higher for the CAZ-AVI arm compared to meropenem in HAP/VAP caused by both MDRE and MDRPA, respectively.

## CONCLUSION

- **CAZ-AVI is a cost-effective alternative to meropenem in the treatment of HAP/VAP caused by MDRE or MDRPA in China.**