Evaluation of Ceftazidime/avibactam Utilization and Clinical Outcomes in Patients with Multidrug-Resistant Gram-Negative Infections

M. HWANG[1], S. YANG[1], J. CHOI[1], H. HAN[1].
[1]ASAN MEDICAL CENTER, PHARMACY, SEOUL, KOREA- SOUTH.
jjj2214@amc.seoul.kr, +82-10-7510-4239.

ASAN Medical Center

Background

Background

2019 Global Burden of Disease Study
: Antimicrobial resistance caused 1.27 million deaths and contributed to 4.95 million deaths.

Carbapenem-resistant Enterobacteriaceae (CRE)
: Classified as a Critical Group in the WHO BPPL(Bacterial Priority Pathogens List).

Domestic Trends
: In 2022, CRE infections increased by 155.5% compared to 2018.

Ceftazidime/avibacatm(CZA)

Ceftazidime + avibactam (β-lactamase inhibitor)

- **Mechanism**
  : Inhibits β-lactamase, demonstrating antibacterial activity against carbapenem-resistant and multidrug-resistant Gram-negative bacteria.
- **Guidelines**
  : Recommended for CRE treatment by IDSA and ESCMID guidelines.
- **Domestic Introduction**
  : Introduced in July 2023 and covered by insurance starting February 2024.
- **Necessity**
  : Systematic studies on its real-world usage and efficacy are still lacking.

Objectives

- The reimbursement approval is expected to contribute to an increased use of CZA.
- Critical time to evaluate current usage patterns and establish strategies for appropriate future use

▶ **To optimize CZA use by monitoring its efficacy and indications while providing data for improving strategies against multidrug-resistant organisms.**

Methods

1. **Study design** : Observational, retrospective study
2. **Study period** : July 2023 ~ July 2024 (total 13 months)
3. **Study patients** : Adult patients who received CZA treatment for 3 days or more after hospitalization at Seoul Asan Medical Center
4. **Study method**
   1) **Status of CZA use**
   2) **Efficacy evaluation**
      - **Treatment success rate**
        : Treatment completion without additional antibiotic treatment for the same indication treated with CZA
      - **30-day mortality rate**
        : 30-day mortality rate from the last day of CZA administration
5. **Statistics** : SPSS version 21 (IBM CO, Armonk, NY, USA) program

Results

[1] Status of CZA use

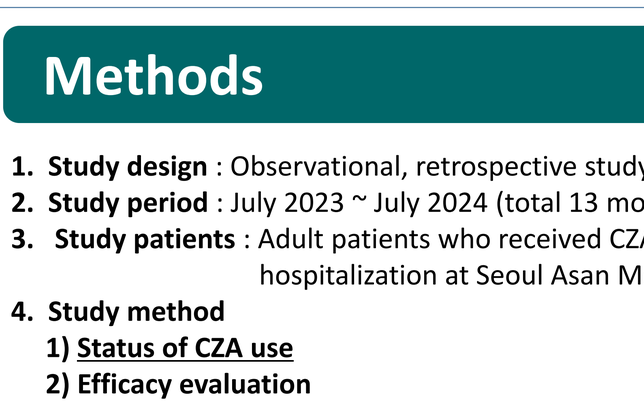

Figure 1. CZA prescriptions per month

- **175 patients** included in study
- Total prescriptions: **3,437**
- **Increase in prescriptions after reimbursement approval (Feb 2024)**
- **Top prescribing departments**
  : LTS (26%), HEM (16%), ONC (16%)
- **Most common pathogen**
  : *Klebsiella pneumoniae* (159, 91%)

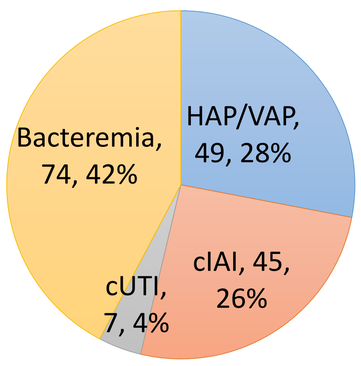

Figure 2. Indications for CZA use

- **Most frequent approved indication:** HAP/VAP (49, 28%)
- **Most frequent off-label indication:** Bacteremia (74, 42%)
- **Adherence to recommended dosage:** 168 (96%)
- **Among 7 inappropriate cases:**
  - 4 adjusted to 24-hour infusion due to cost concerns
  - 3 did not undergo proper dose adjustment based on renal function

[2] Treatment success rate

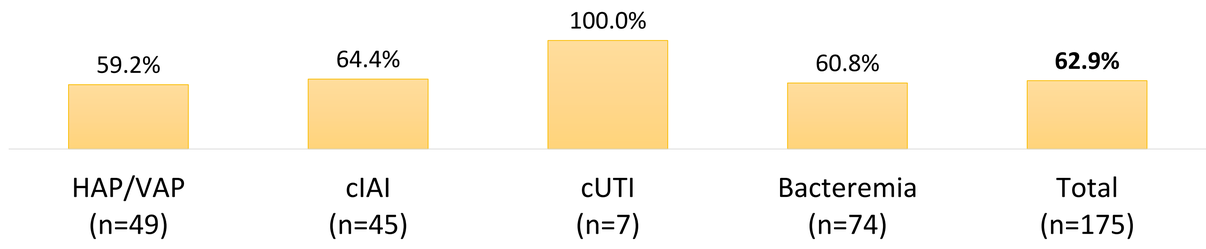

Figure 3. Treatment success rate

- The overall treatment success rate of CZA: **63%** (110 out of 175 patients)
- The difference in treatment success rate according to indication type was not statistically significant.

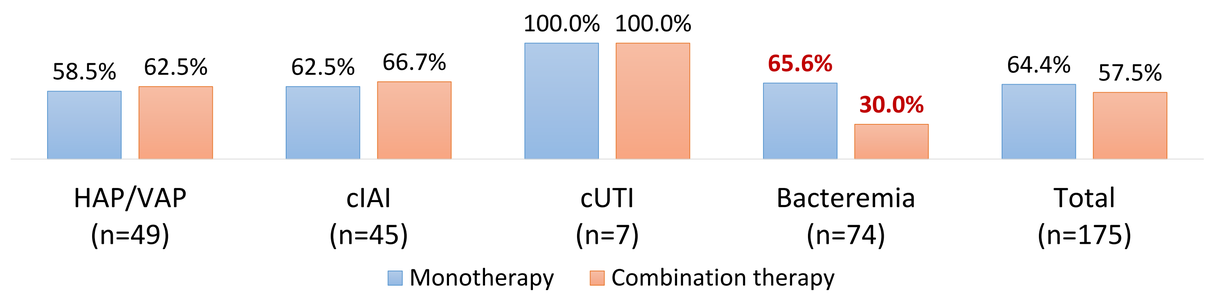

Figure 4. Treatment success rate categorized by treatment regimen

- **A significant difference in treatment success rate was observed only in patients with bacteremia, depending on whether CZA was used in combination therapy ($p<0.05$)**
- Although monotherapy patients showed higher treatment success rates, their greater need for renal replacement therapy and longer hospitalization suggest higher severity.
  → However, the small number of combination therapy patients (n=7) limits the ability to clearly compare or generalize treatment effects.

[3] 30-day mortality rate

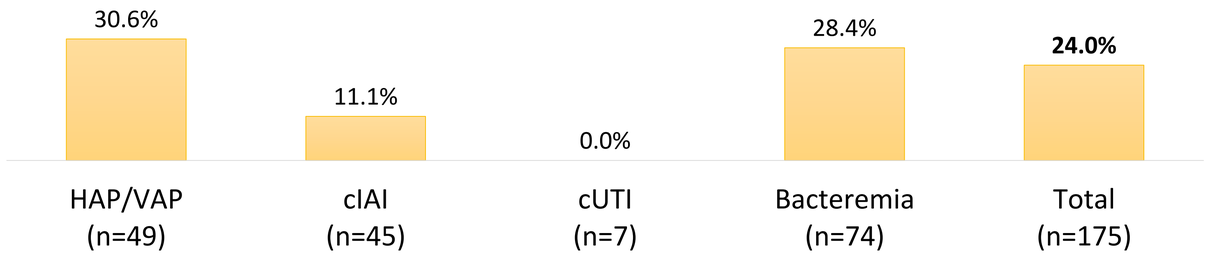

Figure 5. 30-day mortality rate

- The overall 30-day mortality rate of CZA: **24%** (42 out of 175 patients)
- The difference in 30-day mortality rate according to indication type was not statistically significant.

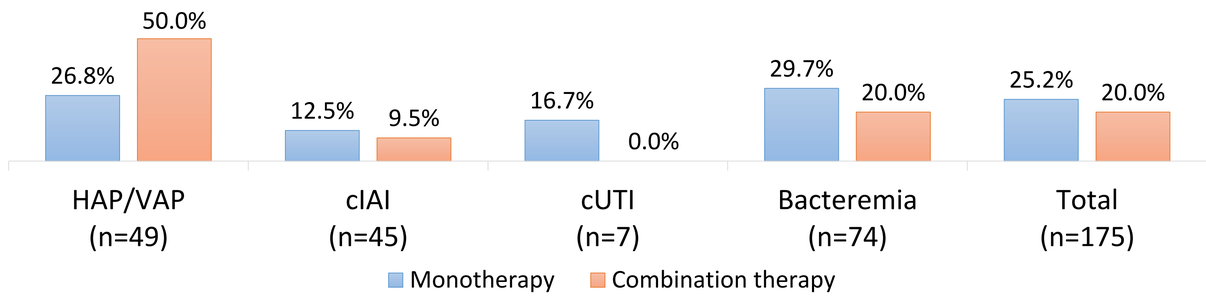

Figure 6. 30-day mortality rate categorized by treatment regimen

- The difference in 30-day mortality rate according to treatment regimen was not statistically significant.

Conclusion

- **Treatment success rate (62.9%) lower than previous study (77.3%)**
  30-day mortality rate (24.0%) similar to previous study (24.6%)
  → Differences likely due to baseline characteristics, sample size, and success criteria
- **No significant difference in effectiveness between monotherapy and combination therapy**
  - **2019 Meta-analysis (Int J Antimicrob Agents)**
    : No significant difference in mortality or microbiological success
  - **2024 Meta-analysis (Infection)**
    : No additional clinical benefit from combination therapy

▶ **A minimal antibiotic approach may achieve sufficient treatment outcomes and reduce costs.**

▶ **Further studies with diverse patients and larger data are needed to clarify the optimal CZA treatment strategy and improve clinical outcomes in resistant infections.**

References

1. The Use and Effectiveness of Ceftazidime-Avibactam in Real-World Clinical Practice: EZTEAM Study. Infect Dis Ther. 2023 Mar; 12(3): 891-917.2.
2. Efficacy of ceftazidime/avibactam in monotherapy or combination therapy against carbapenem-resistant Gram-negative bacteria: A meta-analysis. Int J Antimicrob Agents. 2019 Dec;54(6):735-740.
3. Ceftazidime-avibactam combination therapy versus monotherapy for treating carbapenem-resistant gram-negative infection: a systemic review and meta-analysis. Infection. 2024 Oct;52(5):2029-2042.

5PSQ-066