Real-life Experience of Imipenem-cilastatin-relebactam for Treatment of Extensively Drug-resistant and Difficult-to-treat *Pseudomonas* Infections at a Large Academic Medical Center

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Background

- According to IDSA 2022 guidance, imipenem-cilastatin-relebactam (IMI/REL) is considered one of the preferred antibiotics to treat extensively drug-resistant (XDR) and difficult-to-treat (DTR) *Pseudomonas aeruginosa*
- RESTORE-IMI-1 evaluated 24 patients with imipenem-non-susceptible *P. aeruginosa* and demonstrated favorable clinical response in 13/16 (81%) of IMI-REL versus 5/8 (63%) of colistin+IMI
- Since approval in 2019, there remains limited published data on the real-world experience of IMI/REL for the treatment of *Pseudomonas* infections

Objective

- To describe our experience using IMI/REL for the treatment of MDR, XDR, and DTR *Pseudomonas sp*. infections

Methods

Study design:

- A retrospective, observational study was conducted at Jackson Memorial Hospital, a 1550-bed academic teaching hospital in Miami, Florida

Inclusion Criteria

- Age ≥18 years
- Positive respiratory cultures for MDR *Pseudomonas aeruginosa* between Jan 2020- Feb 2022
- Received 72 hours of IMI/REL

Exclusion Criteria

- Patients with index culture non-susceptible to IMI/REL
- Vulnerable populations (e.g., prisoners, pregnancy)

Primary outcome:

- Clinical success: defined as resolution of clinical signs and symptoms of infection and no requirement for additional antibacterial treatment within 72 hours for the same infection

Secondary outcomes:

- 30-day all-cause mortality
- 30-day recurrence = microbiologic failure + concomitant signs and symptoms of a new infection within 30 days of end of therapy
- 60-day infection-related hospital readmission
- Adverse effects

Results

Table 1. Baseline characteristics (n=10)

Male, n (%)	**6 (60)**
Age in years, median (range)	63 (31-85)
Race	
White	5 (50)
Black	5 (50)
Ethnicity	
Non-Hispanic	6 (60)
Hispanic	4 (40)
BMI kg/m^2, median (range)	27 (21-36)
Comorbidities, n (%)	
Cardiovascular Disease	6 (60)
Chronic Kidney Disease	4 (40)
Diabetes Mellitus	4 (40)
Hypertension	4 (40)
Solid Organ Transplant	3 (30)
Congestive Heart Failure	3 (30)
Liver Disease	3 (30)
Active Malignancy	1 (10)
COPD or Other Chronic Lung Disease	1 (10)
ICU at time of index culture, n (%)	8 (80)
APACHE II	
Median (range)	26 (10-40)
>15, n (%)	9 (90)
Receiving pressors at time of index culture, n (%)	3 (30)
HD or CRRT at index culture, n (%)	5 (50)
Type of Infection, n (%)	
VAP	7 (70)
HAP	1 (10)
Empyema	2 (20)
Bloodstream Infection	2 (20)
Presence of Concomitant Infection, n (%)	
None	4 (40)
Bloodstream Infection (other than *Pseudomonas*)	3 (30)
Fungemia	3 (30)
Urinary Tract Infection	2 (20)
Peritonitis	1 (10)
Polymicrobial VAP with *Klebsiella pneumoniae*	1 (10)
Polymicrobial empyema with *Stenotrophomonas maltophilia*	1 (10)
Cytomegalovirus viremia	1 (10)
Treatment regimen, n (%)	
Monotherapy	4 (40%)
Combination therapy with additional inhaled antibiotic	2 (20%)
Combination therapy with additional inhaled + intravenous antibiotic	4 (40%)

SOT = solid organ transplant; VAP = ventilator-associated pneumonia; HAP = hospital-acquired pneumonia; COPD = chronic obstructive pulmonary disease

Results

Primary outcome:

- Clinical success: 7/10 (70%)

Secondary outcomes:

- Median duration of therapy: 7 (range 4-14 days)
- 30-day all-cause mortality: 3/10 (30%)
- 30-day recurrence: 2/8 (25%)
- 60-day infection-related hospital readmission: 0/4 (0%)
- Adverse effects (while on therapy, unclear if drug-related)
  - Hypertension: 9/10 (90%)
  - AST or ALT ≥5x upper limit normal: 2/10 (20%)
  - Nausea/vomiting: 1/10 (10%)
  - Diarrhea: 2/10 (20%)
  - Seizures: 1/10 (10%)

Additional findings:

- Two patients (20%) had MIC increases after IMI/REL exposure
  - 1 µg/mL (susceptible) → 3 µg/mL (non-susceptible)
  - 1.5 µg/mL (susceptible) → >32 µg/mL (resistant)

Conclusion

- We describe our single-center experience using IMI-REL for the treatment of DTR *Pseudomonas* infections in a small cohort of critically ill patients
- We observed clinical success in a majority of patients; however, these results require validation using a larger study
- In the era of emerging resistance, future studies comparing IMI/REL to other first-line drugs for DTR *Pseudomonas* are urgently needed

References

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Correspondence & Disclosures

All authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject of this presentation

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