Ceftolozane-Tazobactam (C/T) Treatment Outcomes in Immunocompromised Patients with Multidrug-Resistant (MDR) *Pseudomonas aeruginosa* (PA) Infections

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***Presented on behalf of the authors by Mike Wong, MD[3]**

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Background

- C/T is a novel anti-pseudomonal cephalosporin combined with an established beta-lactamase inhibitor active against MDR *P. aeruginosa* (PA)
- Data assessing clinical use and real-world outcomes following C/T treatment in immuno-compromised patients are limited
- This study evaluated treatment patterns and clinical outcomes of immunocompromised patients treated with C/T for MDR PA across 15 U.S. hospitals

Methods

Study design & inclusion criteria

- Retrospective, 15-center cohort study
  - Treatment with C/T for ≥24 hours; positive index culture for PA
  - Immunocompromised status at C/T treatment included: previous solid organ transplant (SOT), diseases suppressing resistance to infection (HIV/AIDS, leukemia, lymphoma), or receipt of immunosuppressive agents

Statistical analysis

- Classification and regression tree (CART) analysis was used to identify 30-day mortality split in APACHE II scores
- Two-tailed unpaired *t* test and Kruskal-Wall test (continuous variables), and Fisher's exact test (categorical variables) were used to compare baseline characteristics and outcomes

Outcomes

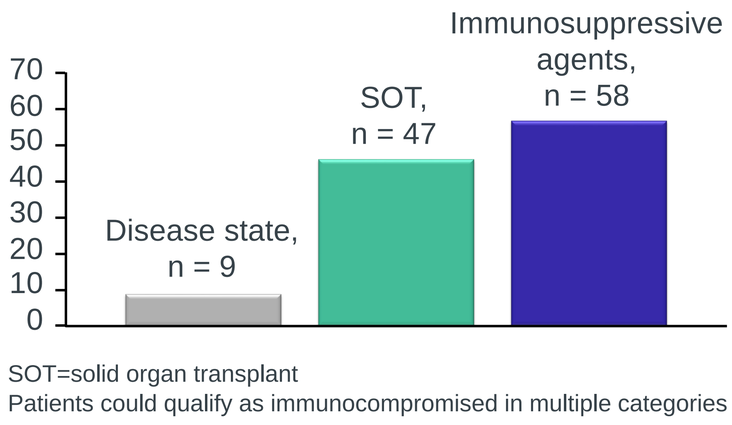
- Clinical cure and 30-day all-cause mortality

Definitions

Clinical cure	No escalation/additional therapy and improved signs and symptoms from baseline to end of therapy
MDR	Non-susceptible to ≥1 agent in ≥3 classes of anti-PA agents
Immuno-suppressive agents	Receipt of immunosuppressive agents, chemotherapy, radiation, steroids at doses capable of immuno-suppression (≥10 mg prednisone for ≥1 month prior to hospitalization or >15 mg/kg/day of hydrocortisone/>3 mg/kg/day methyl-prednisolone for >5 days)

Results

Figure 1. Immunocompromised status



SOT=solid organ transplant
Patients could qualify as immunocompromised in multiple categories

Table 1. Baseline characteristics

Characteristic	Total (n = 70)	APACHE II score >25 (n = 15)	APACHE II score ≤25 (n = 55)	*P*-value (APACHE II group comparisons)
Age (years), mean ± SD	57 ± 14	58.1 ± 14.4	56.1 ± 14	0.64
In ICU on day 1, n (%)	33 (47%)	11 (73%)	22 (40%)	**0.04**
APACHE II score, median (IQR)**	18 (11.75)	28 (3.5)	14 (10.5)	--
Charlson comorbidity index, median (IQR)**	5 (3.75)	5 (4.5)	5 (3.5)	0.81
Comorbidities, n (%)				
Chronic pulmonary disease	32 (46%)	9 (60%)	23 (42%)	0.25
Chronic kidney disease	28 (40%)	6 (40%)	22 (40%)	1.00
Diabetes	17 (24%)	5 (33%)	12 (22%)	0.50
Myocardial infarction	10 (14%)	3 (20%)	7 (13%)	0.44
Heart failure	10 (14%)	4 (27%)	6 (11%)	0.20
Peptic ulcer disease	9 (13%)	1 (6.7%)	8 (15%)	0.67
Liver dysfunction	9 (13%)	3 (20%)	6 (11%)	0.39
Peripheral vascular disease	8 (11%)	5 (33%)	3 (5.5%)	**<0.01**
Cerebrovascular disease	5 (7%)	1 (6.7%)	4 (7.3%)	1.00
Metastatic solid tumor	5 (7%)	0 (0%)	5 (9%)	0.58
Hemiplegia/paraplegia	2 (3%)	0 (0%)	2 (3.6%)	1.00
Concurrent antibiotics, n (%)	31 (44.3%)	9 (60%)	22 (40%)	0.24
Aminoglycoside	15 (48.4%)	5 (55.6%)	10 (45.5%)	0.70
Fluoroquinolone	9 (29%)	2 (22.2%)	7 (31.8%)	0.69
Polymyxin	7 (22.6%)	1 (11.1%)	6 (27.3%)	0.64
Beta-lactam	2 (6.5%)	0 (0%)	2 (20%)	1.00

**APACHE II and Charlson comorbidity index scores were calculated based on labs from Day 1 of suspected infection.

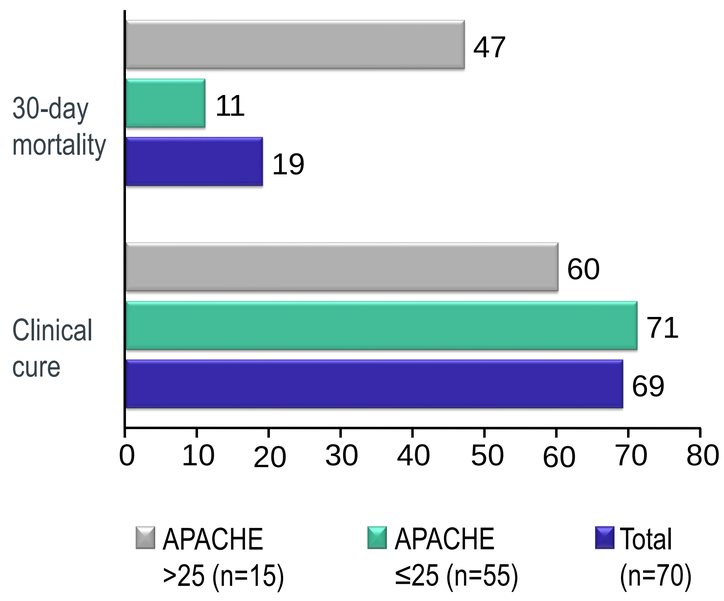
Table 2. Clinical outcomes

Outcome	Total (n = 70)	APACHE II score >25 (n = 15)	APACHE II score ≤25 (n = 55)	*P*-value (APACHE II group comparisons)
Clinical cure, n (%)	48 (69%)	9 (60%)	39 (71%)	0.36
30-day all-cause mortality, n (%)	13 (19%)	7 (47%)	6 (11%)	**<0.01**
Length of C/T therapy (days), mean ± SD	13 ± 10.8	9.1 ± 4.8	13.9 ± 11.7	0.13
Length of hospital stay (days), mean ± SD	57 ± 59.7	72.7 ± 68.4	53.2 ± 57.3	0.28
Polymicrobial infection, n (%)	25 (36%)	7 (47%)	18 (29%)	0.37
Source of infection, n (%)				
Pneumonia (PNA)	39 (56%)	8 (53%)	31 (56%)	1.00
Wound	8 (11%)	1 (6.7%)	7 (13%)	1.00
Intra-abdominal (IAI)	7 (10%)	1 (6.7%)	6 (11%)	1.00
Bloodstream (BSI)	6 (9%)	1 (6.7%)	5 (9%)	1.00
Urinary tract (UTI)	6 (9%)	2 (13%)	4 (7.3%)	0.60
Bone/joint	4 (6%)	1 (6.7%)	3 (5.5%)	1.00
Other source	4 (6%)	0 (0%)	4 (7.3%)	0.57
Central nervous system (CNS)	3 (4%)	1 (6.7%)	2 (3.6%)	0.52

Results (cont'd)

Figure 2. Outcomes by source of infection

Figure 3. Outcomes breakdown by APACHE II score 30-day mortality split



Conclusion

- Of 70 immunocompromised patients treated with C/T for MDR PA, clinical cure was achieved in 69% and 30-day mortality was 19%, which is consistent with other real world evaluations in a more heterogeneous population.
- CART identified a significant split in 30-day mortality at an APACHE II score >25 (n = 15; 47%); in patients with APACHE II ≤ 25, 30-day mortality was 11%.
- C/T represents a promising agent for treatment of PA resistant to many traditional anti-pseudomonal agents in this high-risk population.

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