systemic signs of infection from other causes. Therefore, the possibility of false-positive healthcare facility–onset CDI (*C. difficile* colonization) cannot be fully ruled out. We attempted to mitigate this possibility through appropriate testing and redundant clinician review of tested subjects. Also, the number of CDI PCR tests completed in each group was comparable at 8 (OVP group) and 14 (control group) (P = .23). For future studies, if molecular-based testing is utilized alone, baseline testing for *C. difficile* colonization may provide further discernment.

While our hospital has 961 beds, daily census can vary considerably. The letter writers believe that our eligibility criteria were not excessively restrictive, but our criteria may be more restrictive than one might realize. We included patients ≥60 years of age who had been admitted twice in a short period of time, who received systemic antibiotics at each admission, and did not meet any of our exclusion criteria. Six hundred forty-four patients were screened during the study period; 429 did not meet study criteria (252 did not receive systemic antibiotics during their index hospitalization, 84 were not hospitalized or anticipated to be hospitalized for >72 hours at screening, 65 were receiving an excluding medication, 7 were unable to take oral medications, 5 had active CDI at screening, and 16 were unable to be evaluated in the appropriate time frame), leaving 215 potential patients (~ 1 patient per day). Of these, 109 refused or were unable to consent. As we reported, 106 patients were included with 6 patients excluded after enrollment.

We agree with McCreery et al that there are important statistical considerations to a small study that could affect its conclusions. As we stated, we fully endorse further prospective studies on this issue and are not suggesting that the use of oral vancomycin for the prevention of *C. difficile* is yet an established prevention modality. Our understanding is that a few larger prospective studies are ongoing currently and it will be interesting to see what those studies find. If oral vancomycin prophylaxis is found to be safe and effective, the biggest opportunity will be establishing more effective predictive models so that patients who would most benefit from prophylaxis can be accurately identified.

Notes

Author contributions. All authors have seen and approved the reply and contributed significantly to the work.

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Clinical Efficacy of Ceftolozane-Tazobactam Versus Other Active Agents for the Treatment of Bacteremia and Nosocomial Pneumonia due to Drug-Resistant *Pseudomonas aeruginosa*

To the Editor—We read with great interest the recent study by Pogue et al [1] entitled "Ceftolozane-tazobactam vs polymyxin or aminoglycoside-based regimens for the treatment of drug-resistant *Pseudomonas aeruginosa*." We thank the authors for addressing the demands of better managing patients suffering from these serious infections with limited therapeutic options. However, we think some points merit further discussion.

First, there was an imbalance in the distributions of sites of infection between groups (ie, 12% and 24% of ceftolozane/tazobactam [C/T]–treated and colistin/aminoglycoside–treated patients had hospital-acquired pneumonia, respectively; P = .04), which may have influenced results. Second, infectious disease consultations, which have been associated with improved outcome in other studies [2, 3], were more frequent in patients receiving ceftolozane-tazobactam than colistin/aminoglycosides [1].Third, actual polymyxin dosages were not assessed, with real-life experiences suggesting a nonnegligible risk of inadequate colistin dosages [4].

To evaluate the effect of ceftolozane-tazobactam for the treatment of severe drug-resistant *P. aeruginosa* infections without the above-mentioned limitations, we performed a retrospective 1:2 matched case-control analysis at 9 centers in Italy. All patients with a diagnosis of nosocomial pneumonia (either hospital-acquired pneumonia or ventilator-associated pneumonia) or bloodstream infection due to multidrug-resistant or extensively drug-resistant *P. aeruginosa* during the period June 2016 to March 2018 were included in the study. Cases comprised patients who received ceftolozane-tazobactam for at least ≥ 72 hours. Controls comprised randomly chosen patients among those who received an intravenous colistin- or aminoglycoside-based regimen for ≥ 72 hours (dosages are detailed in Table 1). Matching was based according to age (±10 years), sex, site of infection, and susceptibility profile of the isolated pathogen. Overall, 16 patients with drug-resistant *P. aeruginosa*

infections treated with ceftolozane-tazobactam were included as cases. These patients were compared with 32 corresponding controls who received a regimen including either colistin or aminoglycosides. Demographic and clinical characteristics of patients are shown in Table 1. All patients had at least 1 infectious disease consultation during their course of disease.

Although not statistically significant, a trend toward more favorable 14-day clinical cure rates was observed in C/T-treated than in colistin/aminoglycoside-treated patients (81.3% vs 56.3%; $P = .11$). A similar trend favoring C/T was observed for crude 30-day mortality (18.8% vs 28.1%; $P = .73$). Finally, we observed an increased prevalence of acute kidney injury (25.0% vs 0%; $P = .04$) in patients treated with colistin/aminoglycoside regimens.

In conclusion, ceftolozane-tazobactam was well tolerated and showed higher cure rates than colistin/aminoglycoside-based regimens for

Table 1. Demographic Characteristics, Clinical Characteristics, and Outcome of the 48 Patients With Bloodstream Infection or Nosocomial Pneumonia Due to Multidrug-Resistant or Extensively Drug-Resistant *Pseudomonas aeruginosa* Infections

Characteristic	Overall	Colistin/Aminoglycoside Group[a] (n = 32)	Ceftolozane-tazobactam Group[a] (n = 16)	*P* Value
Age, y, mean ± SD	62.4 ± 14.5	62.5 ± 14.5	62.2 ± 14.7	.93
Male sex	39 (81.3)	26 (81.3)	13 (81.3)	1
Hospital admission				
Medical	27 (56.3)	17 (53.1)	10 (62.5)	.75
Surgical	8 (16.7)	4 (12.5)	4 (25.0)	.41
ICU	13 (27.5)	11 (34.4)	2 (12.5)	.17
Underlying disease				
Cardiovascular disease	13 (27.1)	7 (21.9)	6 (37.5)	.31
Neurological disease	13 (27.1)	7 (21.9)	6 (37.5)	.31
Chronic renal failure	12 (25.0)	7 (21.5)	5 (31.3)	.50
Diabetes	10 (20.8)	6 (18.8)	4 (25.0)	.71
Neoplasm	9 (18.8)	8 (25.0)	1 (6.3)	.23
Other predisposing condition				
CVC at the time of infection	30 (62.5)	18 (56.3)	12 (75.0)	.34
Previous antibiotic therapy[a]	29 (70.7)	17 (68.0)	12 (75.0)	.73
Previous ICU admission[a]	28 (59.6)	20 (64.5)	8 (50.0)	.36
Iatrogenic immunosuppression	25 (54.3)	14 (43.8)	11 (68.8)	.21
Previous surgery	13 (27.1)	6 (18.8)	1 (6.3)	.90
Neutropenia (PMN ≤500 mm^3)	4 (8.5)	2 (6.5)	2 (12.5)	.59
Type of infection				
Pneumonia	27 (56.3)	18 (56.3)	9 (56.3)	1
Bloodstream infection	21 (43.7)	14 (43.7)	7 (43.7)	
Antibiotic susceptibility profile				
MDR	30 (62.5)	20 (62.5)	10 (62.5)	1
XDR	18 (37.5)	12 (37.5)	6 (37.5)	
Adequate empirical therapy	9 (40.9)	6 (50.0)	3 (30.0)	.41
Combined targeted therapy	38 (79.2)	29 (90.6)	9 (56.3)	**.01**
Colistin	4 (10.3)	…	4 (44.4)	
Piperacillin-tazobactam	6 (15.4)	6 (20.0)	…	
Tigecycline	2 (5.1)	0	2 (22.2)	
Fluoroquinolones	5 (12.8)	4 (13.3)	1 (11.1)	
Carbapenems	18 (46.2)	18 (60.0)	…	
Aminoglycosides[b]	3 (7.7)	1 (3.3)	2 (22.2)	
Overall duration of treatment	12.3 ± 6.6	12.3 ± 7.7	12.1 ± 5.8	.93
14-d clinical cure	31 (64.6)	18 (56.3)	13 (81.3)	.11
30-d mortality	12 (25.0)	9 (28.1)	3 (18.8)	.72
AKI development during antibiotic therapy	8 (16.7)	8 (25.0)	0	**.04**

Data are presented as no. (%) unless otherwise indicated. Values in bold indicate statistical significance ($P < .05$).

Abbreviations: AKI, acute kidney injury; CVC, central venous catheter; ICU, intensive care unit; MDR, multidrug resistant; PMN, polymorphonuclear leukocytes; SD, standard deviation; XDR, extensively drug resistant.

[a]Ceftolozane-tazobactam was dosed either as an intravenous dose of 1.5 g every 8 hours or as an intravenous dose of 3 g every 8 hours according to the infectious disease specialist. Colistin was administered every 12 hours at a daily dose of 9 million International Units (MIU), after a 9 MIU loading dose. Gentamicin and amikacin were administered every 24 hours at a daily per-kilogram dose of 5–7 mg and 15 mg, respectively. Doses were reduced in the presence of renal failure. No systematic therapeutic drug monitoring of antibiotics was performed at each participating center.

[b]One patient received combination therapy including colistin plus aminoglycoside.

severe, resistant *P. aeruginosa* infections. Even with the limitation of the small sample size, our experience corroborates and generalizes Pogue et al's results, thus further supporting the possible preferential use of ceftolozane-tazobactam over colistin or aminoglycosides for the treatment of drug-resistant *P. aeruginosa* infections.

Notes

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Reply to Vena et al

To the Editor—We thank Vena and colleagues for their correspondence related to our recent publication [1]. Their analysis, similar to ours but conducted in Italian hospitals, yields results that are in accordance with our findings. We are in complete agreement with their conclusion, supported now by evidence from North America and Europe, that the treatment of invasive infections due to multidrug-resistant or extensively drug-resistant *Pseudomonas aeruginosa* with ceftolozane-tazobactam is associated with higher rates of clinical cure and lower rates of nephrotoxicity than treatment with colistin- or aminoglycoside-based regimens. Based on these data, ceftolozane-tazobactam should be given preference over these therapies for infections due to susceptible isolates.

We opine that a similar evidence-based preference relative to polymyxins should be given to imipenem-relebactam against carbapenem-resistant *P. aeruginosa* [2], and to ceftazidime-avibactam [3, 4] or meropenem-vaborbactam [5] against carbapenem-resistant Enterobacteriaceae. We acknowledge that use of these agents requires expert guidance by infectious diseases physicians and pharmacists regarding indications and dosing, as well as exclusion of resistance mediated by metallo-β-lactamases and phenotypic confirmation of susceptibility by clinical microbiology laboratories. The lower cost