

BACKGROUND

- Real-world data regarding antibiotic use provide valuable insights into regional variations in treatment practice and the characteristics of patients and pathogens.
- Cefiderocol is a siderophore cephalosporin antibiotic with *in vitro* activity against a broad range of Gram-negative bacteria; it is approved in the USA for treatment of complicated urinary tract infections (including pyelonephritis) and hospital-acquired and ventilator-associated bacterial pneumonia.¹
- PROVE was an international, observational medical chart review study of cefiderocol use in hospitalized patients with serious Gram-negative bacterial infections. This poster reports data for the US cohort.

METHODS

- PROVE collected data between November 2020 and July 2024 from patients hospitalized with confirmed Gram-negative bacterial infections.² Included patients had received cefiderocol for the first time and for ≥72 hours.
- The following data for patients in the US cohort were analyzed descriptively:
 - Baseline demographics, clinical characteristics, and cefiderocol use
 - Clinical cure (resolution or improvement of infection signs or symptoms at end of treatment [EOT], without evidence of later relapse or death)
 - Clinical response (resolution or improvement of signs or symptoms at EOT as judged by the physician, excluding patients who died during therapy)
 - All-cause mortality (ACM; including patients who died within 30 days of cefiderocol initiation).
- Additional analyses are ongoing to collect more detailed results for this subgroup.

RESULTS

- Clinical outcomes data were collected for 508 US patients. Demographics, baseline characteristics, cefiderocol use, and severity of illness for this subgroup are shown in **Table 1** and **Figure 1**.
 - At cefiderocol initiation, 57.3% of patients were in the intensive care unit and 47.6% were receiving organ support
 - Diabetes mellitus (36.0%) was the most frequent comorbidity; sepsis or septic shock were present in 23.2% of patients
 - Most patients (93.3%) had ≥1 risk factor for acquiring carbapenem-resistant (CR) Gram-negative bacteria
 - Almost 75% of patients received cefiderocol for a documented infection.
- Infection characteristics are shown in **Figure 2**; respiratory tract infections (RTIs) were most common (n=272; 53.5%). Monomicrobial *Pseudomonas aeruginosa* infections (29.9%) and polymicrobial infections (29.9%) were reported most frequently.
- Overall rates of clinical cure, clinical response, and 30-day ACM were 70.1%, 77.8%, and 20.7%, respectively. Among patients with RTIs, these rates were 64.7%, 76.5%, and 25.7%, respectively (**Table 2**).
- Clinical cure rates for patients with Enterobacterales and *Pseudomonas aeruginosa* infections were 79.3% and 70.4%, with respective 30-day ACM rates of 17.2% and 20.4% (**Figure 3**).
 - Outcomes for infections caused by *Acinetobacter baumannii* were similar to those for infections with other causative pathogens.
- Rates of clinical cure and clinical response were lower, and 30-day ACM was higher, when cefiderocol was used as salvage therapy compared with empiric treatment or for documented infections (**Figure 4**).

Earlier Cefiderocol Use Was Associated with Better Outcomes for Challenging Gram-Negative Bacterial Infections: US Results From the Global Observational PROVE Study

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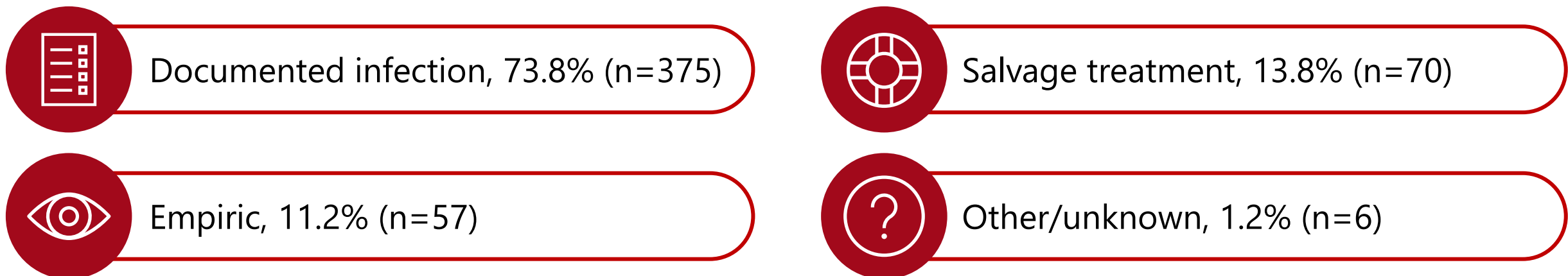
Table 1. Demographics, Baseline Characteristics, and Severity of Illness Among US Patients in the PROVE Study (2020–2024)

Parameter	US Patients (N=508)
Demographics	
Age (years), median (IQR)	58.0 (44.0–67.0)
≥65 years old, n (%)	163 (32.1)
Sex, male, n (%)	311 (61.2)
Most frequent concomitant medical conditions, (%)	
Diabetes mellitus	183 (36.0)
Chronic pulmonary disease	127 (25.0)
Sepsis or septic shock	118 (23.2)
Moderate-to-severe chronic kidney disease	96 (18.9)
Congestive heart failure	83 (16.3)
COVID-19 infection	68 (13.4)
Treatment pattern	
Duration of cefiderocol use (days), median (IQR)	10.0 (7.0–16.0)
Combination therapy, n (%)	168 (33.1)
Severity of illness, n (%)	
ICU stay at time of cefiderocol initiation	291 (57.3)
Receipt of any organ support at time of cefiderocol initiation	242 (47.6)
Mechanical ventilation	210 (41.3)
Use of vasopressor medication	123 (24.2)
Renal replacement therapy	61 (12.0)
ECMO	12 (2.4)

Risk factors for acquiring CR-GNBI, n (%)	
Admitted to hospital in past 6 months	337 (66.3)
Were on ventilator at any point before taking the index culture sample	257 (50.6)
Received carbapenem or non-response to carbapenem in the prior 30 days	167 (32.9)
History of CR-GNBI or colonization within last 6 months	147 (28.9)
Immunocompromised	81 (15.9)
Trauma, major surgery within 1 month before initiation of cefiderocol	17 (3.3)
Other	14 (2.8)
Recent travel history to a foreign country	5 (1.0)
None	34 (6.7)
Number of risk factors for acquiring CR-GNBI, n (%)	
0	34 (6.7)
1	143 (28.1)
2	168 (33.1)
3	112 (22.0)
≥4	51 (10.0)

COVID-19, coronavirus disease 2019; CR-GNBI, carbapenem-resistant Gram-negative bacterial infection; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range.

Figure 1. Reason for Cefiderocol Use in the PROVE US Cohort (N=508)^a



^aReported by the investigator. Documented infection: the pathogen and susceptibilities were known, and cefiderocol use was not due to failure of a prior antibiotic regimen. Empiric use: cefiderocol use started before the pathogen and/or susceptibilities were available to help guide the choice. Salvage therapy: cefiderocol was used after a prior antibiotic regimen had failed; patients usually received at least 3 days of prior antibiotic therapy to see whether there was an adequate response before the next course of antibiotic would be considered salvage. Other, including unknown: any other reason provided by the physician.

Figure 2. Primary Site of Infection and Baseline Pathogen in the US PROVE Cohort (N=508)

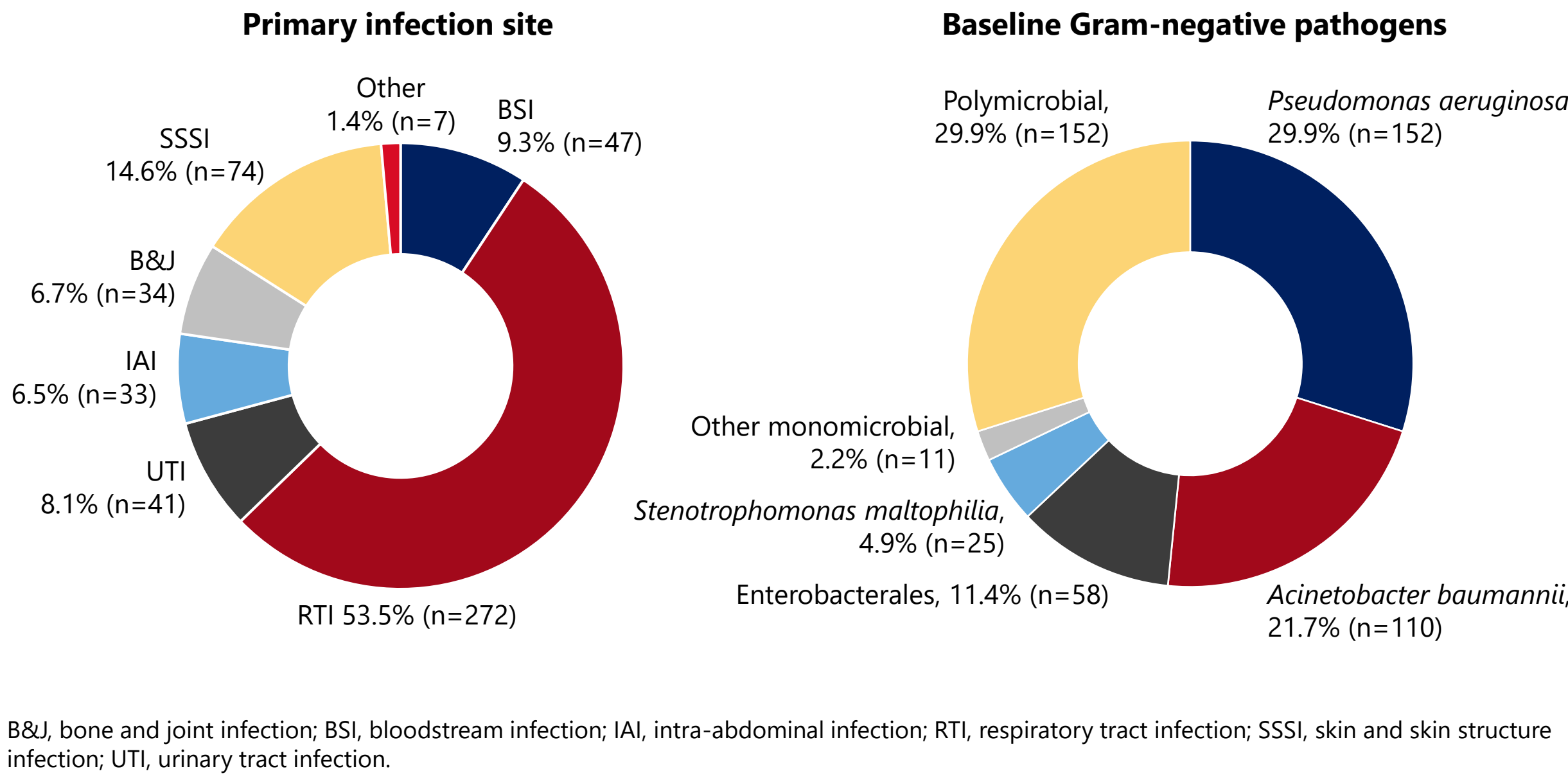


Table 2. Clinical Outcomes by Site of Infection in US Patients Treated With Cefiderocol For Serious Gram-Negative Infections (N=508)

Site of infection	% [95% confidence interval], n/N		
	Clinical cure	Clinical response at EOT	30-day ACM
Overall	70.1% [66.1; 74.1] 356/508	77.8% [74.1; 81.4] 395/508	20.7% [17.2; 24.2] 105/508
RTI	64.7% [59.0; 70.4] 176/272	76.5% [71.4; 81.5] 208/272	25.7% [20.5; 30.9] 70/272
BSI	78.7% [67.0; 90.4] 37/47	80.9% [69.6; 92.1] 38/47	17.0% [6.3; 27.8] 8/47
UTI	85.4% [74.6; 96.2] 35/41	85.4% [74.6; 96.2] 35/41	14.6% [3.8; 25.5] 6/41
SSSI	77.0% [67.4; 86.6] 57/74	79.7% [70.6; 88.9] 59/74	10.8% [3.7; 17.9] 8/74
IAI	54.5% [37.6; 71.5] 18/33	57.6% [40.7; 74.4] 19/33	18.2% [5.0; 31.3] 6/33
B&J	79.4% [65.8; 93.0] 27/34	88.2% [77.4; 99.1] 30/34	17.6% [4.8; 30.5] 6/34
Other	85.7% [59.8; 100] 6/7	85.7% [59.8; 100] 6/7	14.3% [0.0; 40.2] 1/7

ACM, all-cause mortality; B&J, bone and joint infection; BSI, bloodstream infection; EOT, end of treatment; IAI, intra-abdominal infection; RTI, respiratory tract infection; SSSI, skin and skin structure infection; UTI, urinary tract infection. Data are shown as % [95% confidence interval] and n/N; n, number of patients with outcome; N, total number of patients in the category.

CONCLUSIONS

- In this real-world study of US patients at risk for acquiring CR Gram-negative infections, cefiderocol demonstrated good efficacy against a broad range of Gram-negative pathogens in individuals hospitalized with diverse serious infections.
- Outcomes with cefiderocol were comparable for patients treated empirically or for document infection. As might be expected, clinical cure rate was lower for patients receiving salvage therapy, highlighting that cefiderocol treatment prior to clinical decline may be the most beneficial approach.

Figure 3. Clinical Outcomes by Causative Pathogen in US Patients Treated With Cefiderocol in the PROVE Real-World Study (N=508)

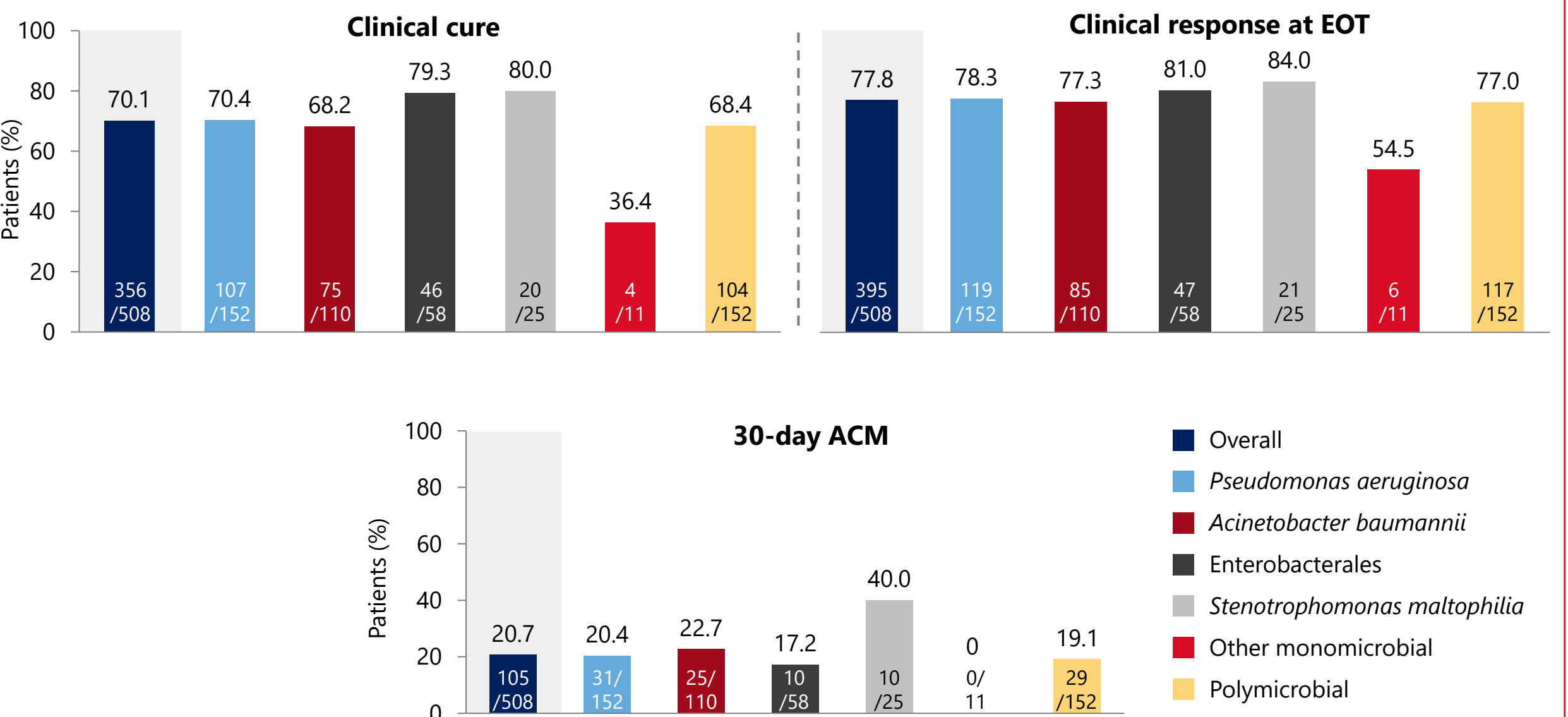


Figure 4. Clinical Outcomes by Reason for Cefiderocol Use Among US Patients With Serious Gram-Negative Infections (N=508)

