

Clinical Outcomes of Cefiderocol for Treatment of Bloodstream Infections Caused by Gram-Negative Bacteria: Subgroup Analysis of the PROVE Study

Emily Drwiega,¹ David W. Wareham,² Massimo Antonelli,³ Stefano Verardi,⁴ Karan Gill,⁴ Anne Santerre Henriksen,⁴ Sean T. Nguyen,⁵

¹Department of Pharmacy Practice, University of Illinois Chicago, Chicago, IL, USA; ²Queen Mary University of London, London, UK; ³Università Cattolica del Sacro Cuore, Rome, Italy; ⁴Shionogi BV, London, UK; ⁵Shionogi Inc., Florham Park, NJ, USA



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BACKGROUND

- Bloodstream infections (BSIs), particularly those caused by Gram-negative pathogens, are associated with increased morbidity and mortality.^{1–3}
- Cefiderocol, a first-in-class siderophore cephalosporin, is indicated in patients ≥18 years for the treatment of complicated urinary tract infections (including pyelonephritis) and hospital-acquired/ventilator-associated bacterial pneumonia caused by susceptible Gram-negative microorganisms.⁴
- The main objective of this subgroup analysis of the real-world PROVE study was to evaluate the clinical outcomes of hospitalized patients with BSIs caused by Gram-negative bacteria, who were treated with cefiderocol.

METHODS

- The PROVE study was an international, multicenter, medical chart review study of real-world first-time cefiderocol use in patients with Gram-negative bacterial infections.⁵
- Eligible patients had a documented Gram-negative bacterial infection, which prompted treatment with cefiderocol for at least 72 hours, and available data detailing the cefiderocol starting dose, description of the Gram-negative bacterial infection for which cefiderocol was prescribed, and discharge data after hospitalization.⁵
 - Primary BSI:** patients with a confirmed Gram-negative pathogen in the bloodstream, which prompted the use of cefiderocol.
 - Secondary BSI:** patients with a confirmed Gram-negative pathogen in the bloodstream, but had a different primary infection site that prompted the use of cefiderocol.
- Clinical cure was defined as the resolution or improvement of signs and symptoms of infection at end of treatment (EOT), as judged by the physician, without evidence of a later relapse or death.
- Clinical response was defined as the resolution or improvement of signs/symptoms of infection at EOT, as judged by the physician, excluding those patients who died during therapy.⁵
- 30-day all-cause mortality (ACM) was analyzed and included patients who died during their hospitalization.⁵
- Data collected were descriptive, and further data analyses are ongoing.

RESULTS

Patients

- Overall, 226 patients enrolled in PROVE had BSI (primary 47.8% [n=108]; secondary 52.2% [n=118]).
- The median (IQR) duration of cefiderocol treatment was 12 (8.0–16.0) days and 41.6% of patients received combination therapy.
- At the time of cefiderocol initiation over half of patients (n=125, 55.3%) were receiving treatment in the intensive care unit and 46.0% of patients (n=104) were in receipt of organ support (**Table 1**).

Pathogens

- The most frequent pathogen was *P. aeruginosa* (35.8%), followed by *A. baumannii* (20.8%) and Enterobacterales (20.8%) (**Figure 1**). Among 199 isolates with known carbapenem susceptibility status, 179 (89.9%) were non-susceptible and 20 (10.1%) were susceptible; 27 isolates had unknown carbapenem susceptibility status.
- Polymicrobial BSIs were reported in 35 patients (15.5%) (**Figure 1**).

Table 1. Demographics, clinical characteristics, and severity of illness in patients with BSI in the PROVE study (2020–2024)

	Patients with BSI (N=226)
Demographics	
Age (years), median (IQR)	60.0 (46.0–69.0)
≥65 years old, n (%)	87 (38.5)
Sex, male, n (%)	133 (58.8)
Country of enrollment, n (%)	
United States of America	97 (42.9)
France	21 (9.3)
Germany	21 (9.3)
Italy	34 (15.0)
Spain	28 (12.4)
United Kingdom	25 (11.1)
Concomitant medical conditions, n (%)	
Diabetes mellitus	63 (27.9)
Chronic pulmonary disease	42 (18.6)
Moderate-to-severe CKD	39 (17.3)
Congestive heart failure	35 (15.5)
Sepsis or septic shock	41 (18.1)
Severity of illness, n (%)	
ICU stay at initiation of cefiderocol	125 (55.3)
Receipt of any organ support at initiation of cefiderocol	104 (46.0)
Mechanical ventilation	83 (36.7)
Vasopressor medication	68 (30.1)
Renal replacement therapy	24 (10.6)
ECMO	4 (1.8)

CKD, chronic kidney disease; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range.

Clinical outcomes

- The overall clinical cure rate was 63.7%; clinical cure rate was 68.5% in patients with primary BSIs and 59.3% in those with secondary BSIs.
- 30-day ACM was 19.4% in primary BSIs and 29.7% in secondary BSIs (**Figure 2**).
- Among 81 patients with monomicrobial *Pseudomonas aeruginosa* BSI, 72.8% had clinical cure. The clinical cure rates in patients with monomicrobial BSIs caused by Enterobacterales species, *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* were 57.4%, 55.3%, and 83.3%, respectively (**Figure 3**).
- 30-day ACM rates were lower in infections caused by *P. aeruginosa* (21.0%) and Enterobacterales (21.3%) than in infections caused by *A. baumannii* (34.0%) and *S. maltophilia* (41.7%) (**Figure 3**).
- Patients who received cefiderocol as empirical treatment had higher clinical cure rate and lower 30-day ACM rate than patients receiving salvage therapy; most patients received cefiderocol for a documented infection (**Figure 4**).
- Patients with BSI had lower clinical cure and clinical response rates and higher 30-day ACM rates when cefiderocol was initiated ≥5 days following culture collection than patients who received cefiderocol earlier (**Figure 5**).

Figure 1. Distribution of Gram-negative pathogens among patients with BSI in the PROVE study (N=226)

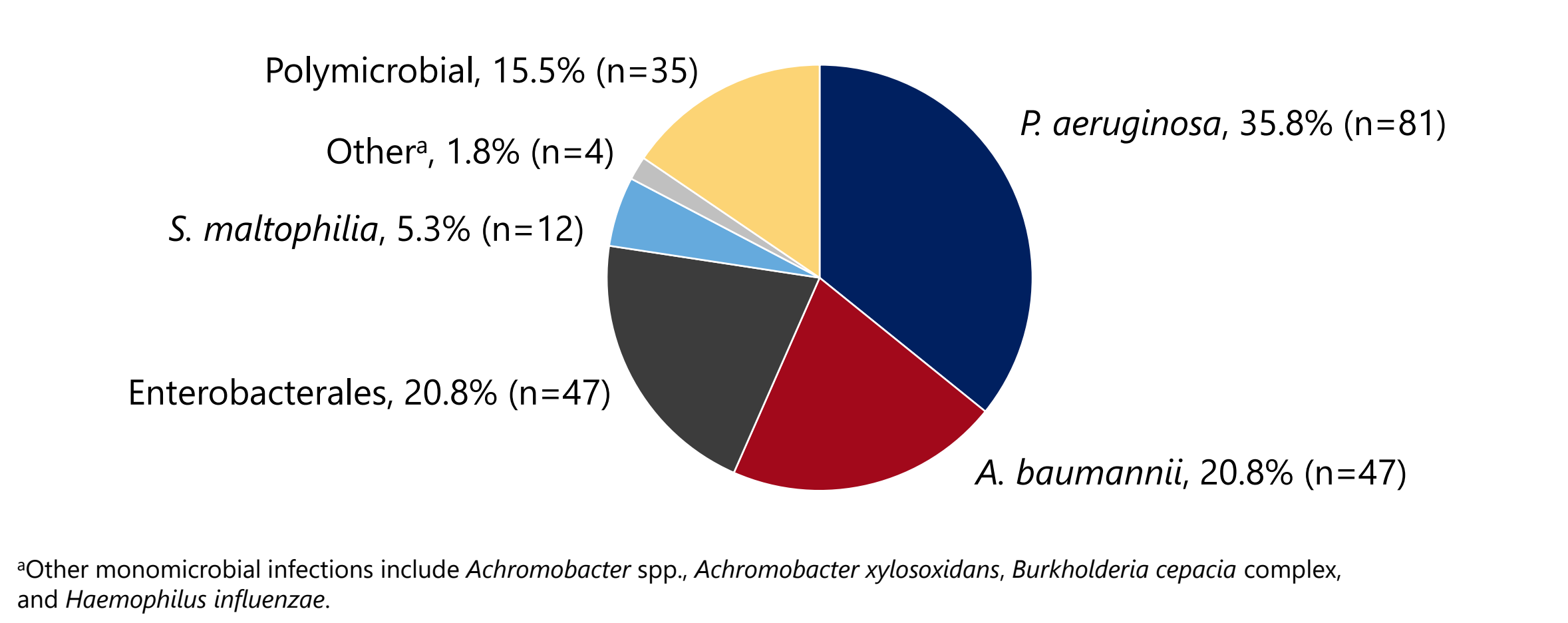


Figure 2. Clinical cure, clinical response rates and 30-day ACM overall in patients with BSI in the PROVE study,^a (N=226)

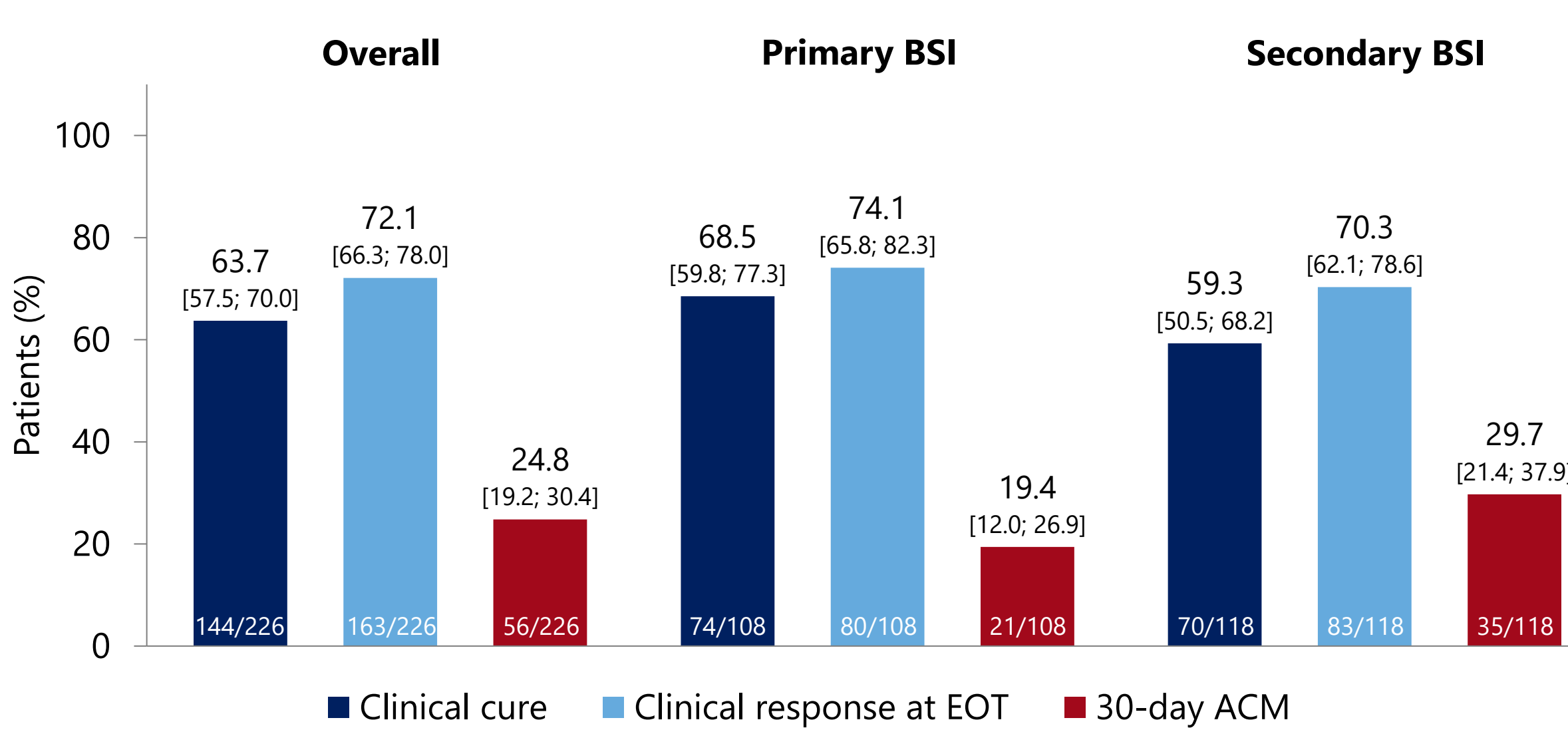
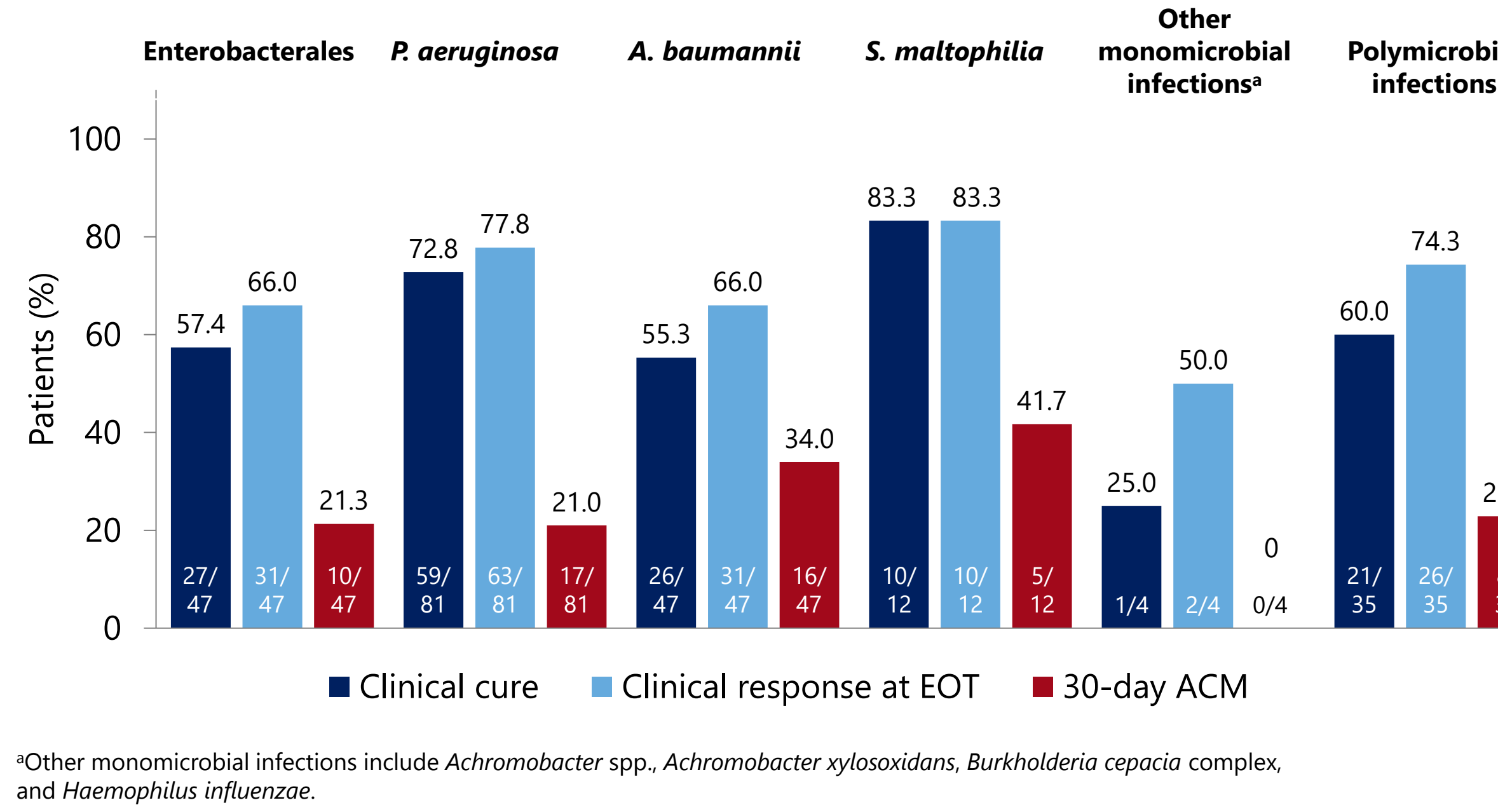


Figure 3. Clinical cure, clinical response rates and 30-day ACM by pathogen in patients with BSI in the PROVE study (N=226)



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Acknowledgements

Editorial support was provided by Highfield, Oxford, UK. This support was funded by Shionogi & Co., Ltd., Osaka, Japan.

Funding

The study was funded by Shionogi & Co., Ltd., Osaka, Japan.

CONCLUSIONS

- Patients with secondary BSI had lower clinical cure rate compared with those with primary BSI.
- Cefiderocol had good efficacy in patients infected by a range of pathogens, including polymicrobial infections.
- Higher clinical cure rates were observed with empiric treatment compared with salvage treatment and in patients who received cefiderocol within 0–4 days of the index culture compared with ≥5 days.
 - However, a similar trend was not observed for 30-day ACM.

Figure 4. Clinical cure, clinical response rates and 30-day ACM by reason for cefiderocol use^a in patients with BSI in the PROVE study (N=226)

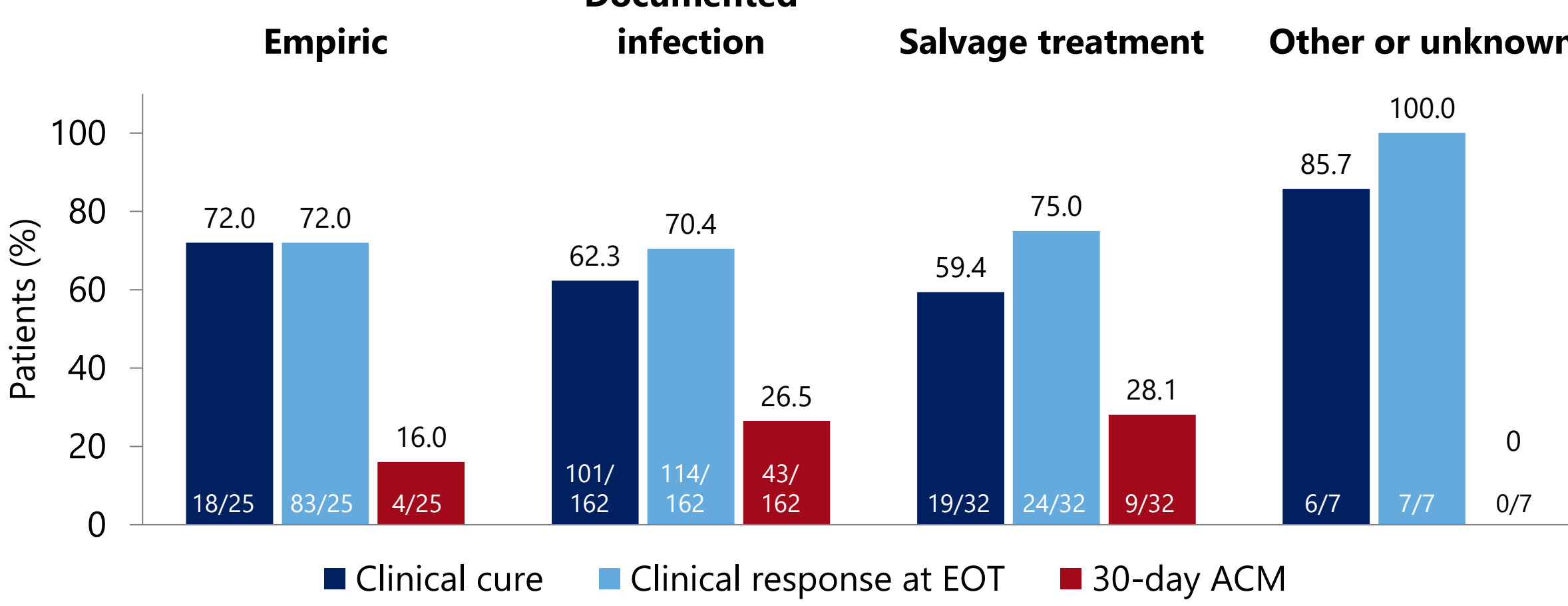
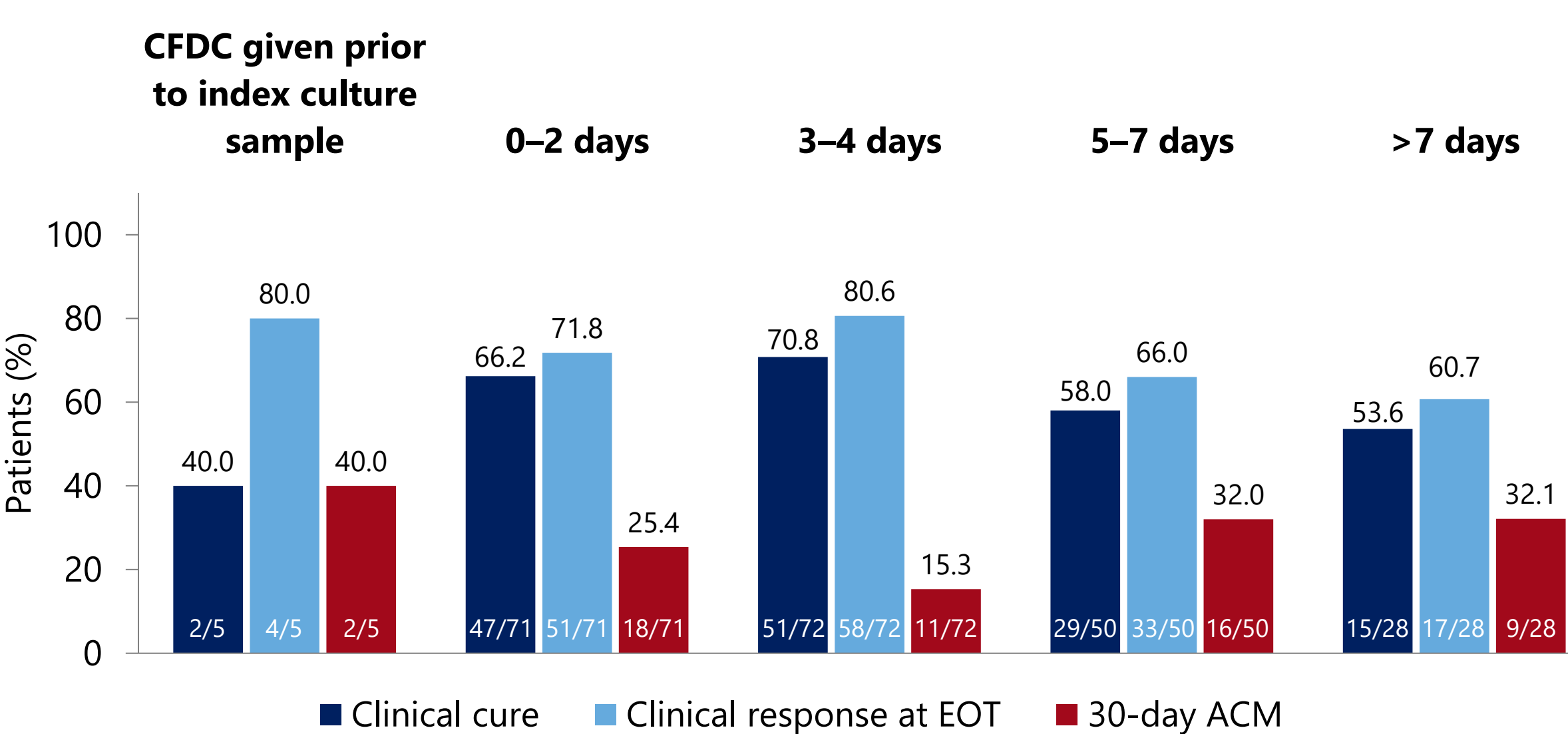


Figure 5. Clinical cure, clinical response rates and 30-day ACM by time from culture to cefiderocol initiation in patients with BSI in the PROVE study (N=226)



Conflict of interest

SV, KG, and STN are employees of Shionogi. ASH is a contractor for Shionogi. ED has nothing to disclose. DWW is a member of ANTRUK (Antimicrobial Research UK) Science Committee, and has received funding for research on antimicrobials from ANTRUK and the Rosetrees Trust (UK) during 2024–2025. MA has received fees for advisory board participation from Shionogi, Menarini, and Pfizer, and research grants from GE Healthcare and Fisher & Paykel Healthcare.