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Cefiderocol Treatment in Patients With Gram-Negative Bacterial Infections: European Results of the Global Retrospective Observational PROVE Study

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KEY POINTS

- Patient and disease characteristics, as well as pathogens, greatly varied across countries in the European cohort of the PROVE study.
- Patients who received cefiderocol earlier for a documented infection or empirically had numerically higher clinical cure rates than those who received cefiderocol salvage therapy.
- Outcomes were similar between monomicrobial and polymicrobial infections.

OBJECTIVE

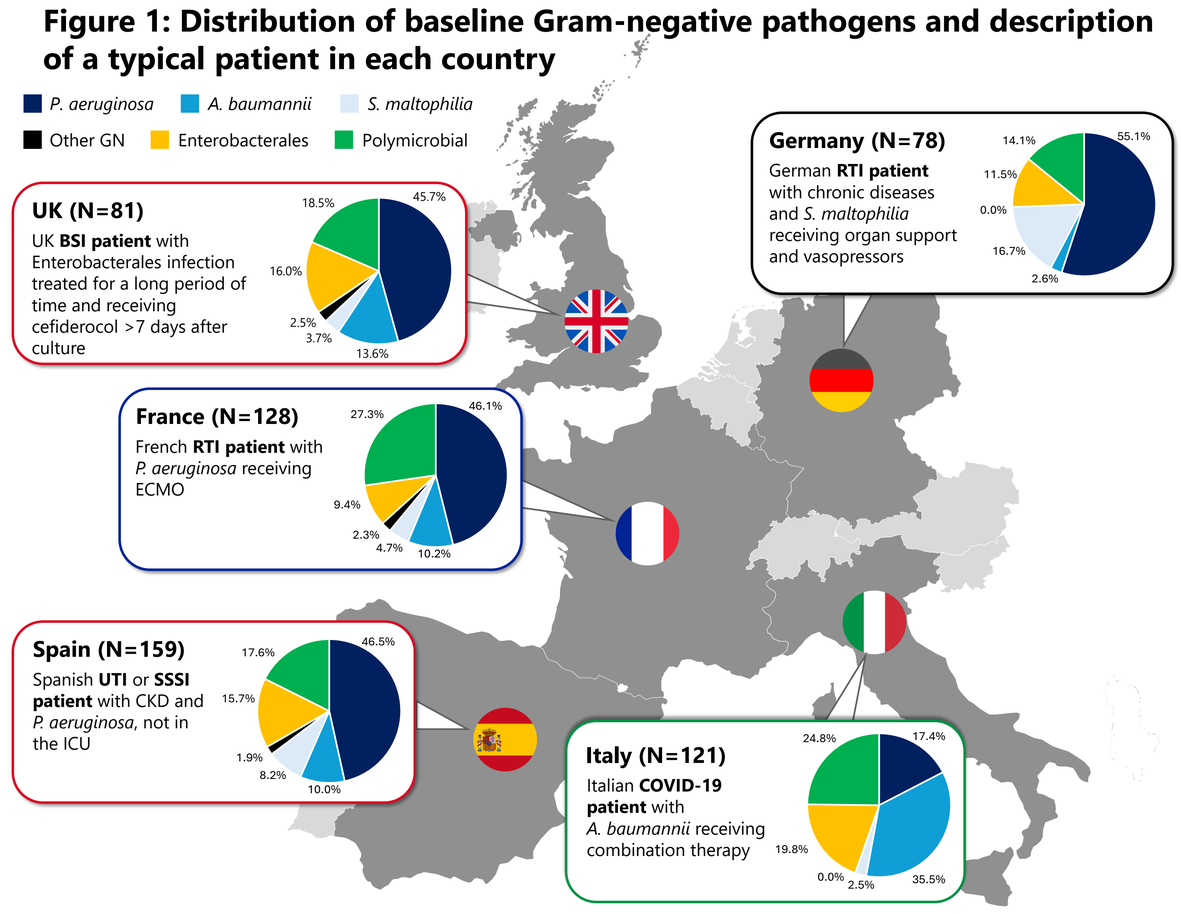
We aimed to elucidate the clinical outcomes of cefiderocol treatment in patients with serious Gram-negative bacterial infections in real-world settings in 42 European centres across 5 countries in the PROVE study.

METHODS

Design: international, retrospective, medical chart review study.
Inclusion criteria: adult hospitalised patients treated with cefiderocol consecutively for ≥72 hours (November 2020–July 2024).
Endpoints: patient and pathogen characteristics, hospitalisation course, antibiotic treatment patterns, clinical cure, and 30-day all-cause mortality (ACM). Clinical cure was defined as resolution or improvement of signs/symptoms at the end of treatment (EOT), as judged by the physician; patients who died during therapy or had a relapse or reinfection due to the same pathogen after EOT during current hospitalisation were considered as clinical failure. ACM included patients who died during their hospitalisation. Only descriptive statistics are provided.

RESULTS

Figure 1: Distribution of baseline Gram-negative pathogens and description of a typical patient in each country



BSI, bloodstream infection; CKD, chronic kidney disease; COVID-19; coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; GN, Gram-negative; ICU, intensive care unit; RTI, respiratory tract infection; SSSI, skin and skin structure infection; UTI, urinary tract infection.

Figure 2: Clinical cure and 30-day ACM rates by index pathogen

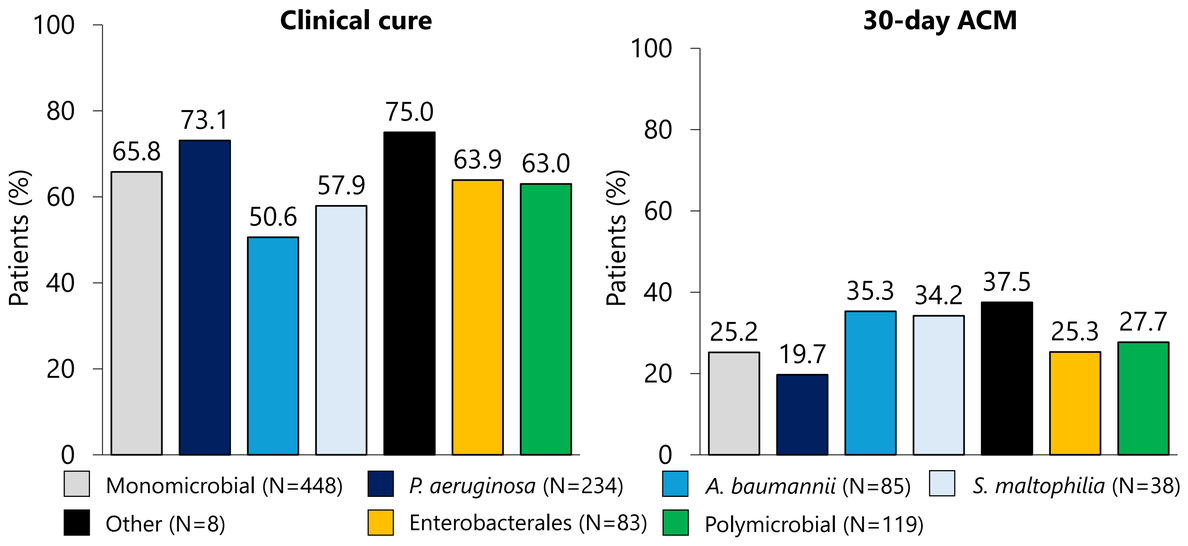
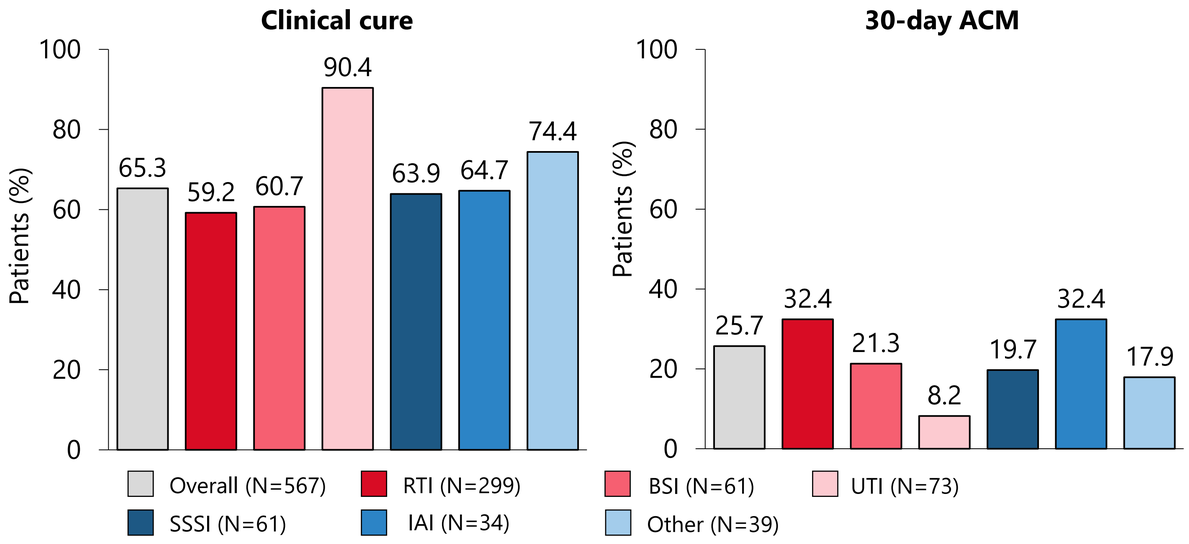


Figure 3: Clinical cure and 30-day ACM rates by infection site



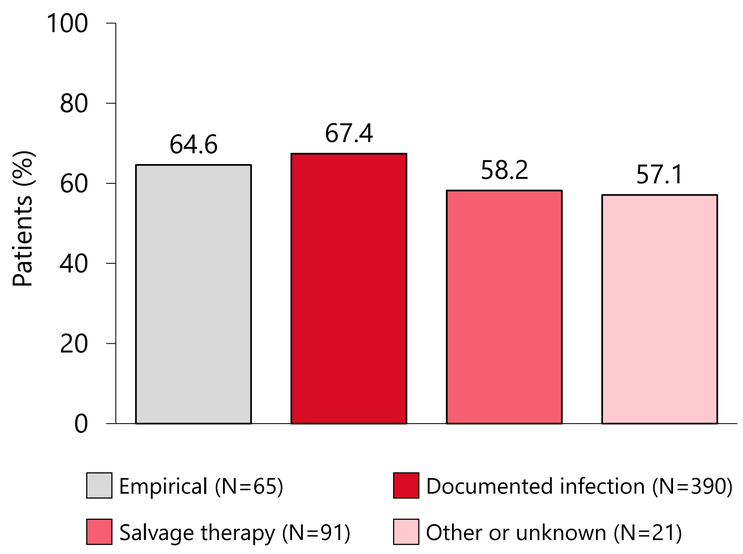
BSI, bloodstream infection; IAI, intra-abdominal infection; RTI, respiratory tract infection; SSSI, skin and skin structure infection; UTI, urinary tract infection.

Table 1: Demographics and baseline characteristics of European patients in the PROVE study

Demographics	Europe (N=567)	Spain (N=159)	France (N=128)	Italy (N=121)	Germany (N=78)	UK (N=81)
Age (years), median (IQR)	62.0 (48.0–71.0)	62.0 (50.0–70.0)	57.0 (45.0–69.0)	66.0 (52.0–74.0)	64.0 (52.0–72.0)	61.0 (42.0–69.0)
≥65 years old, n (%)	238 (42.0)	61 (38.4)	42 (32.8)	66 (54.5)	36 (46.2)	33 (40.7)
Sex, male, n (%)	394 (69.5)	113 (71.1)	94 (73.4)	81 (66.9)	51 (65.4)	55 (67.9)
Most frequent concomitant medical conditions (not mutually exclusive), n (%)						
Diabetes mellitus	140 (24.7)	34 (21.4)	34 (26.6)	31 (25.6)	21 (26.9)	20 (24.7)
COVID-19	115 (20.3)	9 (5.7)	37 (28.9)	41 (33.9)	15 (19.2)	13 (16.0)
Chronic pulmonary disease	92 (16.2)	16 (10.1)	24 (18.8)	25 (20.7)	16 (20.5)	11 (13.6)
Moderate-to-severe CKD	86 (15.2)	28 (17.6)	14 (10.9)	11 (9.1)	17 (21.8)	16 (19.8)
Congestive heart failure	67 (11.8)	21 (13.2)	14 (10.9)	11 (9.1)	14 (17.9)	7 (8.6)
Infection sites, n (%)						
RTI	299 (52.7)	69 (43.4)	82 (64.1)	72 (59.5)	34 (43.6)	42 (51.9)
BSI	61 (10.8)	13 (8.2)	13 (10.2)	16 (13.2)	8 (10.3)	11 (13.6)
UTI	73 (12.9)	34 (21.4)	7 (5.5)	11 (9.1)	11 (14.1)	10 (12.3)
SSSI	61 (10.8)	30 (18.9)	2 (1.6)	11 (9.1)	10 (12.8)	8 (9.9)
IAI	34 (6.0)	5 (3.1)	11 (8.6)	4 (3.3)	9 (11.5)	5 (6.2)
Other	39 (6.9)	8 (5.0)	13 (10.2)	7 (5.8)	6 (7.7)	5 (6.2)
Treatment characteristics						
Duration of cefiderocol use (days), median (IQR)	11.0 (8.0–16.0)	11.0 (8.0–16.0)	12.5 (8.0–16.0)	11.0 (8.0–16.0)	11.0 (8.0–15.0)	12.0 (7.0–17.0)
Combination therapy, n (%)	196 (34.6)	31 (19.5)	40 (31.3)	69 (57.0)	26 (33.3)	30 (37.0)
Severity of illness, n (%)						
ICU stay at initiation of cefiderocol	317 (55.9)	80 (50.3)	76 (59.4)	71 (58.7)	48 (61.5)	42 (51.9)
Receipt of any organ support at time of cefiderocol initiation	234 (41.3)	60 (37.7)	47 (36.7)	50 (41.3)	42 (53.8)	35 (43.2)
Mechanical ventilation	204 (36.0)	49 (30.8)	40 (31.3)	47 (38.8)	38 (48.7)	30 (37.0)
Use of vasopressor medication	149 (26.3)	39 (24.5)	25 (19.5)	32 (26.4)	36 (46.2)	17 (21.0)
ECMO	20 (3.5)	2 (1.3)	13 (10.2)	2 (1.7)	1 (1.3)	2 (2.5)
Renal replacement therapy	54 (9.5)	8 (5.0)	9 (7.0)	4 (3.3)	19 (24.4)	14 (17.3)

BSI, bloodstream infection; CKD, chronic kidney disease; COVID-19; coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; IAI, intra-abdominal infection; ICU, intensive care unit; IQR, interquartile range; RTI, respiratory tract infection; SSSI, skin and skin structure infection; UTI, urinary tract infection.

Figure 4: Clinical cure rates by reason for cefiderocol administration



Clinical cure rates were numerically higher among patients who received cefiderocol as initial **empirical (64.6%)** or **targeted (67.4%) treatment** compared with patients who received it as **salvage therapy (58.2%)**.

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