Poster 1475

IDWeek 2024, Los Angeles, CA, USA
October 16–19, 2024

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Real-World Effectiveness and Safety of Cefiderocol in the Treatment of Patients with Serious Gram-Negative Bacterial Infections: Results of the PROVE Chart Review Study

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Abstract (Revised data)

Background: The PROVE retrospective chart review study aimed to assess real-world outcomes of cefiderocol treatment in patients with serious Gram-negative bacterial infections.
Methods: We analyzed data of 1075 hospitalized patients with suspected or confirmed Gram-negative bacterial infections in Europe and the USA treated with cefiderocol for the first time for ≥72 hours (Nov 2020–Feb 2024). Baseline demographics, clinical characteristics, cefiderocol use, clinical cure, clinical response at end of treatment (EOT), in-hospital all-cause mortality (ACM), and adverse drug reactions (ADRs) were assessed.
Results: Of 1075 patients analyzed, 705 (65.6%) were men and the median age (interquartile range [IQR]) was 60 (46–69) years; 88.7% of patients had ≥1 risk factor for carbapenem-resistant infections. Overall, 56.6% were in the intensive care unit (ICU) and 44.3% received organ support. Cefiderocol was used for a documented infection in 71.2% of patients; the median (IQR) duration was 11 (7–16) days. The most frequent infection site was the respiratory tract (RTI; 53.1%), and the most frequent species in monomicrobial infections was *Pseudomonas aeruginosa* (35.9%), followed by *Acinetobacter baumannii* (18.1%). Overall, 67.5% of patients had clinical cure and 75.1% responded to cefiderocol treatment at EOT. ACM rate at day 30 was 23.3%. Clinical cure and clinical response rates were 61.8% and 71.6% in patients with RTI, and 68.5% and 74.1% in patients with bloodstream infection (BSI), respectively. Among patients with RTI or BSI, 29.2% and 19.4%, respectively, died by Day 30. Among patients with *P. aeruginosa* infection, 72.0% and 79.3% had clinical cure and clinical response, respectively, and 19.9% died by Day 30. In monomicrobial and polymicrobial infections, clinical cure rates were 67.8% and 66.1%, while ACM rates were 23.5% and 22.9% at Day 30, respectively. A total of 25 patients had 29 ADRs or serious ADRs, which led to discontinuation of cefiderocol for 16 events.
Conclusions: Cefiderocol was efficacious and well tolerated in the treatment of serious Gram-negative bacterial infections in real-world settings in a patient population with high rates of ICU admission and organ support.

Objectives

- The main objectives of the PROVE study were to describe the patient characteristics and clinical outcomes in patients treated with cefiderocol for Gram-negative bacterial infections in real-world settings between 2020 and 2024.

Methods

- PROVE was an international, multicenter, retrospective medical chart review study of first-time cefiderocol use in patients with Gram-negative bacterial infections.[1]
- Eligibility criteria included having a documented Gram-negative bacterial infection, which prompted the use of cefiderocol for at least 72 hours, and availability of data on cefiderocol starting dose, description of the Gram-negative bacterial infection for which cefiderocol was prescribed, and discharge data after hospitalization.[1]
- Clinical cure was defined as resolution or improvement in infection signs and symptoms, without evidence of a later relapse or death. Clinical response was defined as resolution or improvement of signs/symptoms at EOT as judged by the physician, excluding patients who died during therapy.[1]
- Only descriptive data are collected. Further data analyses are ongoing.

Conclusions

- Cefiderocol treatment, administered primarily for patients with documented carbapenem-resistant Gram-negative bacterial infections and including a large proportion of critically ill patients, was effective and well tolerated in real-world settings in the USA and Europe.
- Similar effectiveness was demonstrated across a range of Gram-negative infections, including those that were polymicrobial.

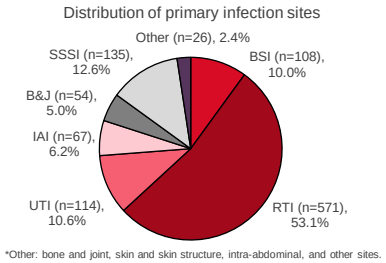
Results

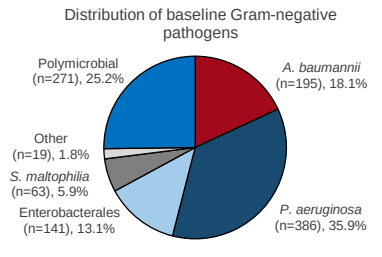
- A total of 1075 hospitalized patients were enrolled, and 65.6% were male.
- The median age was 60 years (IQR: 46–69) and the median CCI was 2 (IQR: 1–4).
- Participating countries: USA 47.3%, Spain 14.8%, France 11.9%, Italy 11.3%, UK 7.5%, Germany 7.3%.
- The median cefiderocol treatment duration was 11 days (IQR: 7–16), and 33.9% of patients received combination therapy.

Comorbidities

20.4%	Chronic pulmonary disease	11.5%	Diabetes with end-organ damage
18.5%	Uncomplicated diabetes	9.4%	Myocardial infarction
17.0%	COVID-19	4.1%	Cystic fibrosis
16.9%	Moderate-severe renal disease	3.9%	Burns
14.0%	Congestive heart failure	2.5%	Bronchiectasis

Infection characteristics





*Other: bone and joint, skin and skin structure, intra-abdominal, and other sites.

Disease severity

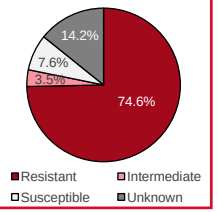
56.6% were treated with cefiderocol in the ICU

11.0% had secondary bacteremia

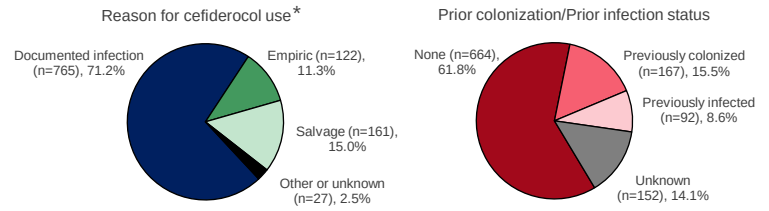
38.5% required mechanical ventilation

25.3% received vasopressor support

Carbapenem susceptibility status

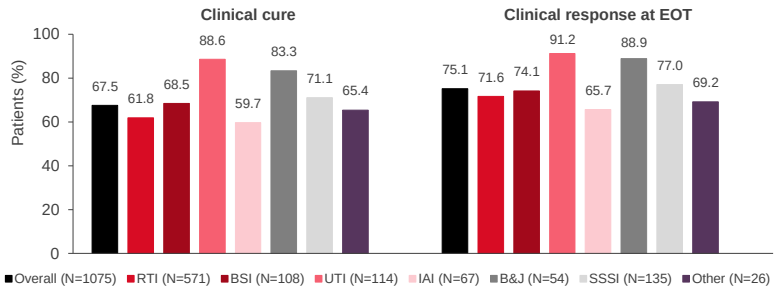


▼ 25 patients had a total of 29 ADRs, of which 3 were serious ADRs (i.e., interstitial nephritis and acute kidney injury; elevation of liver enzyme; hepatic cytolysis). Cefiderocol was discontinued for 16 events (in 13 patients).

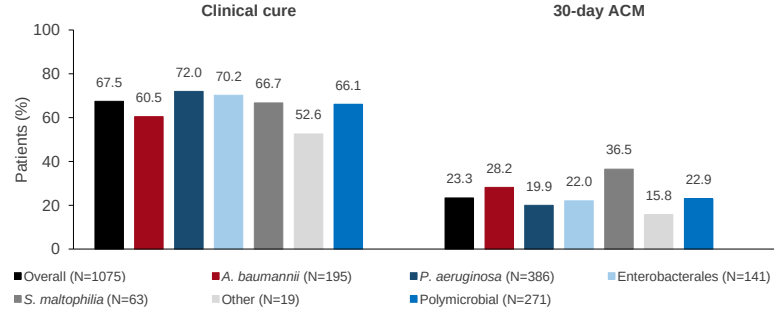


*Reported by the investigator. Documented infection: the pathogen and susceptibilities were known, and cefiderocol use was not due to failure of a prior antibiotic regimen. Empiric use: cefiderocol use started before the pathogen and/or susceptibilities were available to help guide the choice. Salvage therapy: cefiderocol was used after a prior antibiotic regimen had failed; patients usually received at least 3 days of prior antibiotic therapy to see if 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.

Clinical cure and clinical response at EOT by infection site



Clinical cure and 30-day ACM by pathogen



Abbreviations: ACM, all-cause mortality; B&J, bone and joint infection; BSI, bloodstream infection; CCI, Charlson Comorbidity Index; COVID-19, coronavirus disease-2019; EOT, end of treatment; 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.

Reference. 1. EUPAS40551. Retrospective chart review study of cefiderocol real world outcomes and safety in the treatment of patients with Gram-negative bacterial infections (GNBI) in the US and Europe (PROVE). https://catalogues.ema.europa.eu/node/2635/administrative-details.

This study was funded by Shionogi & Co., Ltd., Osaka, Japan. CS, STN, FK, SV, CL, SM, BC are or were employees of Shionogi during the conduct of the study.