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Effectiveness of cefiderocol in patients with intra-abdominal infections caused by Gram-negative bacteria in the PERSEUS study in Spain

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Revised abstract

Background: Cefiderocol has potent *in vitro* activity against multidrug-resistant strains of Enterobacterales and non-fermenting Gram-negative bacteria, including *Pseudomonas aeruginosa*. Data on its effectiveness in patients with complicated intra-abdominal infections (cIAIs) are limited. This subgroup analysis of the PERSEUS study aimed to evaluate the effectiveness of cefiderocol in patients with cIAIs in the Shionogi early access programme in Spain.

Methods: PERSEUS was a retrospective, multicentre, observational, medical chart review study (2018–2022) enrolling hospitalised patients with confirmed Gram-negative bacterial infections, excluding *Acinetobacter baumannii* infections, and for whom other treatment options had failed or were not available. Patients were treated with cefiderocol for the first time for ≥72 hours. Patient demographics, baseline clinical characteristics, rates of clinical success, clinical cure and Day 28 all-cause mortality, and safety were evaluated. Only descriptive statistics were used.

Results: Among 261 eligible patients, 14.6% (n=38) had cIAIs. The median age of this subgroup was 62 years (range: 51–71) and 81.6% (31/38) were male. Comorbidities were present in 86.8% (33/38) of patients. At baseline, up to 44.7% of patients were in the intensive care unit (ICU), 26.3% had septic shock and 23.7% received renal replacement therapy while in the ICU. Secondary bacteraemia was reported for 18.4% of patients with cIAIs. The most frequent Gram-negative pathogens were *P. aeruginosa* (60.5%, 23/38), *Klebsiella pneumoniae* (18.4%, 7/38) and *Pseudomonas* spp. (7.9%, 3/38). Polymicrobial infections were detected in 21.1% (8/38) of patients, and >50% of patients were previously colonised. The median cefiderocol treatment duration was 10.0 days (range: 7.0–17.0). The frequent reasons for starting cefiderocol treatment included resistance to all tested antibiotics (63.2%), treatment failure with prior antibiotics (50.0%) and adverse events (10.5%). Of patients with cIAIs, 76.3% (29/38) of patients achieved clinical success, 68.4% (26/38) had clinical cure and 23.7% (9/38) died by Day 28. No adverse drug reactions related to cefiderocol were reported for these patients.

Conclusions: Cefiderocol was effective and well tolerated in patients with cIAIs caused by Gram-negative bacteria in a complex, ICU, real-world population with no alternative treatment option in Spain.

OBJECTIVES

The PERSEUS retrospective study enrolled hospitalised patients with Gram-negative bacterial infections, who were treated with cefiderocol through the early access programme (EAP) in Spain [1]. Of 261 eligible patients, 80.5% (210/261) achieved clinical cure and 21.5% (56/261) died by Day 28 [1]. Clinical data in patients with complicated intra-abdominal infections (cIAIs) treated with cefiderocol are limited. The objective of this subgroup analysis was to describe the baseline characteristics and the clinical outcomes in patients with cIAIs treated with cefiderocol for up to 28 days in the PERSEUS study.

METHODS

Study design: a retrospective, multicentre, observational study in patients receiving cefiderocol for the first time in the EAP in Spain.

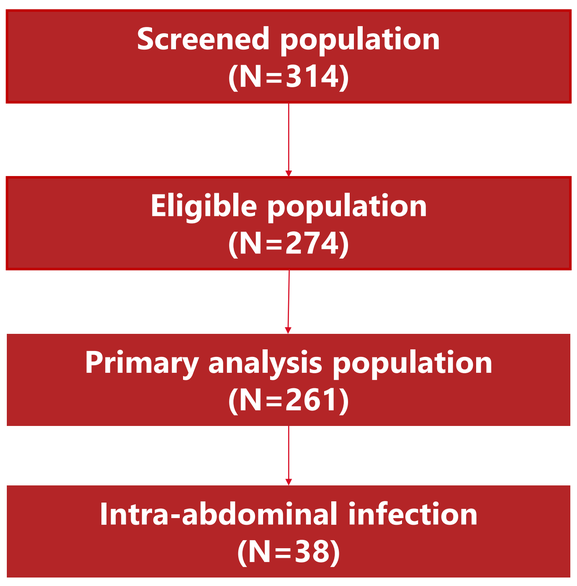
Inclusion criteria: adult hospitalised patients treated with cefiderocol consecutively for ≥72 hours for a confirmed Gram-negative bacterial infection.

Exclusion criteria: confirmed *Acinetobacter* spp. at baseline; confirmed cefiderocol-resistant Gram-negative pathogen at baseline; incomplete medical records; enrolled into other clinical studies of investigational product.

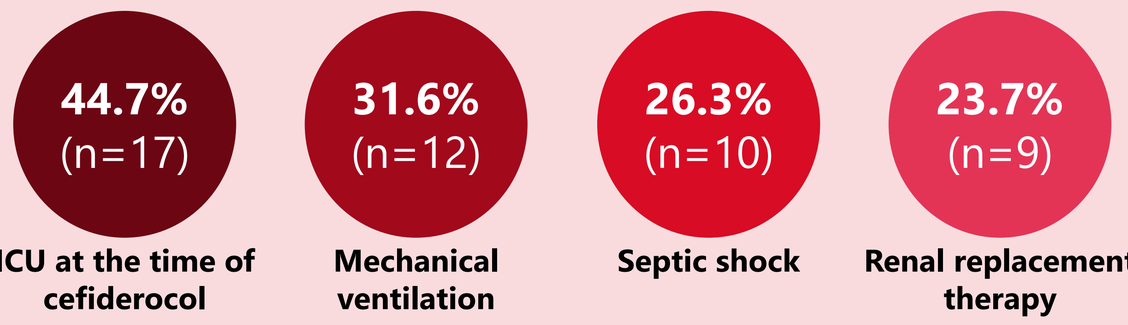
Endpoints: baseline patient characteristics, Gram-negative bacterial pathogens, clinical success (composite of clinical cure and/or survival at Day 28), clinical cure (cessation of antibiotic treatment due to clinical resolution of signs and symptoms) at end of treatment and all-cause mortality at Day 28.

RESULTS

Patient attrition



Patient characteristics (N=38)		Main comorbidities	
Sex, male	31 (81.6%)	Solid/haematological cancer	18 (47.4%)
Age, median (Q1–Q3), years	62 (51–71)	Immunosuppression	15 (39.5%)
CCI score, median (Q1–Q3)	4 (2–5)	Transplant	12 (31.6%)
APACHE II score, median (Q1–Q3)	12.5 (8.5–17.5)	Chronic kidney disease	6 (15.8%)
LOS, median (Q1–Q3), days	59.5 (38–94)	Chronic liver disease	6 (15.8%)
ICU LOS, median (Q1–Q3), days	50.0 (33–64)	Symptomatic COVID-19	3 (7.9%)

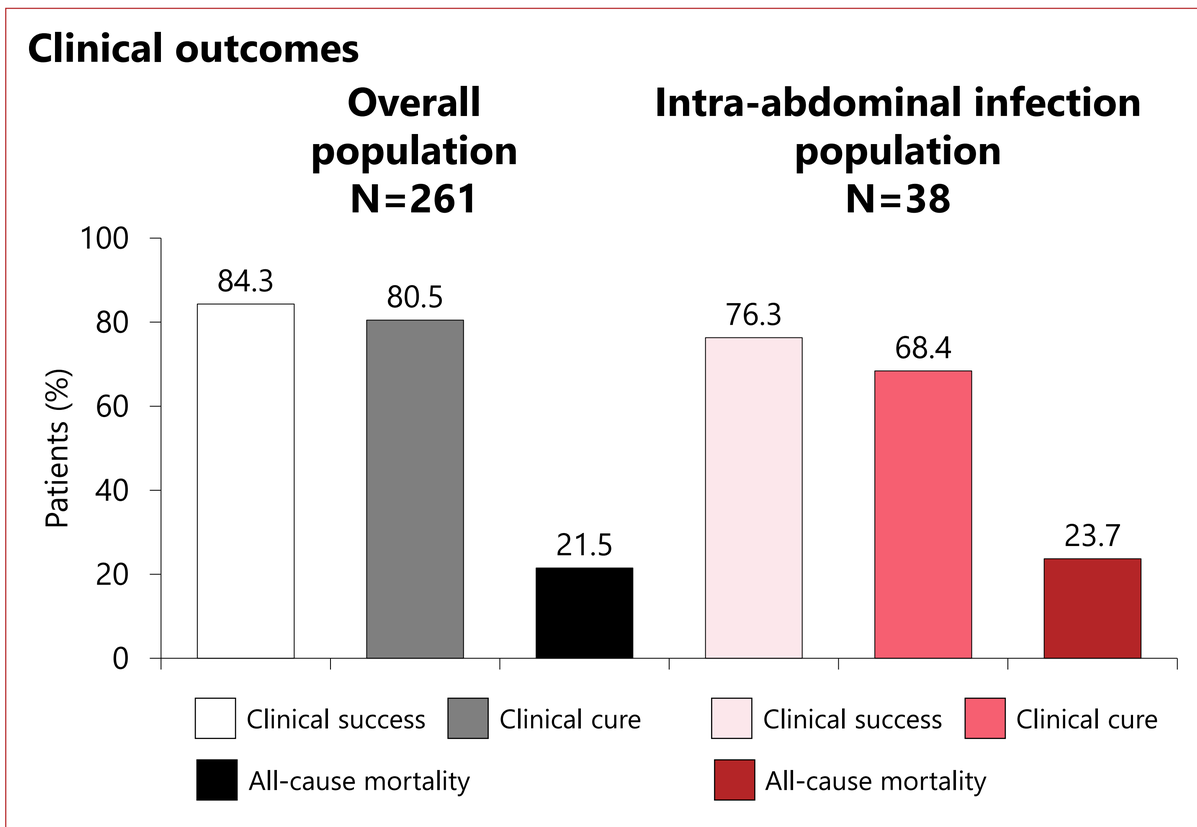


RESULTS CONT'D

Baseline Gram-negative pathogens and rationale for cefiderocol administration in patients with intra-abdominal infections (N=38)	
Gram-negative pathogen, n (%)	
Pseudomonas aeruginosa	**23 (60.5)**
Klebsiella pneumoniae	**7 (18.4)**
Stenotrophomonas maltophilia	**2 (5.3)**
***Pseudomonas* spp.**	**3 (7.9)**
***Burkholderia cepacia* complex**	**1 (2.6)**
Other Enterobacterales[a]	**2 (5.3)**
Secondary bacteraemia, n (%)	**7 (18.4)**
Polymicrobial infection, n (%)	**8 (21.1)**
Previous colonisation, n (%)	**20 (52.6)**
Previous treatment with antibiotics, n (%)	**35 (92.1)**
Rationale for administering cefiderocol[b]	
Resistance to all tested antibiotics	**24 (63.2)**
Treatment failure with prior antibiotics	**19 (50.0)**
Adverse events to other susceptible antibiotics	**4 (10.5)**
Other	**2 (5.3)**
Cefiderocol treatment duration, median (range), days	**10.0 (7.0–17.0)**
Cefiderocol combination therapy, n (%)	**14 (36.8)**
Adverse drug reactions, n (%)	**0 (0)**

[a]*Klebsiella oxytoca* (1), *Citrobacter freundii* (1); [b]Not mutually exclusive.

Clinical outcomes



CONCLUSIONS

- Cefiderocol was effective and well tolerated in patients with cIAIs caused by Gram-negative bacteria in a complex, ICU, frequently colonised, real-world population with limited treatment options in Spain.
- Cefiderocol may be an appropriate antibiotic option for the treatment of patients with Gram-negative bacterial cIAIs.

Reference

1. Ramirez P, et al. Real-world effectiveness and safety of cefiderocol in patients with Gram-negative bacterial infections in the early access programme in Spain: results of the PERSEUS study. Presented at 34th ECCMID, Barcelona, Spain; 27–30 April 2024. Poster 2523.

Acknowledgements

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Abbreviations

CCI, Charlson Comorbidity Index; COVID-19, coronavirus disease 2019; ICU, intensive care unit; LOS, length of stay; Q, quartile.