Cefiderocol as Rescue Therapy for *Pseudomonas aeruginosa* and Other Difficult-To-Treat Gram-negative Infections

Andrew Chou MD MSc, Eva Amenta MD, David Ramsey PhD, Barbara W Trautner MD PhD
Michael E. DeBakey VA Medical Center, Baylor College of Medicine

U.S. Department of Veterans Affairs
Veterans Health Administration
Michael E. DeBakey VA Medical Center

IQUEST CENTER FOR INNOVATIONS IN QUALITY, EFFECTIVENESS & SAFETY

Baylor College of Medicine

Background:

- Cefiderocol is a novel siderophore cephalosporin with broad spectrum activity.
- Cefiderocol is the only beta-lactam with *in vitro* activity against metallo-beta-lactamase producing organisms.
- Post-approval real-world clinical data of cefiderocol use are limited and mostly for treatment of *Acinetobacter baumannii* infections.

Hypothesis/Goals:

- To describe nationwide, real-world, prescribing characteristics, and clinical & microbiological outcomes associated with cefiderocol therapy.

Methods:

Inclusion criteria:

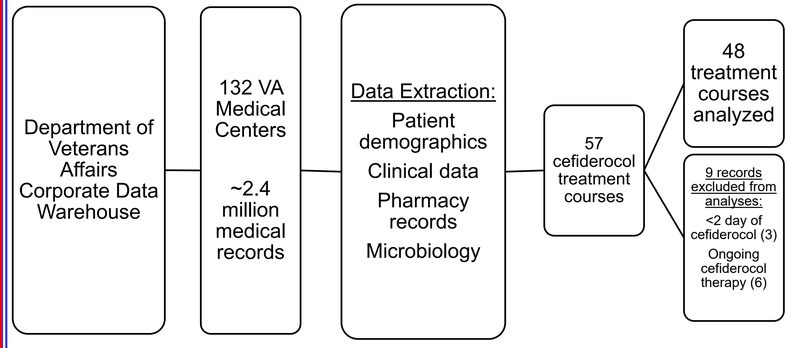
- Receiving care in any VA medical center during FY20 (start 10/1/2020) to 8/31/2022.
- Received cefiderocol therapy for at least 2 days length of therapy (LOT).
- Only the first eligible episode was included in the outcomes analyses.

Exclusion criteria:

- Cefiderocol LOT was <2 days.
- Patients with ongoing follow-up were not included in outcomes analysis.

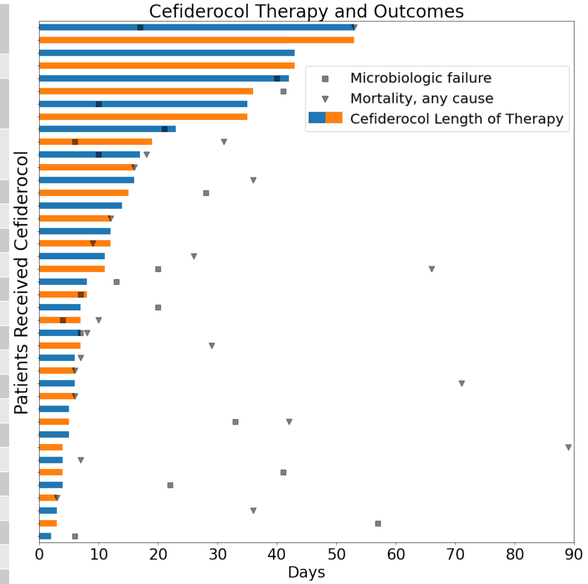
Data source:

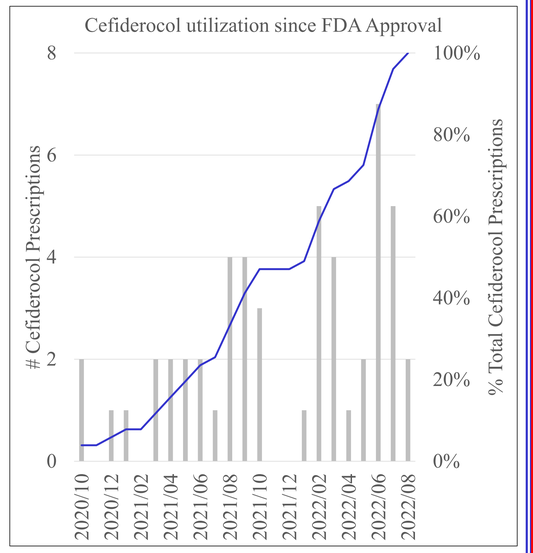
- Structured data were extracted from Veterans Health Administration (VHA) Corporate Data Warehouse and included data from 132 VA Medical Centers.
- All eligible episodes underwent manual chart review to validate extracted structured data and to extract unstructured data, including clinical notes.
- Microbiologic failure was defined as isolation of the same bacterial species following ≥7 days after initiation of therapy.



Age (median)	70.5 years (IQR: 61 – 75)
Male Gender	95%
Charlson comorbidity score, age-unadjusted, median (IQR)	6 (IQR: 3 – 9)
Charlson comorbidity score, age-adjusted, median (IQR)	8 (IQR: 6–11)
Renal function	
Renal replacement therapy	7 (17%)
Augmented Renal Clearance[1]	9 (21%)
Healthcare setting	
ICU	27
Floor	15
Spinal Cord Injury Unit	6
Infectious syndromes*	
Pulmonary	24 (50%)
Urinary	16 (33%)
Endovascular	9 (19%)
Osteomyelitis	4 (8%)
Other	7 (15%)
Gram-negative organism[2]	
Pseudomonas aeruginosa	34 (71%)
Acinetobacter baumannii complex	9 (19%)
Stenotrophomonas maltophilia	5 (10%)
Enterobacterales	19 (40%)
Other	3 (6%)
No growth (empiric therapy)	2 (4%)
Median days (LOT) of cefiderocol therapy (IQR)	8 (5 – 17)
30-day all-cause mortality	11/41 (27%)
90-day all-cause mortality	18/41 (44%)
30-day microbiologic failure	16/41 (39%)
90-day microbiologic failure	22/41 (54%)

1: Augmented Renal Clearance: CLcr >120 ml/min; per FDA Package Insert
2: A patient may have more than one syndrome and/or organism.





Results:

- Forty-eight cefiderocol prescriptions were administered to forty-two unique patients.
- Patients were older, male, had multiple comorbidities, and treated in the ICU.
- Most patients had pulmonary or urinary sources of infection.
- The most common organisms causing infections was *P. aeruginosa* (71%), followed by Enterobacterales (40%) and *A. baumannii* complex (19%).
- The median duration of cefiderocol was 8 days, and LOT was up to 53 days of cefiderocol.
- The 30-day mortality rate was 27%, and the 90-day mortality was 44%.
- The 30-day microbiologic failure rate was 39%, and the 90-day microbiologic failure rate was 54%.
- Cefiderocol utilization has steadily increased over FY20, FY21, and FY22.

Conclusions:

- Patients prescribed cefiderocol had multiple comorbidities and severe infections.
- Patients had high mortality rates and microbiological failure rates.

Funding

VA CSR&D IK2 CX001981 and the Center for Innovations in Quality, Effectiveness and Safety (CIN 13-413)