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# Activity of Cefiderocol and Comparator Agents Against Isolates from Hospitalized Pediatric Patients with Pneumonia Collected During 2020–2022 as Part of the SENTRY Antimicrobial Surveillance Program

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## BACKGROUND

Treatment of pneumonia in hospitalized pediatric patients can be complicated due to antibiotic resistance, which limits the choice of antibiotics.

Cefiderocol is approved in Europe for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options, and in the United States for the treatment of patients with complicated urinary tract infections and hospital-acquired/ventilator-associated bacterial pneumonia caused by susceptible Gram-negative pathogens.[1,2]

## OBJECTIVE

We aimed to evaluate the *in vitro* activity of cefiderocol and comparator agents against Gram-negative isolates collected from pediatric patients (0–17 years old) with pneumonia in 2020–2022 in the SENTRY Antimicrobial Surveillance Program.

## METHODS

- A total of 1,389 isolates from the respiratory tract of pediatric pneumonia patients were collected from 30 European and 31 North American medical centers as part of the SENTRY Antimicrobial Surveillance Program in 2020–2022. Overall, 318 isolates were collected from Europe and 1,071 isolates were from the USA.
- 608 Enterobacterales, 459 *Pseudomonas aeruginosa*, 161 *Stenotrophomonas maltophilia*, 124 *Acinetobacter* spp., and 37 other isolates were tested for susceptibility. Other organisms included: *Achromobacter xylosoxidans* (3), *Burkholderia cepacia* species complex (13), *Burkholderia gladioli* (1), *Chryseobacterium indologenes* (2), unspeciated *Achromobacter* (18) (**Figure 1**).
- Minimum inhibitory concentrations were determined according to CLSI guidelines using broth microdilution with cation-adjusted Mueller–Hinton broth (CAMHB) for comparator agents and iron-depleted CAMHB for cefiderocol.
- Susceptibility was assessed according to 2023 CLSI, FDA, and EUCAST breakpoints (**Table 1**).
- Carbapenem-non-susceptible subsets were defined as non-susceptibility to meropenem and imipenem.

**Table 1. Susceptibility breakpoints by CLSI, US FDA, and EUCAST**

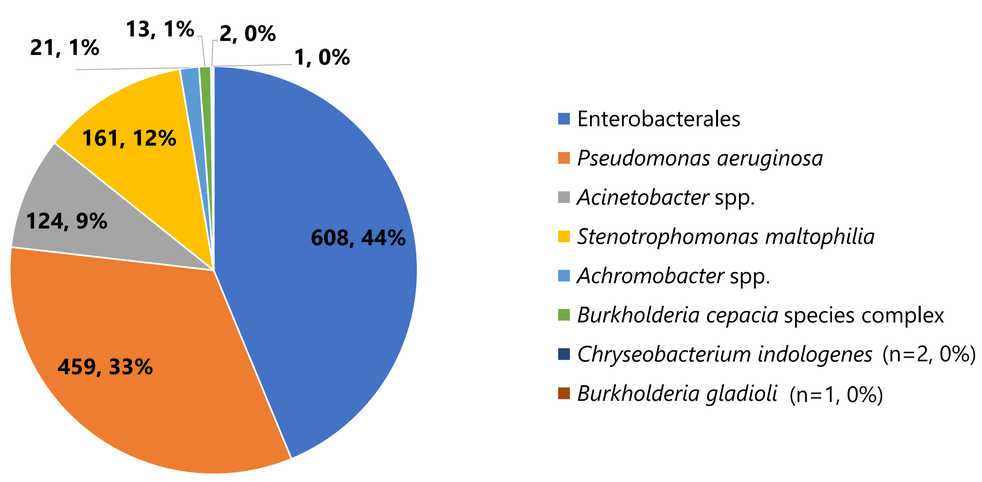
| Organism | Breakpoint (µg/mL) by organization* | | |
|---|---|---|---|
| | CLSI | FDA | EUCAST |
| Enterobacterales | ≤4/8/≥16 | ≤4/8/≥16 | ≤2/–/>2 |
| *Pseudomonas aeruginosa* | ≤4/8/≥16 | ≤1/2/≥4 | ≤2/–/>2 |
| *Acinetobacter* spp. | ≤4/8/≥16 | ≤1/2/≥4 | ≤2/–/>2† |
| *Stenotrophomonas maltophilia* | ≤1/–/– | – | ≤2/–/>2† |

*Susceptible/intermediate/resistant. †EUCAST non-species-specific pharmacokinetic/pharmacodynamic breakpoints used.

## RESULTS

- Carbapenem-non-susceptibility was found in 10.5% of both *P. aeruginosa* and *Acinetobacter* spp., and 100% of *S. maltophilia* isolates, whereas only 0.4% (n=2) of Enterobacterales isolates were carbapenem-non-susceptible.

**Figure 1. Prevalence of organisms from pediatric patients with pneumonia from the SENTRY Antimicrobial Surveillance Program (2020–2022)**




Enterobacterales organisms include: *Citrobacter freundii* species complex (10), *C. koseri* (4), *Cronobacter sakazakii* (1), *Enterobacter asburiae* (2), *E. cloacae* (15), *E. cloacae* species complex (73), *Escherichia coli* (88), *Klebsiella aerogenes* (26), *K. oxytoca* (67), *K. pneumoniae* (136), *K. variicola* (4), *Morganella morganii* (1), *Pantoea calida* (1), *P. piersonii* (1), *Pluralibacter gergoviae* (5), *Proteus mirabilis* (8), *P. vulgaris* group (1), *Providencia rettgeri* (3), *Raoultella ornithinolytica* (2), *Serratia liquefaciens* (5), *S. liquefaciens complex* (2), *S. marcescens* (150), unspeciated *Providencia* (1), unspeciated *Raoultella* (2).

## CONCLUSIONS

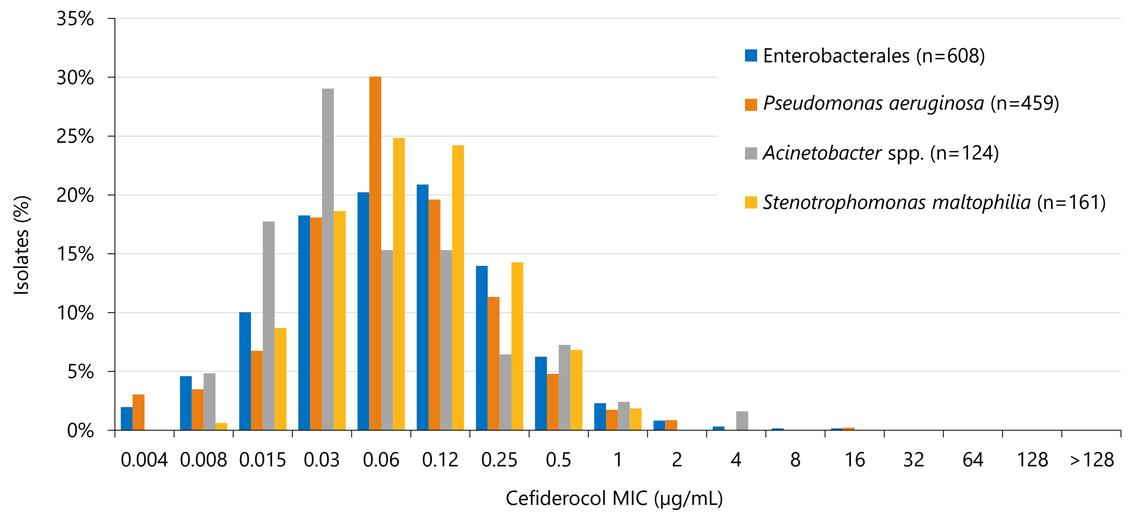
- Cefiderocol displays potent *in vitro* activity against Gram-negative isolates from pediatric pneumonia patients, including carbapenem-non-susceptible subsets.
- These data suggest cefiderocol may be a valuable treatment option for respiratory infections in pediatric patients caused by Gram-negative bacteria.
- Clinical studies are currently ongoing in pediatric subjects.[3,4]

**Table 2. *In vitro* activity of cefiderocol and selected comparator agents against pediatric respiratory isolates from the SENTRY Antimicrobial Surveillance Program (2020–2022)**

| Organism group<br>Agent | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | MIC range (µg/mL) | %S[a] CLSI | %S[a] FDA | %S[a] EUCAST |
|---|---|---|---|---|---|---|
| **Enterobacterales all (n=608)** | | | | | | |
| Cefiderocol | 0.06 | 0.5 | ≤0.004 – 16 | 99.7 | 99.7 | 99.3 |
| Meropenem | 0.03 | 0.06 | ≤0.015 – >32 | 99.5 | 99.5 | 99.5 |
| Imipenem-relebactam | 0.12 | 0.5 | 0.06 – 4 | 97.7 | 97.7 | 99.3 |
| Meropenem-vaborbactam | 0.03 | 0.06 | ≤0.015 – 4 | 100 | 100 | 100 |
| Ceftazidime-avibactam | 0.12 | 0.25 | ≤0.015 – >32 | 99.8 | 99.8 | 99.8 |
| Ceftolozane-tazobactam | 0.25 | 1 | ≤0.12 – >16 | 96.1 | 96.1 | 96.1 |
| **CarbNS Enterobacterales (n=2)** | | | | | | |
| Cefiderocol | NA | NA | 0.03 – 0.5 | 100 | 100 | 100 |
| Imipenem-relebactam | NA | NA | 4 – 4 | 0.0 | 0.0 | 0.0 |
| Meropenem-vaborbactam | NA | NA | 0.06 – 4 | 100 | 100 | 100 |
| Ceftazidime-avibactam | NA | NA | 0.25 – >32 | 50.0 | 50.0 | 50.0 |
| Ceftolozane-tazobactam | NA | NA | 0.5 – >16 | 50.0 | 50.0 | 50.0 |
| ***Pseudomonas aeruginosa* (n=459)** | | | | | | |
| Cefiderocol | 0.06 | 0.25 | ≤0.004 – 16 | 99.8 | 98.9 | 99.8 |
| Meropenem | 0.5 | 4 | ≤0.015 – >32 | 86.9 | 86.9 | 86.9 |
| Imipenem-relebactam | 0.25 | 1 | ≤0.03 – >16 | 98.3 | 98.3 | 98.3 |
| Meropenem-vaborbactam | 0.5 | 4 | ≤0.015 – >8 | NA | NA | 95.8 |
| Ceftazidime-avibactam | 2 | 4 | 0.12 – >32 | 98.7 | 98.7 | 98.7 |
| Ceftolozane-tazobactam | 0.5 | 1 | ≤ 0.12 – >16 | 98.0 | 98.0 | 98.0 |
| **CarbNS *Pseudomonas aeruginosa* (n=48)** | | | | | | |
| Cefiderocol | 0.06 | 0.25 | ≤0.004 – 0.5 | 100 | 100 | 100 |
| Imipenem-relebactam | 1 | 4 | 0.12 – >16 | 83.3 | 83.3 | 83.3 |
| Meropenem-vaborbactam | 8 | >8 | 2 – >8 | NA | NA | 60.4 |
| Ceftazidime-avibactam | 4 | 16 | 0.5 – >32 | 87.5 | 87.5 | 87.5 |
| Ceftolozane-tazobactam | 1 | 8 | 0.25 – >16 | 89.6 | 89.6 | 89.6 |
| ***Acinetobacter* spp. (n=124)** | | | | | | |
| Cefiderocol | 0.06 | 1 | 0.015 – 8 | 98.4 | 96.0 | 98.4 |
| Meropenem | 0.5 | 8 | 0.06 – >32 | 87.9 | 87.9 | 87.9 |
| Imipenem-relebactam | 0.12 | >8 | ≤0.03 – >8 | NA | 89.5 | 89.5 |
| Ampicillin-sulbactam | 2 | 32 | ≤0.5 – >64 | 83.1 | 83.1 | NA |
| Colistin | 0.5 | 2 | 0.12 – >8 | NA | NA | 94.4 |
| **CarbNS *Acinetobacter* spp. (n=13)** | | | | | | |
| Cefiderocol | 0.25 | 2 | 0.03 – 8 | 92.3 | 84.6 | 92.3 |
| Imipenem-relebactam | >8 | >8 | >8 – >8 | NA | 0.0 | 0.0 |
| Ampicillin-sulbactam | 64 | >64 | 4 – >64 | 15.4 | 15.4 | NA |
| Colistin | 0.5 | >8 | 0.25 – >8 | NA | NA | 84.6 |
| ***Stenotrophomonas maltophilia* (n=161)** | | | | | | |
| Cefiderocol | 0.06 | 0.25 | 0.008 – 1 | 100 | NA | 100 |
| Levofloxacin | 1 | 4 | 0.12 – >32 | 86.9 | NA | NA |
| Trimethoprim-sulfamethoxazole | ≤0.12 | 0.5 | ≤0.12 – >4 | 96.9 | NA | NA |
| Minocycline | 0.5 | 1 | ≤0.06 – 4 | 100.0 | NA | NA |

[a]According to 2023 CLSI, FDA, and EUCAST breakpoints. CarbNS, carbapenem non-susceptible; MIC, minimum inhibitory concentration; $MIC_{50/90}$, MIC required to inhibit the growth of 50%/90% of organisms; n, number of isolates; NA, not applicable; S, susceptible.

**Figure 2. Cefiderocol MIC distribution against Enterobacterales, *P. aeruginosa*, *Acinetobacter* spp., and *S. maltophilia* of pediatric respiratory isolates in SENTRY 2020–2022**




MIC, minimum inhibitory concentration.

- Cefiderocol was highly active with most isolates being susceptible, including carbapenem-non-susceptible isolates; 99.5% and 99.6% of pediatric respiratory isolates had MIC values of ≤2 µg/mL and ≤4 µg/mL, respectively.

**Table 3. *In vitro* activity of cefiderocol and selected comparator agents against pediatric respiratory isolates of *Burkholderia cepacia* complex and *Achromobacter* spp. from the SENTRY Antimicrobial Surveillance Program 2020–2022**

| Organism<br>Agent | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | MIC range (µg/mL) |
|---|---|---|---|
| ***Burkholderia cepacia complex* (n=13)** | | | |
| Cefiderocol | 0.06 | 0.25 | ≤0.004 – 0.5 |
| Ceftazidime | 4 | 8 | 1 – 8 |
| Meropenem | 2 | 4 | 0.25 – 4 |
| Levofloxacin | 2 | 32 | 0.5 – >32 |
| Trimethoprim-sulfamethoxazole | 1 | >4 | ≤0.12 – >4 |
| Minocycline | 2 | 16 | 0.25 – 32 |
| ***Achromobacter* spp. (n=21)** | | | |
| Cefiderocol | 0.03 | 0.25 | 0.008 – 4 |
| Ceftazidime | 4 | 16 | 2 – >32 |
| Cefepime | 32 | >32 | 8 – >32 |
| Meropenem | 0.12 | 4 | 0.06 – >32 |
| Ciprofloxacin | 4 | >4 | 1 – >4 |
| Trimethoprim-sulfamethoxazole | ≤0.12 | 1 | ≤0.12 – 2 |
| Minocycline | 1 | 2 | 0.5 – 4 |

MIC, minimum inhibitory concentration; $MIC_{50/90}$, MIC required to inhibit the growth of 50%/90% of organisms.

- 100% of *Burkholderia cepacia* complex isolates had an MIC ≤4 µg/mL.
- 95.2% and 100% of *Achromobacter* isolates had an MIC ≤2 µg/mL and MIC ≤4 µg/mL, respectively.

**References**

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