**Antimicrobial Activity of Ceftolozane-Tazobactam Tested against Contemporary (2015–2017) P. aeruginosa Isolates from a Global Surveillance Program**

**INTRODUCTION**

- Ceftolozane-tazobactam is an antibacterial combination of an antipseudomonal cephalosporin and a β-lactamase inhibitor.
- Ceftolozane-tazobactam is active against isolates with common β-lactam resistance mechanisms found in Pseudomonas aeruginosa, including AmpC production, up-regulated efflux pumps, and outer membrane proteins.
- Ceftolozane-tazobactam is approved in >50 countries, including the United States since 2016 and in Europe since 2015, for susceptible infections that include acute pyelonephritis and complicated intra-abdominal infections associated with MDR P. aeruginosa.
- Clinical trial results for hospital-acquired bacterial pneumonia ventilator-associated bacterial pneumonia are currently in progress (clinicaltrials.gov Identifier: NCT02070757).
- The Program to Assess Ceftolozane-Tazobactam Susceptibility (PACTS) is a global surveillance program that monitors resistance of gram-negative bacteria against ceftolozane-tazobactam.
- PACTS data for Pseudomonas aeruginosa isolates consecutively collected from various infection types in hospitalized patients from 2015–2017 were analyzed for this study.

**MATERIALS AND METHODS**

- A total of 7157 P. aeruginosa isolates were collected from 104 hospitals from 40 countries on 4 continents and tested for susceptibility to ceftolozane-tazobactam by CLSI broth microdilution methodology at JMI laboratories using CLSI (2018) breakpoints.
- Isolate distribution: 2710 from North America (US-only), 2384 from Europe, 695 from Latin America, and 503 from Asia-Pacific (not including China or India).
- Other agents tested were amikacin, cefepime, ceftriaxone, colistin, gentamicin, levofloxacin, meropenem, and piperacillin-tazobactam.
- Ceftolozane-tazobactam and piperacillin-tazobactam were tested with a fixed 4 mg/L concentration of tazobactam.
- Antimicrobial resistance phenotypes analyzed included:
  - Ceftolozane-nonsusceptible (CSS), colistin-nonsusceptible (CSNs), levofloxacin-nonsusceptible (LNS), ceftriaxone-nonsusceptible (CNS), and piperacillin-tazobactam-nonsusceptible (PTNS).
- Antimicrobial activity of ceftolozane-tazobactam tested against contemporary P. aeruginosa isolates from various infection types in hospitalized patients from 2015–2017 were collected from 104 hospitals from 40 countries on 4 continents and tested for susceptibility to ceftolozane-tazobactam by CLSI broth microdilution methodology at JMI laboratories using CLSI (2018) breakpoints.

**RESULTS**

- The most common infection type involved was pneumonia, followed by skin and soft tissue infections.
- Other infection types included intra-abdominal infections (IAI) and urinary tract infections (UTI).
- The distribution of P. aeruginosa isolates by infection type and continent is shown in Figure 1.
- Multiresistant (MDR) isolates were defined as nonsusceptible to ≥1 drug in ≥1 drug classes.
- Extensively drug-resistant (XDR) was nonsusceptible to at least 1 agent in all but 2 or fewer antimicrobial classes.
- Classically tested antimicrobial resistance phenotypes included: antipseudomonal cephalosporins, antipseudomonal carbapenems, quinolones, and antipseudomonal penicillin β-lactamase inhibitor combinations.

**CONCLUSIONS**

- Ceftolozane-tazobactam had activity against most P. aeruginosa isolates from patients hospitalized with various infections in 40 countries.
- Ceftolozane-tazobactam was more active than all comparators, except colistin, and maintained activity against MDR and XDR isolates and isolates nonsusceptible to all tested β-lactams.
- Ceftolozane-tazobactam was active against 12/16 colistin-nonsusceptible isolates that were 77% susceptible to colistin.
- Ceftolozane-tazobactam may be a useful treatment for infections caused by P. aeruginosa, including infections with various resistant phenotypes.

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**References**


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