Antimicrobial Activity of Cefepime-Taniborbactam and Comparators Against Clinical Isolates from ICU and Non-ICU Patients; 2018-2020 Global Surveillance

INTRODUCTION
Taniborbactam is a novel cysteine-biocidal-based broad spectrum β-lactamase inhibitor with selective direct inhibitory activity against both serine- and metallo-β-lactamases. Taniborbactam restores the activity of cefepime against many difficult to treat organisms, including eaeavibactam, and ceftazidime-taniborbactam. Enterobacterales and Pseudomonas aeruginosa. Antimicrobial resistance is typically higher in isolates collected from ICU, leaving clinicians with limited treatment options. In this study, we evaluated the in vitro activity of cefepime-taniborbactam and comparator agents against clinical isolates of Enterobacterales and Pseudomonas aeruginosa collected from ICUs and non-ICUs in 2018-2020 global surveillance study.

METHODS
MICs of cefepime with taniborbactam fixed at 4 mg/L (FTB) and comparators were determined using the CLSI reference method [1] against Enterobacterales (n=12,428) and P. aeruginosa (n=3,314) collected in 2018-2020. Quality control (QC) testing was performed each day of testing as specified by the CLSI [1, 2]. Isolates were collected from community and hospital infections from 266 sites in 56 countries. Only isolates collected from patients in wards designated ICU (n=2,225 Enterobacterales; 2,367 P. aeruginosa) and non-ICU (n=7,223 Enterobacterales; 2,367 P. aeruginosa) were included in this analysis. Isolates were sorted from (n-percent of total): respiratory tract infections (6,911.4%); urinary tract infections (3,254.1%); intra-abdominal infections (2,537.2%); bloodstream infections (2,341.1%); skin/soft tissue infections (1,416.3%); and unknown (15.3%). Cefepime was tested at a fixed concentration of 4 mg/L in combination with ceftazidime, taniborbactam was tested at a fixed concentration of 4 mg/L in combination with ceftriaxone, pipacaravacil, and vaborbactam was tested at a fixed concentration of 8 mg/L in combination with meropenem.

RESULTS
Cefepime-taniborbactam restored activity of ceftazidime against P. aeruginosa (MIC >16/57.4 mg/L compared to MIC >16/80.9 mg/L susceptibility). A meteoric increase was seen across all antibiotic classes tested as ceftazidime, and cefepime were compared to the FTB comparator. When compared to comparators in Enterobacterales and Pseudomonas aeruginosa, the MIC >16/57.4 mg/L comparing cefepime-taniborbactam to ceftazidime-taniborbactam (8/97.9 mg/L compared to <8/94.8 mg/L susceptibility respectively). Cefepime-taniborbactam was compared against an additional group of patients to isolate MIC >16/57.4 mg/L comparing cefepime-taniborbactam to ceftazidime-taniborbactam (8/97.9 mg/L compared to <8/94.8 mg/L susceptibility respectively). Cefepime-taniborbactam was compared against an additional group of patients to isolate MIC >16/57.4 mg/L comparing cefepime-taniborbactam to ceftazidime-taniborbactam (8/97.9 mg/L compared to <8/94.8 mg/L susceptibility respectively). Cefepime-taniborbactam was compared against an additional group of patients to isolate MIC >16/57.4 mg/L comparing cefepime-taniborbactam to ceftazidime-taniborbactam (8/97.9 mg/L compared to <8/94.8 mg/L susceptibility respectively).

CONCLUSIONS
- Cefepime-taniborbactam showed in vitro activity against Enterobacterales, with MIC90 values of 0.25 mg/L for isolates from non-ICU patients and 0.5 mg/L for isolates from ICU patients (Table 1, Figure 1). Greater than 99% of all Enterobacterales from both wards were inhibited by ≤16 mg/L of cefepine-taniborbactam.
- Cefepime-taniborbactam maintained activity against resistant phenotypes of P. aeruginosa in both wards with 99.8% of isolates inhibited at ≤16 mg/L. The percent susceptible to comparator agents against the resistant subsets ranged from 1.6% to 92.6% for Enterobacterales (Table 1, Figure 3).
- Cefepime-taniborbactam showed in vitro activity against P. aeruginosa, with an MIC90 value of 8 mg/L and inhibiting at least 99.8% of isolates at ≤16 mg/L, for both ICU and community isolates (Table 2, Figure 2).
- Cefepime-taniborbactam maintained activity against resistant phenotypes of P. aeruginosa in both ward types, with 84.7% to 92.5% inhibited at ≤16 mg/L (Table 2). The percent susceptible to comparator agents against the resistant subsets of P. aeruginosa ranged from 35.2% to 68.4% (Table 2, Figure 3).
- Against the particularly challenging subset of MDR P. aeruginosa from ICU patients, cefepime-taniborbactam was the most active agent tested as it inhibited 64.7% of isolates at ≤16 mg/L compared to 43.1% susceptible to ceftazidime-avibactam, 36.0% susceptible to ceftazidime-balbavactam, and 36.0% susceptible to meropenem-vaborbactam.

REFERENCES
3 CLSI Performance Standards for Antimicrobial Testing. Wayne, PA.

DISCLOSURES
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