MHT. Modified Hodge Test, APB: boric acid synergy; EDTA: EDTA synergy; Pos: positive; Neg: negative. KPC (Klebsiella pneumoniae Carbapenemase), VIM (Verona integron-mediated metallo-β-lactamase), NDM (New Delhi metallo-β-lactamase), OXA (oxacillinase 48-like carbapenemase (OXA-48)).

Conclusion. Conventional phenotypic synergy tests with boric acid and EDTA used for detecting carbapenemases are suboptimal and their routine use should be reconsidered. They depend on the degree of enzyme expression and the distance between disks. Lateral flow immunoassay tests are a rapid and cost-effective tool to detect and differentiate carbapenemases, improving clinical outcomes through targeted therapy and prevention.

Disclosures. Diego Josa, Msc, AlIFAX (Speaker’s Bureau) German Esparza, n/a, Biomerieux (Consultant/Pfizer (Speaker’s Bureau) Luis Reyes, n/a, MSD (Speaker’s Bureau))

1252. In Vitro Activity of Aztreonam-Avibactam and Comparator Agents Against Enterobacterales Isolates with Bloodstream Infections collected during the ATLAS Global Surveillance Program, 2015-2019

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Session: P-72. Resistance Mechanisms

Background. Treatment options for β-lactamase-producing Enterobacterales are limited, particularly for infections caused by metallo-β-lactamase (MBL)-producing strains. The β-lactam/非-β-lactam inhibitor combination aztreonam-avibactam (ATM-AVI) is active in vitro against Enterobacterales isolates carrying MBLs, including those co-producing β-lactamases of Class A, C, and some class D enzymes. This study evaluated the in vitro activity of ATM-AVI and comparators against Enterobacterales isolates collected in 2015-2019 from patients with bloodstream infections (BSI) as part of the ATLAS program.

Methods. Non-duplicate clinical isolates were collected in 53 countries in Europe, Latin America, Asia/Pacific (excluding mainland China and India), and Middle East. Asia. Susceptibility testing was performed by CLSI broth microdilution and interpreted using CLSI 2021 and FDA (tigecycline) breakpoints. ATM-AVI was tested at a fixed concentration of 4 µg/mL. MDR was defined as resistant (R) to ≥3 of 7 sentinel drugs: amikacin, aztreonam, cefepime, colistin, levofloxacin, meropenem, and piperacillin-tazobactam. PCR and sequencing were used to identify the β-lactamase genes present in all isolates with meropenem MIC >1 µg/mL, and Escherichia coli, Klebsiella spp. and Proteus mirabilis phenotypically positive for ESBL activity (2015) or with aztreonam or ceftazidime MIC >1 µg/mL (2016-2019).

Results. Of in vitro active in vitro against Enterobacterales isolates from BSI (MICβ < 0.12 µg/mL), with 99.97% of isolates inhibited by ≤8 µg/mL of ATM-AVI, including 100% of isolates that produced MBLs. ATM-AVI tested with MICβ values of 0.5 µg/mL against subsets of ceftazidime-non-susceptible (NS), meropenem-NS, amikacin-NS, colistin-resistant, and MBL-positive Enterobacterales (Table). The tested β-lactam comparators showed susceptibility of < 79% against these subsets of resistant isolates.

Results Table

| MICβ (µg/mL) | MBL-positive (%) |
|--------------|-----------------|
| ATM-AVI       | 79              |
| ATM           | 79              |
| FEP           | 79              |
| CTA           | 79              |
| MEV           | 79              |
| TF P          | 79              |

Conclusion. Taniborbactam significantly restored the in vitro activity of ceftazidime against Enterobacterales, including isolates nonsusceptible to recently-approved BL/BLI combinations and expressing serine and metallo-β-lactamases. This support the continued development of FTB as a potential new treatment option for challenging infections due to resistant Gram-negative pathogens.

Disclosures. Meredith Hackel, PhD MPH, IHMA (Employee/Pfizer, Inc (Independent Contractor)) Mark G G. Wise, PhD, IHMA (Employee/Pfizer, Inc (Independent Contractor)) Daniel F Sahm, PhD, IHMA (Employee/Pfizer, Inc (Independent Contractor))

1254. Molecular Epidemiology of Escherichia coli causing Urinary Tract Infections in United States and in vitro Activity of Tepibenem, Including Against Strain Lineage and Resistant subsets (2018-2020)

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Session: P-72. Resistance Mechanisms

Background. Tepibenem (TB) is an oral carbapenem in clinical development for treating complicated urinary tract infections (UTIs), including pyelonephritis. This study investigates the epidemiology of E. coli (EC) causing UTI in U.S. patients and the activity of TB and comparators against various subsets.

Methods. A total of 2,395 EC recovered from urine samples during the 2018-2020 STEWARD Surveillance Program were included. Isolates were collected from medical centers in all 9 US Census Regions and centrally tested by reference broth microdilution method. MIC interpretation was based on CLSI criteria. Isolates that met MCR criteria were subjected to genome sequencing, followed by screening for extended-spectrum β-lactamase (ESBL) genes and epidemiology typing (MLST).

Results. A total of 16.1%, 15.4% and 14.6% of EC met the ESBL screening criteria in 2018, 2019, and 2020, respectively. 369/360 (74.7%) carried blaCTX-M and 259/360 (72.1%) had bala. bala and bala were detected in 2015-2017 at frequencies of 0.06% and 0.6%, respectively. MICβ for meropenem was ≤2 µg/mL (n=406) was evaluated for the presence of MBLs, KPC, ESBLs, and OXA-48 group genes via PCR and sequencing. Forty-eight isolates with FTB MIC values of 16 µg/mL or greater were interrogated by WGS.

Results. Overall, 23.0% and 15.9% of isolates were nonsusceptible (NS) to ceftazidime and piperacillin-tazobactam (TZP), respectively. FTB had potent activity against all Enterobacterales, with MICβ values of 0.06/0.25 µg/mL and 99.5% inhibited at ≤8 µg/mL. FTB maintained activity against MBL-, KPC-, OXA-48 group, and ESBL-positive isolates (MICβ range, 1 to 16 µg/mL; 80.5% to 100% inhibited at ≤8 µg/mL). Isolates with elevated FTB MICs had IMP-type enzymes, variation in the cephalosporin target (penicillin binding protein 3), permeability defects in combination with acquired β-lactamases, and/or possible up-regulated efflux.

Results Table

| Resistance Phenotype | N (%) | MICβ (µg/mL) | Percent susceptible |
|----------------------|-------|--------------|---------------------|
| ATM-AVI              | 79    | 0.06/0.25    |                      |
| ATM                  | 79    | 0.06/0.25    |                      |
| FEP                  | 79    | 0.06/0.25    |                      |
| CTA                  | 79    | 0.06/0.25    |                      |
| MEV                  | 79    | 0.06/0.25    |                      |
| TF P                 | 79    | 0.06/0.25    |                      |

Conclusion. Taniborbactam significantly restored the in vitro activity of ceftazidime against Enterobacterales, including isolates nonsusceptible to recently-approved BLI/BLI combinations and expressing serine and metallo-β-lactamases. This support the continued development of FTB as a potential new treatment option for challenging infections due to resistant Gram-negative pathogens.

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1255. Modified Hodge Test, APB: boric acid synergy; EDTA: EDTA synergy; Pos: positive; Neg: negative. KPC (Klebsiella pneumoniae Carbapenemase), VIM (Verona integron-mediated metallo-β-lactamase), NDM (New Delhi metallo-β-lactamase), OXA (oxacillinase 48-like carbapenemase (OXA-48)).

Conclusion. Conventional phenotypic synergy tests with boric acid and EDTA used for detecting carbapenemases are suboptimal and their routine use should be reconsidered. They depend on the degree of enzyme expression and the distance between disks. Lateral flow immunoassay tests are a rapid and cost-effective tool to detect and differentiate carbapenemases, improving clinical outcomes through targeted therapy and prevention.

Disclosures. Diego Josa, Msc, AlIFAX (Speaker’s Bureau) German Esparza, n/a, Biomerieux (Consultant/Pfizer (Speaker’s Bureau) Luis Reyes, n/a, MSD (Speaker’s Bureau))
with the majority of isolates being ST131 (56.2%). 21 (6.7%) and 19 (6.0%) iso-
lates belonged to ST38 and ST1193, respectively, followed by ST5 represented by 8 or less isolates. Among ST131, 56.5% carried bla\_\text{CTX-M-15}, from group 1 and 35.6% had genes associated within group 9. Overall, TBP showed consistent MIC\_\text{values} values throughout the subsets. ERT had activity (29.7 - 90.6%) against the various subsets. The majority of resistance genotypes (85.7 - 90.6%) were again isolated carrying plasmid AmpC. Other agents (ceftazidime and ceftazolin) had activity only against non-ESBL producers.

**Conclusion.** bla\_\text{CTX-M-15} comprised the majority of acquired genes detected among ESBL producing isolates of \textit{H. influenzae}. This further solidifies the expanded ESBL gene transfer within this species, and its potential to be transferred to other bacteria. These data support the clinical development of TBP as a convenient oral treatment option for UTI caused by \textit{EC}.

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**1255. External Validation and Systematic Quantification of the Predictive Performance of Carbapenem Resistant Enterobacteriaceae Risk Prediction Models in Hospitalized Patients**

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**Session:** P-72. Resistance Mechanisms

**Background.** Accurately predicting the presence of a carbapenem resistant enterobacteriaceae (CRE) in hospitalized patients presents itself as an opportunity that would support timely initiation of CRE active agents. The aim of this study is to determine how reliably the existing risk prediction models identify patients likely to require empiric anti-CRE treatment, preliminary results of which are presented herein.

**Methods.** A systematic search identified all existing CRE prediction models for validation in our patient population. Medical records of hospitalized patients within the Mount Sinai Health System in New York were subsequently reviewed. Data was gathered on model predictors, baseline demographics, clinical information, microbiology results, antibiotic utilization history and index infection. Besides calculating the AUROC, the main outcome of our study was to establish optimal prediction score cutoffs and false positive rates (FPR) where corresponding model performance maintains a false negative rate (FNR) of < 10%, < 20% and < 30%, respectively.

**Results.** 12 models were retained for validation. We identified 106 patients, 41 of which were treated for a CRE infection. Previous admission, organ transplantation, CKD, infection type, and carbapenem use were baseline variables that significantly differed between the groups treated for a CRE or non-CRE related infection (Table 1). The models ability to discriminate varied as evidenced by the AUROC range of 0.5 to 0.77 (Figure 1), suggesting the Seligmen et al. model as the overall best. When evaluated at the pre-specified FNR intervals of < 10%, < 20% and < 30%, the model differed by 12.5% between the groups treated for a CRE or non-CRE related infection (Table 2).