Total number of tests and proportion of IGRA:TST obtained by month, from October 2015–January 2021.

Conclusion. While most TB infection tests in this age group were TSTs, the monthly proportion of tests that were IGRA.s increased over time between 2015–2021. IGRA.s were obtained in varied clinical settings. This low burden setting, rates of invalid/indeterminate IGRA.s were low among children < 2 years old, which suggests that IGRA.s are reasonable TB testing options for patients < 2 years old, and may be preferred given limitations of TSTs.

Disclosures. Gabriella S. Lamb, MD, MPH, Nothing to disclose

656. Sulbac-tam-Durlobactam MIC Determination: Comparative Evaluation of the New ETEST SUD to the CLSI 2021 Broth Microdilution Method

Background. Species belonging to the Acinetobacter baumannii-calcoaceticus (ABC) complex, such as A. baumannii, A. pittii and A. nosocomialis, are a major cause of hospital acquired infections and outbreaks with increasing occurrence of multidrug-resistance. Sulbac-tam-durlobactam (SUD), a combination of one active β-lactam antibiotic (sulbac-tam) with a new β-lactamase inhibitor (durlobactam), is currently being tested in a phase 3 clinical trial by Entasis Therapeutics for the treatment of serious infections caused by ABC, including multidrug-resistant strains. At the same time, an ETEST SUD (sulbac-tam-durlobactam - MIC range 0.004/4-64/4 µg/mL) has been developed and calibrated versus the broth microdilution reference method (BMD) as described by the Clinical and Laboratory Standards Institute (CLSI). This test is intended to determine the MIC of sulbac-tam-durlobactam for species of the ABC complex. The aim of this study was to perform a first comparative study of ETEST SUD with the CLSI BMD method on a panel of 263 isolates.

Methods. The panel consisted of 204 A. baumannii, 29 A. pittii, 30 A. nosocomialis, including 24 SUD-resistant strains, and one CLSI QC strain. BMD was performed using the 2021 CLSI guidelines. ETEST SUD was evaluated using the standard ETEST procedure for Acinetobacter spp. (inoculum 0.5 McFarland, Mueller Hinton medium, incubation at 35°C for 20–24h). For each method, the MIC was read at complete inhibition of visible growth. To determine category agreement (CA) and error rates, the sulbac-tam-durlobactam provisional breakpoint point of 4 µg/mL was applied.

Results. The QC strain MICs were in the expected range with reproducible results. The essential MIC agreement [EA, ±1 dilution] was 97.7% without any tendency to over- or underestimate the MIC when compared to BMD. The CA was 98.5%. Two Very Major Errors, both within the EA, and two Major Errors, one within the EA, were observed.

Conclusion. In this study, the ETEST SUD was found to be equivalent to the CLSI reference method. MIC end points were easy to read. With a 15-dilution range and simplicity of use, ETEST SUD could represent a valuable tool for MIC determination and could be an alternative to BMD.

Disclosures. All Authors: No reported disclosures

657. Genomic Insights into Virulence Factors Affecting a Tissue-invasive Klebsiella pneumoniae Infection

Klebsiella pneumoniae is one of the hypervirulent Klebsiella pneumoniae (hvKp) endemic areas, resulting in an alarming issue in actual clinical settings. However, little is known regarding key virulence factors responsible for hvKp infection.

Methods. We analyzed K. pneumoniae isolates collected between 2017 and 2019, and defined hvKp as a pyogenic infection. Classical K. pneumoniae (cKp) involved a non-invasive infection or uncomplicated bacteremia. Isolates belonging to the K. pneumoniae species complex were excluded.

Results. We analyzed 112 isolates, including 19 hvKp, 67 cKp, and 26 colonizers, by whole-genome sequencing. Population genomics revealed that the K1–sequence type (ST) 82 clade was distinct from that of K1-ST23 clone (Figure 1). The virulence gene profiles also differed between K1-ST82 (aero-bactin and rmpA) and K1-ST23 (aero-bactin, yersiniabactin, salmochelin, colibactin, and rmpA/rmpA2). The K2 genotype was more diverse than that of K1. A neighboring subclone of K1-ST23 (comprising ST29, ST412, ST36, and ST268) showed multidrug-resistance and hypervirulence potentials. Logistic-regression analysis revealed that diabetes mellitus was associated with K. pneumoniae infection (odds ratio [OR]: 4.11; 95% confidence interval [CI]: 1.14–14.8). No significant association was found between hvKp diagnosis and clinical characteristics, such as diabetes mellitus or community acquisition (Table 1). The K1 genotype (OR: 9.02; 95% CI: 2.49–32.7; positive likelihood ratio [LR] 4.08, rmpA (OR: 8.26; 95% CI: 1.77–38.5; positive LR: 5.83), and aerobactin (OR: 4.59; 95% CI: 1.22–17.2; positive LR: 3.49) were substantial diagnostic predictors of hvKp (Table 2).

Figure 1. Phylogenetic distribution of genetic virulence factors in 112 K. pneumoniae isolates

Table 1. Variables analyzed for predicting hvKp infection

| Variables            | OR (95% CI) | p value |
|----------------------|-------------|---------|
| Diabetes mellitus    | 1.49 (0.52–4.23) | 0.46    |
| Liver cirrhosis      | 12.4 (1.21–127) | 0.034   |
| Community-acquired   | 1.34 (0.48–3.73) | 0.58    |
| Positive string test | 4.07 (1.08–15.3) | 0.038   |
| K1                   | 9.02 (2.49–32.7) | 0.001   |
| K2                   | 0.94 (0.32–2.82) | 0.92    |
| Aerobactin           | 4.59 (1.22–17.2) | 0.024   |
| Yersiniabactin       | 2.11 (0.74–6.04) | 0.16    |
| Salmochelin          | 2.56 (0.83–7.91) | 0.11    |
| Colibactin           | 1.86 (0.63–5.52) | 0.26    |
| rmpA                 | 8.20 (1.77–38.5) | 0.007   |
| rmpA2                | 1.26 (0.44–3.37) | 0.71    |

hvKp, hypervirulent K. pneumoniae; OR, odds ratio; CI, confidence interval

Table 2. Microbiological diagnostic predictive values for hvKp

| Characteristics | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | LR+ | LR− |
|----------------|----------------|-----------------|---------|---------|-----|-----|
| Positive string test | 84.2 | 43.3 | 29.6 | 90.6 | 1.49 | 0.37 |
| K1 genotype       | 61.5 | 84.9 | 42.1 | 92.5 | 4.08 | 0.45 |
| Aerobactin        | 30.8 | 91.2 | 84.2 | 46.3 | 3.49 | 0.76 |
| rmpA              | 33.3 | 94.3 | 89.5 | 49.3 | 5.83 | 0.71 |

hvKp, hypervirulent K. pneumoniae; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio

The highlighted strains are clinically pathogenic (orange, hypervirulent K. pneumoniae; yellow, classical K. pneumoniae; sky blue, colonization). The non-highlighted strain (NTUH-K2044) is a reference K. pneumoniae strain.

Disclosures. Nothing to disclose
Conclusion. In hvKp-rich settings, diabetes mellitus, community-acquisition, and sideroses other than aerobactin were not remarkable predictors of hvKp infection. However, the K1 genotype, rmpA, and aerobactin were found to be substantial predictors, warranting clinical assessment of any possible/further pyogenic (metastatic) infection. We believe that these findings shed light on key hvKp virulence factors.

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658. Diagnostic Testing Among Patients with Suspected Recurrent Clostridioides difficile Infection (rCDI) in ECOSPOR III: A Phase 3 Clinical Trial: Implications for Clinical Practice vs Clinical Trials
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Background. Accurate diagnosis of rCDI is challenging because of limitations in test performance and alternative causes of recurrent diarrhea, such as post-infectious irritable bowel syndrome (IBS). Stool enzyme immunoassay (EIA) toxin testing (TOX) is the best predictor of active disease, but may miss cases of CDI when toxins are below the limit of detection. In contrast, glutamate dehydrogenase (GDH) or PCR have high sensitivity but cannot differentiate colonization from infection, leading to possible overdiagnosis due to low specificity. In ECOSPOR III, SER-109, an investigational purified microbiase therapeutic, was superior to placebo in reducing rCDI (12.4% vs 39.8%, respectively; p-value < 0.001). We examined diagnostic testing patterns among screened subjects.

Methods. Patients with ≥2 prior episodes and ≥3 unformed bowel movements over 48 hours were screened. To ensure enrollment of patients with active CDI, toxin testing was required at entry via a local certified or central lab (Eurofins; Framingham, MA). Subjects with discordant GDH+/TOX- tests at the central lab had reflex confirmatory testing with a cell cytotoxicity neutralization assay (CCNA), considered the "gold standard" for toxin testing.

Results. The leading reason for screen failure among 281 subjects screened was a negative test toxin (50/99; 50.5%). Of 182 patients enrolled, 59 (32.4%) qualified with EIA TOX+ at the local lab (33 TOX+; 25 GDH+/TOX+) and 122 (67.0%) qualified by "gold standard" for toxin testing.

Conclusions. These diagnostic testing patterns suggest a subset of patients with suspected rCDI have toxin concentrations below the EIA threshold for detection or may have an alternative cause of diarrhea, such as post-infectious IBS. Thus, the limitations of EIA toxin testing need to be considered in clinical practice when evaluating patients with compatible symptoms of rCDI and a high prior probability of infection. In contrast, in trials of investigational agents, toxin testing assures enrollment of patients with compatible symptoms of rCDI and a high prior probability of infection. In contrast, in trials of investigational agents, toxin testing assures enrollment of patients with compatible symptoms of rCDI and a high prior probability of infection.