

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 IGRAs increased over time between 2015-2021. IGRAs were obtained in varied clinical settings. In this low-burden setting, rates of invalid/indeterminate IGRAs were low among children < 2 years old, which suggests that IGRAs 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. Sulbactam-Durlobactam MIC Determination: Comparative Evaluation of the New ETEST<sup>®</sup> SUD to the CLSI 2021 Broth Microdilution Method

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**Session:** P-29. Diagnostics: Bacteriology/mycobacteriology

**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. Sulbactam-durlobactam (SUD), a combination of one active  $\beta$ -lactam antibiotic (sulbactam) with a new  $\beta$ -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<sup>®</sup> SUD (sulbactam-durlobactam - MIC range 0.004/4-64/4  $\mu$ g/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 sulbactam-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 sulbactam-durlobactam provisional breakpoint of 4  $\mu$ g/mL was applied.

**Results.** The QC strain MICs were in the expected range with reproducible results. The essential MIC agreement [EA,  $\pm 1$  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.

*For Research Use Only. The performance characteristics of this product have not been established yet.*

**Disclosures.** All Authors: No reported disclosures

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

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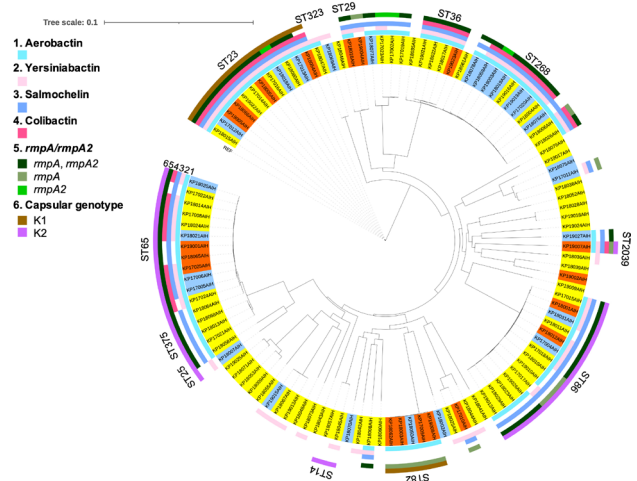
**Session:** P-29. Diagnostics: Bacteriology/mycobacteriology

**Background.** Japan 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 (aerobactin and *rmpA*) and K1-ST23 (aerobactin, yersiniabactin, salmochelin, colibactin, and *rmpA/rmpA2*). The K2 genotype was more diverse than that of K1. A neighboring subclade 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



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.

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
<i>rmpA</i>	8.26 (1.77-38.5)	0.007
<i>rmpA2</i>	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
<i>rmpA</i>	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