### Table 1: *A. C. Uhlemann, Merck: Investigator, Grant recipient.

| Strain  | CKB (μg/mL) | Colistin (μg/mL) | Polymyxin B (μg/mL) | phaP | phaQ | pmxK | pmrC | pmrK |
|---------|-------------|------------------|---------------------|------|------|------|------|------|
| NR 5803 | 1.87V       | >128              | 3.2                 | 2.2  | 0.8  | 0.9  |      |      |
| NR 5803 ramb | 1.60      | 0.38              | 1.5                 | 2.0  | 0.8  | 0.6  | 0.9  | 0.9  |
| NR 5337 | 2.05 WT     | 0.125             |                     |      |      |      |      |      |
| NR 5337 ramb | 1.60    | 0.125             |                     |      |      |      |      |      |

### Background

**Relebactam (REL), formerly MK-7655, is a β-lactamase inhibitor of class A and C β-lactamases that is in clinical development in combination with imipenem (IMI). In this study, we evaluated the activity of IMI/REL and the susceptibility of NPE to IMI/REL in ICUs among the United States as part of the SMART surveillance program from patients with lower respiratory tract infections (RTI) in ICUs, where antimicrobial resistance is typically higher than in non-ICU wards.**

**Methods**

In 2015–2017, 26 hospitals in the United States each collected up to 100 consecutive Gram-negative pathogens from RTI per year. Antimicrobial susceptibility was determined for 1,298 non-Proteus Enterobacteriaceae (NPE) and 638 P. aeruginosa isolated in ICUs, using broth microdilution and breakpoints. For comparision purposes, the IMI susceptibility breakpoint was applied to IMI/REL. Protease were excluded due to intrinsic nonsusceptibility to IMI. Susceptibility was calculated for the 4 United States census regions and overall.

### Results

Susceptibility of NPE was lowest in the Midwest to ceftazidime (81%) and cefepime (87%) and highest in the Northeast (88% and 94%, respectively); susceptibility to imipenem (89–93%) and piperacillin–tazobactam (86–90%) showed less variability across regions. Susceptibility of P. aeruginosa to the four agents was lowest in the West (57–65%) and highest in the Northeast (68–76%). Susceptibilities to IMI/REL of NPE and P. aeruginosa as well as of phenotypes nonsusceptible (NS) to β-lactams are shown below.

#### Initial

| Organism/phenotype | Midwest | Northeast | South | West | United States |
|--------------------|---------|-----------|-------|------|---------------|
| NPE                | 96.2 (95) | 93.3 (119) | 96.4 (34) | 97.5 (429) | 97.0 (2306) |
| Cefazeime-NS       | 94.6 (61) | 70.7 (461) | 97.1 (93) | 98.2 (50) | 98.0 (1533) |
| Cefuzidime-NS      | 93.0 (68) | 100 (14)  | 97.0 (46) | 96.0 (70) | 96.6 (218)  |
| Imipenem-NS        | 40.6 (93) | 83.1 (12) | 70.0 (31) | 70.9 (39) | 76.5 (177)  |
| Piperacillin-ampenem-NS | 98.5 (87) | 100 (13)  | 96.4 (38) | 98.0 (51) | 98.1 (1568) |
| P. aeruginosa       | 94.6 (224) | 97.3 (101) | 96.5 (190) | 95.9 (150) | 92.2 (686)  |
| Cefazeime-NS       | 82.9 (58) | 81.3 (10) | 73.9 (45) | 78.6 (66) | 77.8 (165)  |
| Cefuzidime-NS      | 67.3 (55) | 96.5 (13) | 79.4 (49) | 79.1 (67) | 82.4 (200)  |
| Imipenem-NS        | 82.6 (69) | 79.0 (19) | 74.1 (58) | 74.0 (73) | 77.2 (219)  |
| Piperacillin-ampenem-NS | 83.6 (71) | 80.5 (29) | 77.4 (53) | 79.8 (82) | 80.3 (228)  |

#### Subsequent

| % of NPE/REL-susceptible (total a) |
|-----------------------------------|
|                                    |
| MIDWEST                           |
| Northeast                         |
| South                            |
| West                             |
| United States                     |
| NPE                               |
| IMI/REL                           |
| Cefazeime-NS                      |
| Cefuzidime-NS                     |
| Imipenem-NS                       |
| Piperacillin-ampenem-NS           |

#### Conclusion

The study β-lactams showed some variability in activity against pathogens from RTI patients in ICUs across census regions, whereas IMI/REL maintained activity in all regions against NPE (>96%) and P. aeruginosa (90–95%). IMI/REL remained active against ≥98% of resistant phenotypes of NPE, except the imipenem-NS subset (67.5% susceptible), which was composed mainly of Serratia spp., and remained active against 77–88% of resistant phenotypes of P. aeruginosa, including 72.2% of imipenem-NS isolates. IMI/REL may provide a valuable therapeutic option for the treatment of ICU patients with respiratory tract infections caused by organisms resistant to commonly used β-lactams.

### Session: 68. Resistance Mechanisms: Gram-Positive

**Thursday, October 4, 2018: 12:30 PM**

#### 710. Increased Clinical Failure Rates Associated with Reduced Meropenem Susceptibility in Cladobiotic difficile

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**Session:** Resistance Mechanisms: Gram-Positive

**Thursday, October 4, 2018: 12:30 PM**

**Background.** Reduced susceptibility to meropenem (ME) was observed in C. difficile isolates from stool samples that tested positive for C. difficile infection (CDI). However, the reason for these increased failure rates is unclear. We hypothesized an increase in the minimum inhibitory concentration (MIC) of ME to C. difficile to contribute to these failure rates.

**Methods.** In 2017–2018, stool samples from 2,293 ME-resistant patients were assessed in patients that received treatment for CDI. Treatment failure rates were assessed in patients that were treated with metronidazole (MTZ). The objective of this study was to determine clinical response rates in patients with CDI who received ME therapy vs. other therapies stratified by MTZ susceptibility.

**Results.** Stool samples that tested positive for C. difficile (2017–2018) were collected from two large academic hospital systems in Texas. C. difficile isolates were recovered from stool and visually screened for growth on heme-containing agar plates at MTZ at 2 mg/L (defined as reduced susceptibility). Blinded investigators reviewed electronic medical records to identify the treatment received and determine clinical success or failure of each patient. Treatment failure rates were assessed in patients that received ME therapy vs. other therapies stratified by MTZ susceptibility. Results were analyzed using multivariate logistic regression analysis.

**Conclusion.** A total of 172 C. difficile isolates were included of which 55.8% displayed reduced susceptibility to ME (reduced susceptibility; MS) and were subjected to in vitro susceptibility testing with various antibiotics. Clinical success rates with ME varied widely (40%) and were not associated with reduced susceptibility to ME. This study was limited by the small number of isolates assessed; however, the results suggest that C. difficile isolates with reduced susceptibility to ME may contribute to poor response to ME therapy in the treatment of CDI.

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**Disclosures.** B; blood; IA; intra-abdominal; L; lung; R; rectal; S; skin soft tissue; U; urine; EC, Enterobacter cloacae; ECO, Escherichia coli; KP, Klebsiella pneumoniae

**Conclusion.** Incidence of CI in carriers is low. Patients with IA and respiratory CI in the preceding 93 days are candidates for CPCTRE treatment; empiric therapy should be active against the carbapenemase identified in the index episode.

**Disclosures.** All authors No reported disclosures.

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### 709. Activity of Key β-Lactam Agents Against Gram-Negative Bacilli from ICU Patients with Lower Respiratory Tract Infections, SMART United States 2015–2017

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**International Health Management Associates, Inc., Schaumburg, Illinois**

**Session:** Resistance Mechanisms: Gram-Negative

**Thursday, October 4, 2018: 12:30 PM**