Influenza A viruses are responsible for seasonal epidemics and the attributes of potency, broad recognition of a highly conserved epitope, and high stringency for FcγR engagement are barriers to effective prophylaxis. Our findings bolster available benchtop and clinical data suggesting that breath testing may be a useful diagnostic modality for influenza infection. The next step will be to study the predictive algorithm developed in this protocol in a blinded validation cohort. If the predictive algorithm performs well in a validation study, adaptation for its use in a portable, tabletop GC would be warranted to allow for an accurate, universal point-of-care influenza diagnostic test.

**Background.**

The C. Andrew Tazobactam (PIP/TAZ) with Imipenem/Cilastatin (IMI)/Relebactam (REL) Versus Piperacillin/Tazobactam (PIP/TAZ) study, adaptation for its use in a portable, tabletop GC would be warranted to allow for a rapid, accurate, universal point-of-care influenza diagnostic test.

**Conclusion.**

Our findings bolster available benchtop and clinical data suggesting that breath testing may be a useful diagnostic modality for influenza infection. The next step will be to study the predictive algorithm developed in this protocol in a blinded validation cohort. If the predictive algorithm performs well in a validation study, adaptation for its use in a portable, tabletop GC would be warranted to allow for a rapid, accurate, universal point-of-care influenza diagnostic test.

**Disclosures.**

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1230. Clinical and Microbiologic Outcomes by Causative Pathogen in Hospital-Acquired or Ventilator-Associated Bacterial Pneumonia (HABP/VABP) Treated with Imipenem/Cilastatin (IMI)/Relebactam (REL) Versus Piperacillin/Tazobactam (PIP/TAZ)

Maria C. Losada, BA, Merck & Co., Inc. (Employee, Shareholder) Jiejun Du, PhD, Merck & Co., Inc. (Employee, Shareholder) Michele L. Brown, BS, Merck & Co., Inc. (Employee, Shareholder) Katherine Young, MS, Merck & Co., Inc. (Employee, Shareholder) Merck & Co., Inc. (Employee, Shareholder) Robert Tipping, MS, Merck & Co., Inc. (Employee, Shareholder) C. Andrew DeRyke, PharmD, Merck & Co., Inc. (Employee, Shareholder) Joan R. Burttder, MD, Merck & Co., Inc. (Employee, Shareholder) Amanda Paschke, MD MSCF³; Luke F. Chen, MBBS MPH MBA FRACP PSHEA FIDSA³; Merck & Co., Inc., Rahway, New Jersey; Merck & Co., Inc, Kenilworth, NJ

Session: P-56. New Drug Development

**Background.**

IMI/REL is a combination of IMI and the novel class A and class C β-lactamase inhibitor REL. Here we present per-pathogen outcomes from a recent phase 3 clinical trial (RESTORE-IMI 2), in which IMI/REL was shown to be non-inferior to piperacillin/tazobactam (PIP/TAZ) for empiric therapy of HABP/VABP, in both primary and secondary endpoints. **Methods.**

Randomized, controlled, double-blind, multinational, phase 3, non-inferiority trial in adults with HABP/VABP. Lower respiratory tract specimens were obtained ≤48 hours prior to screening. Participants (pts) were randomized 1:1 to IMI/REL 500 mg/250 mg or PIP/TAZ 4 g/500 mg, given intravenously every 6 h for 7-14 d. Pts also received empiric linezolid until baseline cultures confirmed absence of MRSA. This analysis evaluated outcomes by causative LRT pathogen in modified intent to treat (MITT) pts (randomized pts with ≥1 dose of study drug, excluding pts with only gram-positive cocci present on baseline Gram stain) who had ≥1 baseline LRT pathogen susceptible (according to CLSI criteria) to both study drugs. Outcomes assessed were microbiologic response at end of therapy (EOT), clinical response at early follow-up (EUF), 7-14 d after EOT), and Day 28 all-cause mortality (ACM).

**Results.**

Of 531 MITT pts, 51.4% (130 IMI/REL, 143 PIP/TAZ) had ≥1 baseline LRT pathogen susceptible to both study drugs. The most common causative pathogens in this analysis population were Klebsiella spp (30.4% of patients), Pseudomonas aeruginosa (22.3%), Escherichia coli (22.0%), and Haemophilus influenzae (9.2%), consistent with other recent trials in HABP/VABP and with surveillance data. Outcomes by pathogens were generally comparable between IMI/REL and PIP/TAZ (Table). In a separate subgroup analysis of the microbiologic MITT population, in pts with ≥1 ESBL-positive LRT pathogen (45 IMI/REL, 35 PIP/TAZ), microbiologic response at EOT was 82.2% (IMI/REL) vs 66.6% (PIP/TAZ), clinical response at ETO was 64.4% vs 60.0%, and Day 28 ACM was 20.0% and 22.9%, respectively. In the IMI/REL arm, 8 pts had ≥1 confirmed KPC-positive baseline LRT pathogen; KPC status was not assessed in the PIP/TAZ arm.

**Conclusion.**

IMI/REL is an efficacious treatment option for HABP/VABP, regardless of causative pathogen.

**Table.** Primary and secondary efficacy outcomes in patients who were in the MITT population and had at least 1 baseline LRT pathogen susceptible to both study drugs

| Baseline LRT Pathogen | IMI/REL (%) | PIP/TAZ (%) | p-value |
|-----------------------|-------------|-------------|---------|
| NSBL | 79.9(85.4) | 73.0(72.5) | 0.109 |
| MRSA | 62.5(83.3) | 60.0(76.0) | 0.759 |
| E. coli | 52.5(70.5) | 52.5(70.5) | 1.000 |
| S. marcescens | 8(10.5) | 14(20.5) | 0.334 |
| E. faecalis | 61.5(88.1) | 71.2(93.3) | 0.231 |
| P. aeruginosa | 11.5(18.4) | 22.5(32.5) | 0.118 |
| A. calcoaceticus-balearicus complex | 4(6.5) | 7(10.5) | 0.631 |
| N. influenzae | 12(13.5) | 5(7.5) | 0.201 |

*NSBL app. includes Pseudomonas aeruginosa, Klebsiella oxytoca, and Haemophilus influenzae.

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