with baseline bacteremia could receive up to 14 days; study continued to late follow-up (LFU, 26 ± 2 days). Oral step-down therapy was prohibited. ZTI-01 met the primary endpoint of noninferiority to PIP-TAZ. Secondary objectives included comparing clinical cure rates (assessed by investigator) in the modified intent-to-treat (MITT), microbiologic MITT (m-MITT), clinical evaluable (CE), and microbiologic evaluable (ME) populations at test-of-cure (TOC). Day 18 ± 2 days.

Results. There were 464 patients randomized who received study drug. In all populations, clinical cure rates at TOC were high and similar between treatment groups (>90%) (table). Conclusion. These results demonstrate consistent efficacy in multiple secondary efficacy populations for patients with cUTI and AP who were treated with either ZTI-01 or PIP-TAZ. If approved by FDA, ZTI-01 may provide a new IV option with a different mode of action for patients in the United States with serious Gram-negative infections.

Table: Clinical Response at TOC

| Population       | ZTI-01 | PIP-TAZ | n (%) | n (%) | Difference (%) | 95% CI |
|------------------|--------|---------|-------|-------|----------------|-------|
| MITT             | 233    | 233     |       |       |                |       |
| Cure             | 211    | 212     | 90.2% | 91.6% | -1.4%          | 6.6%  |
| Failure          | 11     | 1 (4.7) | 17 (6.9) | 6.9% |               |       |
| Indeterminate    | 11     | 11 (4.7) | 3 (1.3) | -3.4% |                |       |
| m-MITT           | 184    | 178     |       |       |                |       |
| Cure             | 167    | 167 (90.6) | 191 (96.6) | 6.6% |               |       |
| Failure          | 9      | 4 (9.4) | 16 (8.7) | -1.3% |                |       |
| Indeterminate    | 8      | 8 (3.5) | 3 (1.7) | -1.8% |                |       |
| CE               | 199    | 199     |       |       |                |       |
| Cure             | 188    | 189 (95.4) | 200 (96) | 0.6% |                |       |
| Failure          | 11     | 11 (5.5) | 14 (7.1) | -1.6% |                |       |
| ME               | 155    | 155     |       |       |                |       |
| Cure             | 148    | 148 (95.5) | 151 (93.1) | 8.4% |                |       |
| Failure          | 7      | 4 (5.6) | 10 (6.6) | -1.0% |                |       |

95% confidence intervals (CIs, two-sided) were computed using a continuity-corrected Z-test.

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1368. Assessment of the In Vivo Efficacy of Human-Simulated Epithelial Lining Fluid (ELF) Exposure of Meropenem/Nacubactam (MEM/NAC) Combination Against β-Lactamase-Producing Enterobacteriaceae in Neutropenic Lungen Infection Model

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Background. NAC is being developed as a combination therapy with MEM for the treatment of serious Gram-negative bacterial infections. This study evaluated the efficacy of the human-simulated ELF exposure of MEM/NAC, compared with those of MEM or NAC alone against β-lactamase-producing Enterobacteriaceae isolates in the neutropenic murine lung infection model.

Methods. Eight clinical MEM-resistant Enterobacteriaceae isolates harboring various β-lactamases (IMI, KPC, OXA, TEM, SHV, and AmpC) were utilized in the study. The MICs were tested for susceptibility. The majority of isolates (>70%) were sourced from Wilkins Chalgren agar plates after 48 hours incubation at 37°C, or by agar or microbroth dilution using supplemented Brucella medium following the CLSI guidelines. Regimens in mice that simulated MEM/NAC human-simulated ELF exposure produced enhanced efficacy against MEM-resistant β-lactamase-producing Enterobacteriaceae isolates with MEM/NAC MIC ≤4 mg/L. These data support a potential role for MEM/NAC for treatment of lung infections due to β-lactamase-producing Enterobacteriaceae and warrant further studies.

Results. MEM and MEM/NAC MICs were 8–512 and 0.5–8 mg/mL, respectively. The average log₆ CFU/fung at 0 hours across all isolates was 6.26 ± 0.26. Relative to 0 hours control, the mean bacterial growth at 24 hours in the untreated control mice, MEM HSR, and NAC HSR treatment groups were 2.93 ± 0.29, 2.72 ± 0.42, and 1.75 ± 0.80 log₆ CFU/fung, respectively. MEM/NAC HSR resulted in up to 2-log bacterial reduction in isolates with MEM/NAC MIC ≤4 mg/L.

Conclusion. MEM/NAC human-simulated ELF exposure produced enhanced efficacy against MEM-resistant β-lactamase-producing Enterobacteriaceae isolates with MEM/NAC MIC ≤4 mg/L. These data support a potential role for MEM/NAC for treatment of lung infections due to β-lactamase-producing Enterobacteriaceae and warrant further studies.

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1370. Celipleve/VNRX-5133 Broad-Spectrum Activity is Maintained Against Emerging KPC- and PDC-Variants in Multidrug-Resistant K. pneumoniae and P. aeruginosa

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Background. VNRX-5133 is a cyclic boronate β-lactamase inhibitor (BLI) currently in clinical development with cefepime to treat multidrug-resistant (MDR) infections caused by ESBL- and carbapenemase-producing Enterobacteriaceae (ENT) and...