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 19 ± 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 differentiated MOA for patients in the United States with serious Gram-negative infections.

Table: Clinical Response at TOC

	ZTI-01	PIP-TAZ		
Population	*n* (%)	*n* (%)	Difference (%)	95% CI
MITT	233	231		
Cure	211 (90.6)	212 (91.8)	−1.2	(−6.8, 4.4)
Failure	11 (4.7)	16 (6.9)		
Indeterminate	11 (4.7)	3 (1.3)		
m-MITT	184	178		
Cure	167 (90.8)	163 (91.6)	−0.8	(−7.2, 5.6)
Failure	9 (4.9)	12 (6.7)		
Indeterminate	8 (4.3)	3 (1.7)		
CE	199	196		
Cure	188 (94.5)	182 (92.9)	1.6	(−3.7, 6.9)
Failure	11 (5.5)	14 (7.1)		
ME	155	145		
Cure	148 (95.5)	135 (93.1)	2.4	(−3.5, 8.3)
Failure	7 (4.5)	10 (6.9)		

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

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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 Lung Infection Model

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Session: 144. Novel Agents
Friday, October 5, 2018: 12:30 PM

Background. NAC is a novel dual action β-lactamase inhibitor with *in vitro* activity against class A, class C, and some class D β-lactamases and antibacterial activity against *Enterobactaeriaceae*. 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. MEM and MEM:NAC (1:1) combination MICs were determined in triplicate via broth microdilution. ICR mice were rendered transiently neutropenic, and lungs were inoculated with 50 µL bacterial suspensions of 10^7 CFU/mL. Regimens in mice that simulated the human ELF exposures following doses of MEM 2g q8h and NAC 2g q8h (1.5 hours infusions) as monotherapies and in combination were established. Treatment mice received MEM human-simulated regimen (HSR), NAC HSR, or MEM/NAC HSR and control mice were vehicle-dosed. Treatment was started 2 hours after inoculation and continued for 24 hours. Efficacy was assessed as the change in $\log_{10}$CFU/lung at 24 hours compared with 0 hours controls.

Results. MEM and MEM/NAC MICs were 8–512 and 0.5–8 mg/L, respectively. The average $\log_{10}$CFU/lung 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 $\log_{10}$CFU/lung, 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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1369. Combined Analysis of the In Vitro Activity of Ridinilazole (RDZ) Against More Than 500 *Clostridium difficile* (CD) Clinical Isolates and Impact of RDZ on Cell Morphology

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Session: 144. Novel Agents
Friday, October 5, 2018: 12:30 PM

Background. *Clostridium difficile* infection (CDI) is one of the most urgent bacterial healthcare threats in the United States. RDZ is a targeted spectrum, GI restricted, antibacterial currently in clinical development for the treatment of CDI and reducing the recurrence of CDI. Here we report the combined analysis of previously reported and new independent studies assessing the susceptibility of CD clinical isolates collected in North America and Europe between 2010 and 2015, and the effect of RDZ on cell morphology.

Methods. A total of 570 CD clinical isolates across seven independent studies were tested for susceptibility. The majority of isolates (>70%) were sourced from RDZ Phase 2 clinical trials and North American and European surveillance programs. Minimum inhibitory concentrations (MIC) were determined by agar dilution on 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 M11-A7/A8. Up to 11 comparator antibiotics were tested alongside RDZ. PCR ribotyping was performed on 549 isolates by capillary gel electrophoresis. To investigate the impact of RDZ on cell morphology, CD strain R20291 was incubated with RDZ at 0.125–0.5 × MIC concentrations for 24 hours. DAPI and FM4-64 staining was used to visualize DNA and cell membrane by confocal microscopy.

Results. RDZ was highly active against the isolates collected in North America and Europe with MICs distributed over a narrow range (0.015–0.5 µg/mL) and an overall MIC_{90} of 0.25 µg/mL. There was no variation in activity by geographic region or ribotype, including hypervirulent ribotype 027 isolates ($N = 83$). RDZ also maintained activity against antibiotic-resistant isolates, including isolates with reduced susceptibility to metronidazole and vancomycin. When treated with sub-MIC concentrations of RDZ, CD cells formed filamentous structures with a dose-dependent effect on cell length and decreased septum formation. This preliminary data suggest that RDZ may alter CD cell division.

Conclusion. These data show that RDZ was highly active against recent CD isolates independent of geographic origin, ribotype, and antibiotic resistance profile. Mechanism of action studies are ongoing and further susceptibility profiling will be undertaken during the Phase 3.

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1370. Cefepime/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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Session: 144. Novel Agents
Friday, October 5, 2018: 12:30 PM

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