Results. Of the 28 samples tested, 13 were C-N and 15 C-P. The extraction-free method generated an amplicon in 13/15 C-P cases, with CPs ranging from 26 to 36 cycles *vs.* 100% (15/15) detected with the DNA extraction method and Cps of 19 to 32. Usable sequence length for the extraction-free method was of 359 (interquartile range, 307–390) *vs.* 390 (interquartile range, 308–396) base pairs with DNA extraction. Genus-level concordance between bacteria detected by culture in C-P samples and those found using the extraction-free and extraction methods was 92% (12/13) and 93% (14/15), respectively. Bacteria were detected by the extraction method in 2/13 C-N specimens, with none detected with an extraction-free method.

Conclusion. The described extraction-free method may be suitable for testing SF derived from CIEDs using 16S rRNA gene PCR/sequencing, saving time and cost. More studies are needed to establish clear cutoffs for interpretation of results and to assess for PCR inhibitors in the studied specimen-type.

Disclosures. Robin Patel, MD, ASM and IDSA: Other Financial or Material Support, Travel reimbursement, editor's stipends; CD Diagnostics, Merck, Hutchison Biofilm Medical Solutions, Accelerate Diagnostics, ContraFect, TenNor Therapeutics Limited, Shionogi: Grant/Research Support; Curetis, Specific Technologies, NextGen Diagnostics, PathoQuest, Qvella: Consultant; NBME, Up-to-Date, the Infectious Diseases Board Review Course: Honorarium recipient, Other Financial or Material Support; Patent on Bordetella pertussis/parapertussis PCR issued, a patent on a device/method for sonication with royalties paid by Samsung to Mayo Clinic, and a patent on an anti-biofilm substance issued: Other Financial or Material Support, Patents.

661. Ibalizumab Efficacy and Safety Through 48 Weeks of Treatment: Results of an Expanded Access Protocol (TMB-311)

Brinda Emu, MD[1]; Edwin DeJesus, MD[2]; Mezgebe Berhe, MD[3];
Jason Leider, MD, PhD[4]; Catherine Creticos, MD[5]; Steve Weinheimer, PhD[6];
Zvi Cohen, PhD[7]; [1]Yale University, New Haven, Connecticut; [2]Orlando Immunology Center, University of Central Florida College of Medicine, Orlando, Florida; [3]North Texas Infectious Diseases Consultants, Dallas, Texas; [4]Jacobi Medical Center, Bronx, New York; [5]Howard Brown Health, Chicago, Illinois; [6]TaiMed Biologics USA, Houston, Texas; [7]Theratechnologies Inc., Montreal, QC, Canada

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Ibalizumab (IBA), a humanized monoclonal antibody, is the first CD4-directed post-attachment HIV-1 inhibitor. It was approved by the FDA in March 2018 based on results from the pivotal Phase 3 TMB-301 clinical study.

The TMB-311 expanded access protocol Cohort 2 enrolled treatment-experienced patients with multidrug-resistant (MDR) HIV-1 infection to further evaluate the efficacy, safety and tolerability of IBA in combination with an optimized background regimen (OBR). Here, we report the results through 48 weeks of treatment in these patients.

Methods. Major eligibility criteria included HIV-1 viral load (VL) >1000 copies/mL, resistance to ≥1 antiretroviral (ARV) medication from three different ARV classes and full viral sensitivity to ≥1 ARV agent. Treatment started with IBA 2000 mg intravenously (IV) on Day 0 and then 800 mg IV (maintenance) every 2 weeks thereafter. OBR with ≥1 fully active agent also started at Day 0.

Results. Cohort 2 enrolled 38 patients with a median age of 53 years, mostly male (87%) and white (53%). At Baseline, median VL was 4.7 $\log_{10}$ copies/mL, CD4 cell count was 26 cells/mm^3 and overall susceptibility score of 1. A ≥0.5 $\log_{10}$ decrease in VL from Baseline was achieved in 28 of 37 patients (76%) at Day 7. Of 24 patients who completed the Week 24 visit, 11 (46%) had HIV-1 RNA levels <50 copies/mL. Of 17 patients with a VL assessment at Week 48, 8 (47%) achieved <50 copies/mL. Seven patients did not have a Week 48 endpoint because they withdrew from the study to receive commercial IBA. At both time points, the median change in VL from Baseline was -2.6 $\log_{10}$ copies/mL. The most frequently reported treatment-emergent adverse events (TEAEs) were diarrhea (24%), headache (21%), and nausea, cough, rash, and fatigue (16% each). No injection site reactions related to IBA were reported. Most events were mild; 9 patients reported Grade ≥3 TEAEs. Two events were fatal (sepsis and cardiac arrest); neither related to IBA. One event of immune reconstitution inflammatory syndrome was reported and considered possibly related to IBA.

Conclusion. Results from Cohort 2 patients of TMB-311 (IBA + OBR) demonstrate durable viral suppression in this difficult-to-treat patient population and with a safety profile consistent with pivotal Phase 3 study of IBA.

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

662. Recurrence of Infection and Emergence of Drug Resistance After Treatment with Meropenem/Vaborbactam Compared with Ceftazidime/Avibactam in Carbapenem-Resistant *Enterobacteriaceae* Infections

Renee Ackley, PharmD, BCPS[1]; Danya Roshdy, PharmD, BCPS, BCIDP[2];
Jacqueline Isip, PharmD, BCPS, BCIDP[1];
Sarah B,. Minor, PharmD, BCPS-AQ ID[3];
Amanda L. Elchynski, Doctor of Pharmacy[4]; William E. Anderson, MS[1];
Gerald A. Capraro, PhD, D(ABMM)[1]; Christopher Polk, MD[1]; [1]Atrium Health, Charlotte, North Carolina; [2]Atrium Health - Antimicrobial Support Network, Charlotte, North Carolina; [3]AdventHealth, Winter Springs, Florida; [4]AdventHealth Orlando, Orlando, Florida

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Options for treatment of carbapenem-resistant *Enterobacteriaceae* (CRE) infections were historically limited to antibiotics with limited efficacy and significant toxicities. Ceftazidime/avibactam (CA) and meropenem/vaborbactam (MV) are superior to older regimens; however, a direct comparison of the agents is lacking. This study compared clinical outcomes including recurrence of infection and emergence of drug resistance in patients who received CA vs. MV for CRE infections.

Methods. This was a multicenter, retrospective cohort study of adults with CRE infections who received CA or MV for ≥72 hours from February 2015 to October 2018. Patients with localized urinary tract infection were excluded. The primary endpoint was clinical success (30-day survival, resolution of signs and symptoms of infection, sterilization of blood cultures within 7 days in patients with bacteremia, absence of recurrent infection). Secondary endpoints included 30- and 90-day mortality, adverse events (AE), recurrent CRE infection within 90 days, and development of resistance in patients with recurrent infection. We conducted a post hoc subgroup analysis in patients with recurrence to compare development of resistance in those who received CA monotherapy, CA combination therapy, and MV monotherapy.

Results. 131 patients were included (CA: 105 patients, MV: 26 patients), 40% had bacteremia. No statistical difference in clinical success was observed between groups (62% vs. 69%, respectively, $P = 0.49$). Patients in the CA arm received combination therapy more often than patients in the MV arm (61% vs. 15%, $P < 0.01$). No difference in 30- and 90-day mortality resulted among groups, but numerically higher rates of AE were observed in the CA group (38% vs. 23%, $P = 0.17$). In patients with recurrent infection, development of resistance occurred more often with CA monotherapy, though not statistically significant (Table 1). One case of MV resistance was observed in a patient who had received 4 prior courses of MV, but this episode was outside of the study period.

Conclusion. Clinical success was similar between the groups despite MV being used more often as monotherapy. Development of resistance and rates of AE were higher in the CA group compared with MV therapy.

Table 1. Post-hoc subgroup analysis of patients with recurrent CRE infection

n (%)	CA monotherapy n = 41	CA combination n = 64	MV monotherapy n = 22	P value
Recurrent CRE infection	9 (22.0)	6 (9.4)	3 (13.6)	0.20
MIC increase	5 (12.2)	1 (1.6)	0	0.13
Development of resistance	3 (7.3)	0	0	0.21

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

663. Efficacy and Safety of Lefamulin (LEF) vs. Moxifloxacin (MOX) for *Legionella pneumophila* (*LP*) in Patients with Community-Acquired Bacterial Pneumonia (CABP): Pooled Results From the Lefamulin Evaluation Against Pneumonia (LEAP) 1 and LEAP 2 Phase 3 Clinical Trials

Andrew F. Shorr, MD, MPH, MBA[1]; Jennifer Schranz, MD[2];
Lisa Goldberg, MS[2]; Susanne Paukner, PhD[3]; Anita F. Das, PhD[4];
Gregory J. Moran, MD[5]; Christian Sandrock, MD[6];
Thomas M. File, Jr., MD[7]; Elizabeth Alexander, MD, MSc., FIDSA[2];
Steven P. Gelone, PharmD[2]; [1]Medstar Washington Hospital Center, Washington, DC; [2]Nabriva Therapeutics US, Inc., King of Prussia, Pennsylvania; [3]Nabriva Therapeutics GmbH, Vienna, Wien, Austria; [4]Das Consulting, Guerneville, California; [5]Olive View-UCLA Medical Center, Sylmar, California; [6]UC Davis School of Medicine, Sacramento, California; [7]Summa Health, Akron, Ohio

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. *LP* is associated with severe CABP, rapid onset, and high morbidity/mortality. Poor outcomes in CABP have been linked to receiving inappropriate empiric therapy or delayed treatment (tx). LEF, a novel IV/oral pleuromutilin, demonstrated efficacy/safety in noninferiority studies (LEAP 1/2) vs. MOX in adults with CABP. We report efficacy/safety of LEF in patients with *LP* based on a pooled analyses of LEAP 1/2 data.

Methods. In LEAP 1, PORT III–V patients received LEF 150 mg IV q12h for 5–7 days or MOX 400 mg IV q24h for 7 days, with optional IV-to-oral switch (600 mg LEF q12h or 400 mg MOX q24h). In LEAP 2, PORT II–IV patients received oral LEF for 5 days or oral MOX for 7 days. Both studies assessed early clinical response (ECR) at 96 ± 24 hours after first dose in the intent-to-treat (ITT; all randomized patients) population and investigator assessment of clinical response (IACR) at test-of-cure (TOC; 5–10 days after last dose) in the modified ITT (received ≥1 dose) and clinically evaluable (met predefined evaluability criteria) populations. *LP* was identified from baseline (BL) samples by culture, serology (IgG, Zeus *L. pneumophila* group 1–6 indirect fluorescent antibody assay), urine antigen testing (BinaxNOW), and real-time PCR (positive for *ssrA*). Efficacy analyses herein were done in the microbiological ITT (microITT, treated patients with BL CABP-causing pathogen), microITT-2 (no PCR), and microbiologically evaluable populations; safety analyses included all randomized/treated patients.

Results. Of 65 pooled microITT patients, median age was 60 y, 66% were male, 51% had a normal renal function, and 54%/25% were PORT III/IV. *LP* was identified in 9.3% (34/364) of LEF patients (7 [20.6%]/19 [55.9%]/8 [23.5%] PORT II/III/IV) and in 9.0% (31/345) of MOX patients (7 [22.6%]/16 [51.6%]/8 [25.8%] PORT II/III/IV), primarily by urine antigen or serology (table). Patients with *LP* in both tx groups achieved high and similar responses across all endpoints (Figures 1 and 2). In both tx groups, TEAE rates were low and comparable (~32%) and most were mild to moderate; 5 patients (3 LEF; 2 MOX) had treatment-emergent SAEs, all unrelated to tx. No patients died due to TEAEs; no LEF patients and 2 MOX patients discontinued tx due to TEAEs.

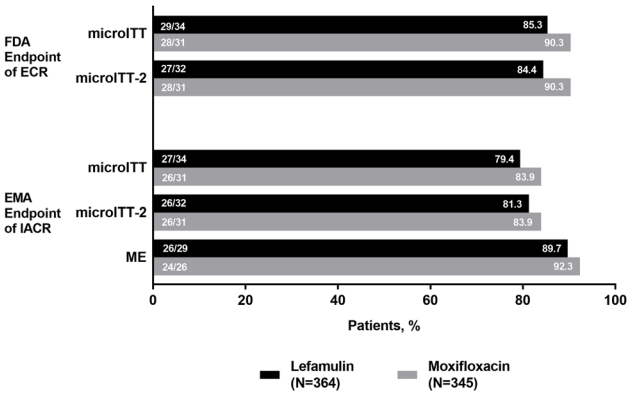
Conclusion. LEF appears to be as safe and effective as MOX in treating patients with *LP*, including when given as short-course (5 days) oral therapy.

Table 1. Diagnostic Modalities and Baseline Pathogen Categories in Patients With *L. pneumophila*

	Lefamulin	Moxifloxacin
microITT, n/N (%)	34/364 (9.3)	31/345 (9.0)
Diagnostic Modality,* n (%)		
Serology	15 (4.1)	22 (6.4)
Urine UAT	8 (2.2)	8 (2.3)
Urine UAT + serology	3 (0.8)	0
Sputum RT-PCR	2 (0.5)	0
Urine UAT + sputum RT-PCR	1 (0.3)	0
Sputum RT-PCR + serology	1 (0.3)	1 (0.3)
≥3 modalities	4 (1.0)	0
Pathogen Category, n (%)		
Monomicrobial	18 (4.9)	16 (4.6)
Polymicrobial†	16 (4.4)	15 (4.3)
microITT-2, n/N (%)	32/209 (15.3)	31/195 (15.9)
Diagnostic Modality, n (%)		
Serology	16 (7.7)	23 (11.8)
Urine UAT	9 (4.3)	8 (4.1)
Urine UAT + serology	5 (2.4)	0
≥3 modalities	2 (1.0)	0
ME, n/N (%)	29/319 (9.1)	26/306 (8.5)
Diagnostic Modality, n (%)		
Serology	15 (4.7)	19 (6.2)
Urine UAT	5 (1.6)	6 (2.0)
Urine UAT + serology	2 (0.6)	0
Sputum RT-PCR	2 (0.6)	0
Sputum RT-PCR + serology	1 (0.3)	1 (0.3)
≥3 modalities	4 (1.2)	0

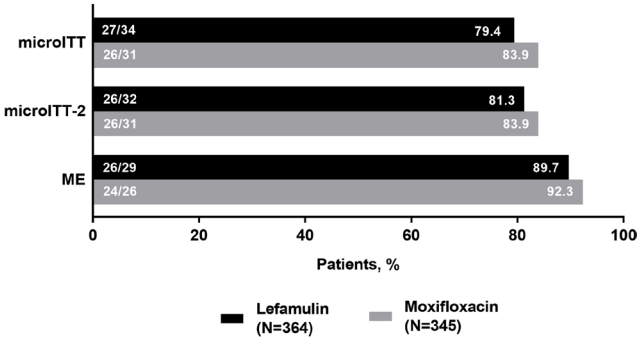
LEF=lefamulin; *LP*=*L. pneumophila*; ME=microbiologically evaluable population includes all pts who met the criteria for both the microITT and the CE analysis sets; microITT=microbiological ITT population includes all pts who had ≥1 baseline pathogen known to cause CABP; microITT-2=microbiological ITT-2 population includes all pts who had ≥1 baseline pathogen known to cause CABP from a diagnostic method other than PCR; MOX=moxifloxacin; RT-PCR=real-time polymerase chain reaction; UAT=urine antigen test.
*Qualification of *LP* as a baseline pathogen with serology testing required a 4-fold or greater increase in *LP* antibody titer to ≥1:128 between the baseline and convalescent samples. In RT-PCR, sample had to test positive for the *ssrA* gene.
†Included >1 atypical pathogen only (6 LEF, 3 MOX); Gram-positive and atypical pathogens only (6 LEF, 9 MOX); Gram-negative and atypical pathogens only (4 LEF, 1 MOX); and Gram-positive, Gram-negative, and atypical pathogens (0 LEF, 2 MOX).

Figure 1. Patients with *L. pneumophila* at Baseline Achieving ECR and IACR



ECR=early clinical response; EMA=European Medicines Agency; FDA=Food and Drug Administration; IACR=investigator assessment of clinical response; ME=microbiologically evaluable population; microITT=microbiological intent-to-treat population.

Figure 2. Microbiological Response in Patients with *L. pneumophila* at Baseline



ME=microbiologically evaluable population; microITT=microbiological intent-to-treat population.

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

664. Efficacy in Adults With Moderate to Severe Community-Acquired Bacterial Pneumonia (CABP) and Pneumonia Outcomes Research Team (PORT) Risk Class III to V: Results of a Pooled Analysis of Lefamulin Evaluation Against Pneumonia (LEAP) 1 and LEAP 2 Study Outcomes

Elizabeth Alexander, MD, MSc, FIDSA[1]; Jennifer Schranz, MD[1]; Anita F. Das, PhD[2]; Gregory J. Moran, MD, FACEP[3]; Christian Sandrock, MD[4]; Thomas M. File, Jr., MD[5]; Steven P. Gelone, PharmD[1]; [1]Nabriva Therapeutics US, Inc., King of Prussia, Pennsylvania; [2]Das Consulting, Guerneville, California; [3]Olive View-UCLA Medical Center, Sylmar, California; [4]UC Davis School of Medicine, Sacramento, California; [5]Summa Health, Akron, Ohio

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

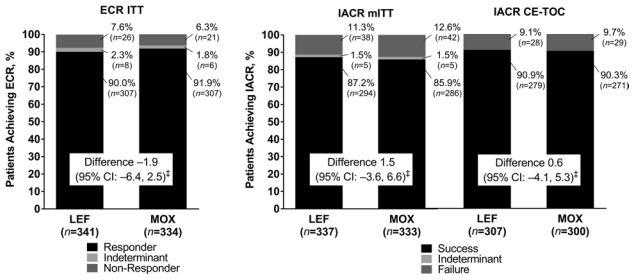
Background. CABP, the second most common cause of hospitalization in the US, has prognoses ranging from rapid resolution to death, the likelihood of which can be estimated via PORT pneumonia severity index. Patients with PORT scores ≤III have predicted mortality rates <3% and may be managed as outpatients; those with scores of IV/V are often hospitalized, owing to higher predicted mortality rates (8%–31%). Lefamulin (LEF), a novel systemic antibiotic, was noninferior to moxifloxacin (MOX) for treatment of adults with CABP in 2 phase 3 trials (LEAP 1 and 2). We report the results of pooled analyses of LEAP 1/2 data in patients with PORT III and IV/V scores.

Methods. In LEAP 1, patients (PORT III–V) received IV LEF 150 mg for 5–7 d or MOX 400 mg for 7 d, with optional IV-to-oral switch. In LEAP 2, patients (PORT II–IV) received oral LEF 600 mg for 5 d or MOX 400 mg for 7 d. In both studies, randomization was stratified by PORT score. The studies assessed early clinical response (ECR; 96±24 h after first dose) in the intent-to-treat (ITT; all randomized patients) population (FDA primary endpoint) and investigator assessment of clinical response (IACR) success at test of cure (5–10 d after last dose) in the modified ITT (received ≥1 dose) and clinically evaluable (met predefined evaluability criteria) populations (EMA coprimary endpoints).

Results. Over 50% of patients (52.8% LEF; 51.9% MOX) were PORT III and >18% (18.7% LEF; 18.2% MOX) were PORT IV/V, reflective of the CABP population. As expected, PORT IV/V patients were older and more likely to have comorbidities (eg, moderate/severe renal impairment) vs. PORT III patients (Table 1). ECR and IACR response rates were high and similar for LEF and MOX in PORT III (Figure 1) and PORT IV/V (Figure 2) patients, with slightly higher rates in PORT III vs. PORT IV/V patients. LEF and MOX had similar safety profiles, with more adverse events overall in PORT IV/V vs. PORT III patients (Table 2). Mortality rates were low, with higher rates in PORT IV/V (4.2% LEF; 5.2% MOX) vs. PORT III (1.5% LEF; 0.6% MOX) patients.

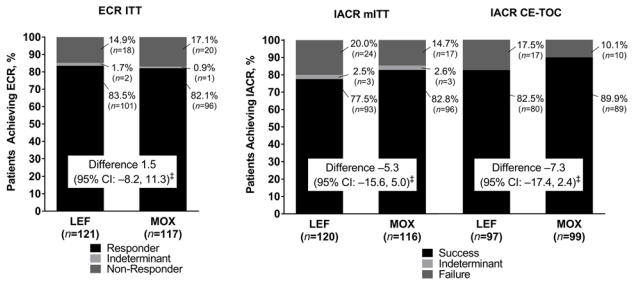
Conclusion. ECR and IACR rates with LEF were high and similar to MOX in patients who are candidates for outpatient (PORT III) and inpatient (PORT IV/V) treatment; LEF may be an alternative oral and IV monotherapy option for empiric CABP treatment in both populations.

Figure 1. PORT Risk Class III Patients Achieving ECR* and IACR†



*Patients achieved ECR if they showed improvement in ≥2 CABP signs/symptoms, had no worsening in any CABP sign/symptom, and had not received a concomitant nonstudy antibiotic for CABP.
†IACR was classified as successful if CABP signs/symptoms resolved or improved such that no additional antibacterial therapy was administered for CABP.
‡Weighted treatment difference and confidence interval (CI) were computed using the method of Miettinen and Nurminen and adjusted for study, with the inverse variance of effect size as stratum weights.

Figure 2. PORT Risk Class IV/V Patients Achieving ECR* and IACR†



*Patients achieved ECR if they showed improvement in ≥2 CABP signs/symptoms, had no worsening in any CABP sign/symptom, and had not received a concomitant nonstudy antibiotic for CABP.
†IACR was classified as successful if CABP signs/symptoms resolved or improved such that no additional antibacterial therapy was administered for CABP.
‡Weighted treatment difference and confidence interval (CI) were computed using the method of Miettinen and Nurminen and adjusted for study, with the inverse variance of effect size as stratum weights.