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**Background.** Daptomycin plus fosfomycin combination has demonstrated synergistic and bactericidal effect in animal models of methicillin-resistant Staphylococcus aureus bacteremia (MRSA), but there is lack of data in humans.

**Method.** A randomized (1:1), open-label, clinical trial involving adults with MRSAB was conducted at 18 medical centers in Spain. Patients were assigned to receive daptomycin, 10 mg/kg IV daily plus fosfomycin, 2 g IV/6 h (combination therapy) or to receive daptomycin 10 mg/kg/24 h IV (monotherapy) during 10 up to 14 days for uncomplicated bacteremia and 28 up to 42 days for complicated bacteremia. The primary efficacy endpoint was treatment success at a 22-Day snapshot (54.1% vs. 42.0%; absolute difference, 12.1%; 95% confidence interval, 0%-27.0%; P < 0.001) at 7 days after starting the therapy: a successful outcome was achieved in 69 of 74 patients who received combination therapy as compared with 62 of 81 patients who received monotherapy (93.2% vs. 76.5%; absolute difference, 16.7%; 95% confidence interval, 5.4%-27.7%). Combination therapy was associated with lower rates of microbiologic failure than monotherapy at ToC visit (0 vs. 9 patients, P = 0.009). Combination therapy, as compared with daptomycin monotherapy, was associated with a nonsignificantly higher rate of adverse events due to study medication leading to treatment failure and discontinuation: 6/74 (8.1%) vs. 1/81 (1.2%); P = 0.31.

**Conclusion.** The combination of daptomycin plus fosfomycin was more effective than daptomycin alone for treating MRSA (NCT01898338).

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

**LB4. A Phase 3, Randomized, Controlled Clinical Trial of Bictegravir in a Fixed-Dose Combination, B/F/TAF, vs. AB/C/3TC in Treatment-Naïve Adults at Week 96.**

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**Session:** 48. Late Breaker Oral Abstracts: HIV and Antibiotic Trials

**Thursday, October 4, 2018: 10:30 AM**

**Background.** Bictegravir (B), a potent INSTI with a high barrier to resistance, is coformulated with emtricitabine (F) and tenofovir alafenamide (TAF) as the FDA-approved single-tablet regimen B/F/TAF. We report Week 96 results from an ongoing phase 3 study comparing B/F/TAF to coformulated dolutegravir, abacavir, and lamivudine (DTG/ABC/3TC) in treatment-naïve adults living with HIV-1. Primary outcome at W48 demonstrated noninferior virologic responses, similar bone and renal profiles, and no viral resistance.

**Methods.** We randomized 1,112 HIV-1+ individuals who were not on antiretroviral therapy, and had ≤ 3 viral load measurements >400 copies/mL within 12 weeks of randomization to receive B/F/TAF (50/200 mg) or DTG/ABC/3TC (50/600 mg) with matching placebos. Primary endpoint was proportion with HIV-1 RNA <50 copies/mL at W48 (FDA snapshot), with secondary analysis at W96. Noninferiority was demonstrated for the absolute difference (AD) CI (12% margin). Other secondary endpoints were safety (adverse events (AEs), laboratory abnormalities) and predefined analyses of bone mineral density (BMD) and measures of renal function (eGFR, proteinuria).

**Results.** A total of 629 adults were randomized/treated (315 B/F/TAF, 314 DTG/ABC/3TC; 87% vs. 89.8%, respectively, achieved HIV-1 RNA <50 copies/mL (difference ~1.9%; 95%CI –6.9% to 3.1%, P = 0.45). In per-protocol analysis, 99.6% on B/F/TAF vs. 98.9% on DTG/ABC/3TC achieved HIV-1 RNA <50 copies/mL (P = 0.33). Most common AEs overall were headache (10.9% B/F/TAF, 9.1% DTG/ABC/3TC) and nausea (6%, 17% respectively). Other AEs leading to treatment discontinuation were ≥ grade 3 (B/F/TAF 3%, DTG/ABC/3TC 1%). Eight (4%) and three (1%) patients on B/F/TAF had elevated lipids compared with no patients on DTG/ABC/3TC. Median % changes in estimated glomerular filtration rate (eGFR) were similar with increased proteinuria with B/F/TAF (1.5% vs. 1.3%, respectively; P = 0.78) and similar bone and renal safety. B/F/TAF was well tolerated with no viral resistance or safety-related discontinuations. B/F/TAF was well tolerated with less nausea than DTG/ABC/3TC and similar bone and renal profile.

**Conclusion.** At W96, B/F/TAF was virologically noninferior to DTG/ABC/3TC, with no viral resistance or safety-related discontinuations. B/F/TAF was well tolerated with less nausea than DTG/ABC/3TC and similar bone and renal profile.

**Table.** Changes from baseline in safety parameters at W96

| Safety Parameter | B/F/TAF | DTG/ABC/3TC |
|-----------------|--------|-------------|
| eGFR, median (ml/min) | 71.8 | 70.9 |
| Renal biomarkers, median (%) | | |
| Albuminuria Albumin-Creatinine Ratio | 0.3 | 0.2 |
| Cystatin C Cystatin C | 21.2 | 22.1 |
| Beta-2-Microglobulin-Creatinine Ratio | 3.0 | 3.0 |

**Disclosures.** D. A. Wohl, Gilead; Grant Investigator and Scientific Advisor, Consulting fee and Research grant. Y. Yazdanpanah, AbbVie: Consultant, Consulting fee. Bristol-Myers Squibb: Consultant, Consulting fee. Gilead: Consultant, Consulting fee. MSD: Consultant, Consulting fee. Pfizer: Consultant, Consulting fee. Johnson & Johnson: Consultant, Consulting fee. ViV Healthcare: Consultant, Consulting fee. A. Baumgard, AbbVie: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium. BMS: Consultant and Speaker, Consulting fee. M. Collins: Consultant, Consulting fee. A. Antinori: Consultant, Speaker fee. Gilead: Consultant and Speaker, Consulting fee and Speaker honorarium. J. C. Kallings: Consultant and Speaker, Consulting fee and Speaker honorarium.
of Nabriva: Consultant, Consulting fee. Healthcare: Gilead: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. Novo Nordisk: Consultant, Consulting fee. Achaogen: Consultant, Consulting fee. Cempra: Consultant, Consulting fee. November 3, 2020: 10:30 AM

Background. Oral Lefamulin is safe and effective in the treatment of adults with community-acquired bacterial pneumonia (CABP). Lefamulin Evaluation Against Pneumonia (LEAP) 2 Study

Disclosures. E. Alexander, Nabriva: Employee and Shareholder, Salary and Stock Options. L. Goldberg, Nabriva: Employee, Employee Stock Options and Salary. A. Das, Achaogen: Consultant, Consulting fee. Compass, Consulting. Consultant, Consulting fee. Contrat: Consultant, Consulting fee. Parexel: Consultant, Consulting fee. Tetraphase: Consultant, Consulting fee. Workhards: Consultant, Consulting fee. Theravance: Consultant, Consulting fee. Zavante: Consultant, Consulting fee. Utility: Consultant, Consulting fee. Former Employee of Nabriva: Employee, Salary. Nabriva: Consultant, Consulting fee. G. J. Moran, Nabriva: Scientific Advisor, Consulting fee. C. Sandrock, Nabriva: Consultant, Consulting fee. L. B. Gasink, Former Employee of Nabriva: Employee, Salary. P. Spera, Nabriva: Employee and Shareholder, Salary. C. Sweeten, Nabriva: Employee, Stock Options and Salary. S. Paulkner, Nabriva: Employee and Shareholder, Salary. W. W. Wicha, Nabriva: Employee and Shareholder, Salary. J. Schranz, Nabriva: Employee and Shareholder, Salary.

LB7. Contract Trajectory Tracking Following First Case of Andes Virus in the United States

Aaron Kofman, MD;1 Paula Eggers, RN;2 Anne Kjemtrup, DVM, MPVM, PhD;3 Rebecca Hall, MPH;4 Shelley Brown, BS;5 Mary Chou, MD, MPH;5 Harley Yaglom, MPH;5 Monique Dowell, MD, MPH;6;1 Barbara Knust, DVM, MPH, DACVP;7 John Klena, PhD;2 Francisco Alvarado-Ramy, MD;2 Trevor Shoemaker, MPH;5 Jonathan Towner, PhD;5 Stuart Nichol, PhD and The Andes Virus Investigation Work Group,1 Epidemiemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia, 1Virual Special Pathogens Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, 2Division of Public Health, Delaware Department of Health and Social Services, Dover, Delaware, 3California Department of Public Health, Sacramento, California, 4Division of Global Migration and

LB6. Oral Lefamulin Is Safe and Effective in the Treatment of Adults With Community-Acquired Bacterial Pneumonia (CABP): Results of Lefamulin Evaluation Against Pneumonia (LEAP) 2 Study

Elizabeth Alexander, MD;1 Lisa Goldberg, MS;1 Anita Das, PhD;2 Gregory J. Moran, MD;2 Christian Sandrock, MD;1 Leanne B. Gasink, MD;1 Patricia Spera, PhD;2 Carolyn Sweeney, BS;2 Susanne Paulkner, PhD;2 Wolfgang W. Wicha, MS;4 and Jennifer Schranz, MD;1 Nabriva Therapeutics US, Inc., King of Prussia, Pennsylvania, 1Das Consulting, Guerneville, California, 2Olive View-UCLA Medical Center, Los Angeles, California, 3UC Davis School of Medicine, Sacramento, California, 4Nabriva Therapies GmbH, Vienna, Austria

Session: 48. Late Breaker Oral Abstracts: HIV and Antibiotic Trials Thursday, October 4, 2018: 10:30 AM

Background. Lefamulin, a first in class pleuromutilin, is being developed as an IV and oral formulation for treating CABP. The second of 2 phase 3 Lefamulin Evaluation Against Pneumonia studies, LEAP 2 (NCT02813694; EudraCT 2015-004782-92) evaluated an oral 5-day regimen, is presented here. LEAP 2 complements the positive results from LEAP 1, an IV-to-oral switch study in patients with PORT Risk Class III-V.

Methods. In this multicenter, randomized, double-blind, double dummy study, patients with CABP were randomized to oral lefamulin 600 mg q12h for 5 days or 7 days of moxifloxacin 400 mg q12h for 7 days. The primary endpoint was oral early clinical response (ECR) (96 ± 24 h after first dose) in the intent-to-treat (ITT) population. The EMA coprimary endpoints (FDA secondary endpoints) were investigational assessment of clinical response (IACR) at test of cure (TOC) (5–10 days after last dose) in the modified ITT (MITT) and clinically evaluable (CEE) TOC populations. For FDA and EMA endpoints, noninferiority was considered if the lower limit of the two-sided 95% CI was greater than –10% (Figure 1).

Results. A total of 738 patients were randomized (n = 370 lefamulin, n = 368 moxifloxacin). Five days of lefamulin was noninferior to 7 days of moxifloxacin for both FDA and EMA primary endpoints (Figure 2). Lefamulin was efficacious regardless of PORT Risk Class (ECR responder rates for PORT II, III, and IV; 91.8% [168/183], 91.0% [132/145], and 85.0% [34/40] for lefamulin; 93.1% [176/189], 90.2% [120/133], and 85.2% [36/42] for moxifloxacin, respectively). Both agents demonstrated similar ECR responder and IACR success rates across baseline CABP pathogens. Rates of serious adverse events (SAEs) and AEs leading to discontinuation were low and similar between groups. Most frequently reported AEs were gastrointestinal, the majority of mild severity with few discontinuations.

Conclusion. Five-day oral lefamulin demonstrated noninferiority for both FDA and EMA efficacy endpoints vs. 7-day oral moxifloxacin. Both agents were safe and generally well tolerated. Lefamulin shows promise as an oral monotherapy with a complete spectrum of antibacterial activity against CABP pathogens.

Figure 1: LEAP 2 Phase 3 Trial Design, Oral Administration.

Figure 2: FDA (ECR) and EMA (IACR) Primary Endpoints

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