honorarium. MSD: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium. ViiV: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium. **A. Clarke**, GSK: Scientific Advisor, Consulting fee. Gilead: Conference attendence, Scientific Advisor and Speaker's Bureau, Conference attendance support, Consulting fee and Speaker honorarium. BMS: Conference attendence, Conference attendance support. Janssen: Conference attendence, Conference attendance support. **M. Thompson**, Bristol Myers Squibb: Research Contractor, Research support. ViiV Healthcare: Research Contractor, Research support. **C. Brinson**, Gilead: Investigator, Scientific Advisor and Speaker's Bureau, Research support and Speaker honorarium. Theratech: Investigator, Research support. BMS: Investigator, Research support. SlieaGen: Investigator, Research support. GSK ViiV: Consultant, Investigator and Scientific Advisor, Consulting fee, Research support and Speaker honorarium. Daiichi Sankyo: Sub Investigator, Research support. Novo Nordisk: Investigator, Research support. Sanofi: Investigator, Research support. Watson: Investigator, Research support. Salix: Investigator, Research support. Janssen: Investigator, Research support. Roche: Investigator, Research support. Colucid: Investigator, Research support. Eisai: Investigator, Research support. Shionogi: Investigator, Research support. Elcelyx: Investigator, Research support. Sangamo: Sub Investigator, Research support. **D. Hagins**, GlaxoSmithKline: Scientific Advisor and Speaker's Bureau, Honoraria and Speaker honorarium. ViiV Healthcare: Scientific Advisor and Speaker's Bureau, Honoraria and Speaker honorarium. Gilead: Scientific Advisor, Honoraria and Speaker honorarium. Bristol-Myers Squibb: Scientific Advisor and Speaker's Bureau, Honoraria and Speaker honorarium. **M. Ramgopal**, Gilead: Grant Investigator, Research grant.**A. Antinori**, AbbVie: Consultant, Consulting fee. BMS: Consultant and Grant Investigator, Consulting fee and Research grant. Gilead: Consultant and Grant Investigator, Consulting fee and Research grant. Janssen-Cilag: Consultant and Grant Investigator, Consulting fee and Research grant. Merck: Consultant, Consulting fee. ViiV Healthcare: Consultant and Grant Investigator, Consulting fee and Research grant. **X. Wei**, Gilead: Shareholder, Salary and Stock. **K. White**, Gilead: Employee and Shareholder, Salary and Stock. **S. Collins**, Gilead: Employee and Shareholder, Salary and Stock. **A. Cheng**, Gilead: Employee and Shareholder, Salary and Stock. **E. Quirk**, Gilead: Employee and Shareholder, Salary and Stock. **H. Martin**, Gilead: Employee and Shareholder, Salary and Stock.

LB5. Safety of In Utero Antiretroviral (ARV) Exposure: Neurologic Outcomes in HIV-Exposed, Uninfected Children

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

Background. Antiretroviral therapy for pregnant women with HIV has dramatically decreased perinatal transmission of HIV, but concerns remain regarding adverse neurologic outcomes from possible mitochondrial dysfunction or other mechanisms in children exposed in utero to antiretroviral (ARV) medications.

Method. We evaluated HIV-exposed uninfected (HEU) children enrolled in the Surveillance Monitoring for ART Toxicities (SMARTT) study, a longitudinal observational cohort study conducted by the Pediatric HIV/AIDS Cohort Study (PHACS) network. The primary outcome of interest was a "neurologic case" (microcephaly, febrile seizures, seizure disorders, ophthalmologic disorders, other neurologic conditions) as determined by clinical review blinded to ARV exposure. Log-binomial regression analysis was used to obtain adjusted relative risks (aRRs) for associations between in utero ARV exposure and neurologic case status, accounting for potential confounders including Hispanic ethnicity, tobacco use during pregnancy, and birth cohort (2011–2014 and 2015–2017 vs. <2011). To account for variable person-time follow-up within the cohort, Poisson regression models for adjusted incidence rate ratios (aIRRs) were also fitted.

Result. Among 3,747 eligible HEU children enrolled in SMARTT (52% male, 68% Black and 31% Hispanic), 237 were diagnosed with neurologic conditions, yielding an event rate of 6.3% (95% CI: 5.6%, 7.2%). Tobacco and alcohol use during pregnancy were common (17% and 8%, respectively). The majority of children had in utero ARV exposure (87%); 60% to PI-based regimens, 16% to NNRTI-based regimens and 7% to PI + NNRTI-based regimens. In adjusted models, there was a trend towards an association between efavirenz exposure (EFV) and neurologic case status (aRR: 1.60, 95% CI: 0.99, 2.58). This association was statistically significant in sensitivity analyses restricted to children enrolled prior to or shortly after birth (aRR: 1.80, 95% CI: 1.06, 3.05), excluding children with confirmed congenital anomalies (aRR: 1.66, 95% CI: 1.02, 2.64), and accounting for person-time follow-up (aIRR: 1.55, 95% CI: 1.00, 2.76).

Conclusion. EFV exposure during pregnancy was associated with a higher risk of neurologic abnormalities in infancy and childhood.

Disclosures. **R. Van Dyke**, Giliad Sciences: Grant Investigator, Research grant. **E. G. Chadwick**, Abbott Labs: Shareholder, stock dividends. AbbVie: Shareholder, stock dividends.

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

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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) evaluating 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 moxifloxacin 400 mg q24h for 7 days. Adults with PORT Risk Class II–IV were eligible (≥50% were to have PORT Risk Class III or IV). The US FDA primary endpoint was 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 investigator assessment of clinical response (IACR) at test of cure (TOC) (5–10 days after last dose) in the modified ITT (mITT) and clinically evaluable (CE) TOC populations. For FDA and EMA endpoints, noninferiority was concluded 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 85.7% [36/42] for moxifloxacin, respectively). Both agents demonstrated similar ECR responder and IACR success rates across baseline CABP pathogens. Rates of serious adverse events (AEs) 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

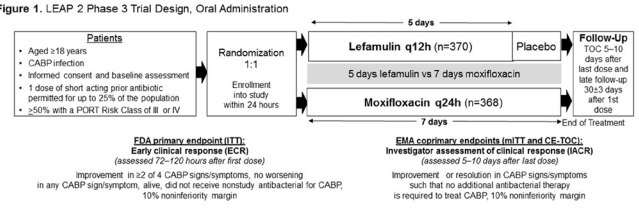
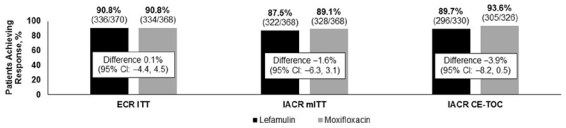


Figure 2. FDA (ECR) and EMA (IACR) Primary Endpoints



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. Cempra: Consultant, Consulting fee. Contrafect: Consultant, Consulting fee. Paratek: Consultant, Consulting fee. Tetraphase: Consultant, Consulting fee. Wockhardt: 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. Sweeney**, Nabriva: Employee, Employee Stock Options and Salary. **S. Paukner**, Nabriva: Employee and Shareholder, Salary. **W. W. Wicha**, Nabriva: Employee and Shareholder, Salary. **J. Schranz**, Nabriva: Employee and Shareholder, Salary.

LB7. Contract Tracing Investigation Following First Case of Andes Virus in the United States

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