1963. Combined Microbiological Response Rates From Two Phase 3 Trials Demonstrating the Activity of Eravacycline in the Treatment of Complicated Intra-abdominal Infections: A Pooled Analysis of IGNITE1 and IGNITE4
Joseph Newman, PhD; Sergey Izmailyan, MS; Corey Fyfe, MS; and Larry Tsai, MD; Tetraphase Pharmaceuticals, Watertown, Massachusetts

Session: 227. Clinical Trials
Saturday, October 6, 2018: 12:30 PM

Background. IGNITE1 and IGNITE4 were randomized, double-blind, double-dummy multinational studies which confirmed the efficacy and safety of eravacycline (ERV) compared with a carbapenem in subjects with complicated intra-abdominal infections (cIAIs). The primary objective of this analysis was to compare the microbiological response at the test-of-cure (TOC) visit for subjects in the two treatment groups.

Methods. Appropriate aerobic and anaerobic specimens for culture at the time of the initial procedure were collected from the site of infection and directly inoculated into transport media. Blood and intra-abdominal specimens were cultured, and species identified according to local laboratory practice. Pure cultures of isolates were sent to a reference laboratory for susceptibility analysis to ERV and comparators. Favorable microbiological response rates at the TOC visit were determined for each baseline pathogen isolated from blood and/or intra- or extra-abdominal specimens in the micro-ITT population.

Results. For subjects with infections caused by Enterobacteriaceae, the overall favorable microbiological response rates for ERV-treated subjects were 86.3% and 91.8% for IGNITE1 and IGNITE4, respectively. The favorable microbiological response rates among pooled ERV-treated subjects are shown in the Table.

| Pathogen or Genotype Category | PLZ (N = 14) | CST (N = 15) | Difference PLZ Minus CST (90% CI) | PLZ (N = 14) |
|------------------------------|-------------|-------------|----------------------------------|-------------|
| Pts with CRE, n/No (%)        | 7/14 (50.0) | 6/15 (40.0) | 0.09 (−0.21, 0.49)              | 7/14 (50.0) |
| E. coli                      |             |             |                                  |             |
| E. faecalis                  | 1/2 (50.0)  | 1/3 (33.3)  | 0.09 (−0.51, 0.69)              | 1/2 (50.0)  |
| Enterobacteriaceae, n/No (%) |             |             |                                  |             |
| A. baumannii                 | 1/1 (100.0)| 0/1 (0.0)   | −1.00 (−0.50, −0.50)            | 1/1 (100.0) |

Conclusion. In IGNITE1 and IGNITE4 studies, high favorable microbiological responses were observed for ERV. More than 88% of five Enterobacteriaceae spp. and B. fragilis, the most common bacteria associated with intraabdominal infections, were eradicated by ERV. Comparable eradication rates were observed following eravacycline and meropenem therapy, further establishing that ERV was at least as effective as carbapenem treatments. These data support in vitro observations that ERV has broad-spectrum activity against common isolates found in intra-abdominal infections.

Disclosures. J. Newman, Tetraphase Pharmaceuticals: Employee, Salary. S. Izmailyan, Tetraphase Pharmaceuticals: Employee, Salary. C. Fyfe, Tetraphase Pharmaceuticals: Employee, Salary. L. Tsai, Tetraphase Pharmaceuticals: Employee and Shareholder, Salary.

Microbial Outcomes With Plazomicin (PLZ) vs. Colistin (CST) in Patients With Bloodstream Infections (BSI) Caused by Carbapenem-Resistant Enterobacteriaceae (CRE) in the CARE Study
Alisa W. Serio, PhD; Alex Smith, MS; Kevin M. Krause, MBA; Irene Galani, PhD; Ana Cristina Gales, MD, PhD; Adrian Jubb, MBChB, PhD, FRCPath; and Lynn E. Connolly, MD, PhD; Achaogen, Inc., South San Francisco, California, and University of California, San Francisco, California, United States

2 Infectious Diseases Research Laboratory, 4th Department of Internal Medicine, University General Hospital Attikon, National and Kapodistrian University of Athens, Athens, Greece, Division of Infectious Diseases, Department of Internal Medicine, Escola Paulista de Medicina/Universidade Federal de São Paulo (EPM/UNIFESP), São Paulo, Brazil

Session: 227. Clinical Trials
Saturday, October 6, 2018: 12:30 PM

Background. PLZ is a next-generation aminoglycoside with structural modifications that protect it from aminoglycoside-modifying enzymes (AMEs) and in vitro activity against multidrug-resistant (MDR) Enterobacteriaceae, including aminoglycoside- and carbapenem-resistant strains. In the CARE study, PLZ was associated with improvement in 28-day all-cause mortality vs. CST in patients with CRE BSI. We report the microbiological outcomes in the CARE study by pathogen and key resistance mechanisms.

Methods. CARE was a multinational, open-label trial that enrolled BSI patients with documented or presumed CRE into two cohorts. Patients in the randomized cohort received PLZ plus investigator’s choice of adjunctive agent. Treatment then 5 mg/kg/day IV plus adjunctive tigecycline or meropenem. Patients in the observational cohort received PLZ alone. Microbiological outcomes were assessed in patients with confirmed CRE who received ≥1 dose of study drug (mITT population).

Results. Of 45 BSI patients enrolled, 43 had confirmed CRE (mITT), including Klebsiella pneumoniae (n = 42) and Enterobacter aerogenes (n = 1). Against CRE, PLZ MICs ranged from 0.12 to >128 μg/mL. 22/28 (78.6%) isolates from PLZ-treated patients had a PLZ MIC ≤4 μg/mL; while 3 had a PLZ MIC ≥2 mg/mL and a confirmed 16S ribosomal methyltransferase gene. CST MICs ranged from 0.25 to >128 μg/mL; 6/16 (37.5%) isolates from CST-treated patients had an MIC ≥2 μg/mL. There were 47 distinct Enterobacteriaceae pathogens isolated from 43 patients, and of these, AME genes were detected in 43 (91.5%), most commonly aac(6’)-Ib-cr (n = 29). Carbapenemase genes were detected in 45/47 (95.7%) isolates, most commonly BlaKPC (n = 33). PLZ demonstrated higher microbiological eradication rates than CST against CRE, including AME- and carbapenemase-producing isolates (table).

Conclusion. The results provide evidence of the efficacy of PLZ-based therapy for patients with BSI due to MDR Enterobacteriaceae, including AME- and carbapenemase-producing organisms.

Disclosures. A. W. Serio, Achaogen, Inc.: Employee and Shareholder, Salary. A. Smith, Achaogen, Inc.: Employee and Shareholder, Salary. K. M. Krause, Achaogen, Inc.: Employee. Salary. I. Galani, Achaogen, Inc.: Scientific Advisor, Research funding and honoraria. MSD: Scientific Advisor, Honoraria. A. C. Gales, MSD-Consultant and Speaker, Consulting fee. Pfizer: Consultant, Consulting fee. BMS: Consultant, Consulting fee. XR3: Consultant, Consulting fee. A. Jubb, Achaogen, Inc.: Employee and Shareholder, Salary. L. E. Connolly, Achaogen, Inc.: Consultant, Consulting fee.

Microbiological Outcomes With Plazomicin (PLZ) vs. Colistin (CST) in Patients With Chronic Hepatitis C Virus Genotypes 1–6 and Human Immunodeficiency Virus–1 Co-Infection: An Integrated Analysis of Two Phase 3 Clinical Trials
Jürgen K. Rockstroh, MD; Sanjay R Bhagani, MD; Chloe Orkin, MBChB; Ruth Soto-Malave, MD; Karine Lacombe, MD, PhD; Zhezhuan Zhang, PhD; Stanley Wang, MD, PhD; Federico Mena, MD and Roger Trinh, MD, MPH; Universitätshilunium Bonn, Bonn, Germany, Royal Free London Foundation Trust, London, UK, The Royal London Hospital, London, UK, Innovative Care PC, San Juan, Puerto Rico, Inserm UMR-S1136, Université Pierre et Marie Curie, Hôpital Saint-Antoine, Paris, France, AbbVie Inc., North Chicago, Illinois

Saturday, October 6, 2018: 12:30 PM

Background. People co-infected with hepatitis C virus (HCV) and human immunodeficiency virus (HIV) may be treated for HCV without special considerations apart from drug interactions with antiretroviral therapies (ART). The once-daily, all-oral, ribavirin-free, pan-genotypic combination of glecaprevir (identiﬁed by AbbVie and Enanta) and pibrentasvir has shown high sustained virologic response at post-treatment Week 12 (SVR12) in HCV mono-infected patients. We evaluated the safety/efficacy of glecaprevir/pibrentasvir in patients co-infected with HCV/HIV-1.

Methods. Data were pooled from two Phase 3 trials for treatment-naïve and -experienced patients co-infected with HCV genotypes (GT) 1–6/HIV-1 without cirrhosis or with compensated cirrhosis who received glecaprevir/pibrentasvir for 8 or 12 weeks.