1974. Ceftriaxone–Sulbactam–EDTA vs. Meropenem in PLEA (a Phase 3, Randomized, Double-Blind Trial): Outcomes by Baseline MIC in Adults With Complicated Urinary Tract Infections or Acute Pyelonephritis

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Background. Ceftriaxone–sulbactam–disodium EDTA (CSE) is being developed for Gram-negative infections caused by multidrug-resistant (MDR) bacteria. PLEA was a Phase 3, double-blind, multicenter, randomized study of CSE vs. meropenem (MR) for treatment of adults with complicated urinary tract infections (cUTI) or acute pyelonephritis (AP). Non-inferiority of CSE over MR at the EMA/FDA primary endpoints has been reported. The effect of baseline MIC on clinical and microbiological outcomes at the test of cure (TOC) visit was investigated.

Methods. Adult patients were randomized 1:1 to receive either CSE (1 g ceftriaxone-one/500 mg Sulbactam/37 mg EDTA) every 12 h or MR 1g every 8 hours as 30 minutes IV infusion for 5–14 days. Oral step-down therapy was not allowed. Prior to dosing, urine specimens were collected, and MICs were conducted using CLSI methods for both study drugs. Patients that were nonsusceptible to MR were not included in the mITT population.

Results. Of 230 subjects randomized, 143 (62.2%) were included in the mITT population. CSE-MR was tested in 131 (91.6%) patients, 67/74 (90.5%) in CSE and 64/69 (92.8%) in MR arm. Mean duration of IV therapy was 7 days. Favorable clinical and microbiological outcomes were observed in 290% patients for all MICs across the two study groups, with the exception of MIC 1µg/mL in MR (associated with >20% failures). Overall, both clinical cure and microbiological eradication rates were higher in CSE as compared with MR (95.9% Vs. 89.9% and 94.6% vs. 88.4% respectively) (Table 1).

CSE | MR
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Conclusion. CSE showed a high in vitro–in vivo correlation of >97% for MICs up to 4 µg/mL and is a potential new treatment option in patients with cUTI or AP.

Disclosures. R. Mallory, MedImmune: Employee, Salary. A. Bandell, AstraZeneca: Employee, Salary. C. S. Ambrose, AstraZeneca: Employee, Salary. J. Yu, GSK: Employee, Salary and Stockholder.

1976. Pooling Analysis of Safety Data From Phases 2 and 3 Clinical Trials Evaluating Eravacycline in Complicated Intra-Abdominal Infections

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Background. Eravacycline is a novel, fully synthetic fluorocycline antibiotic that was evaluated in three comparator-controlled studies for the treatment of complicated intra-abdominal infections (cIAI). The objective of this analysis was to evaluate the safety profile of eravacycline 1 mg/kg IV q12h for the treatment of cIAI.

Methods. Pooled data from one phase 2 and two phase 3 (IGNITE1 and IGNITE4) clinical trials in cIAI were analyzed. Patients in the trials were randomized to receive eravacycline 1 mg/kg IV q12h, ertapenem 1 g IV q24h, or meropenem 1 g IV q8h for 4–14 days. Overall treatment-emergent adverse events (TEAEs), serious TEAEs, and laboratory assessments were evaluated.

Results. Five hundred seventy-six patients were treated with eravacycline 1 mg/kg IV q12h and 547 patients with comparators (ertapenem and meropenem). Demographic and baseline characteristics were similar among the groups. Overall summary and common TEAEs are presented in Table 1. None of the serious TEAEs or those leading to death were related to the study drug. Clinically notable laboratory abnormalities were relatively uncommon and occurred at similar frequencies in eravacycline- and comparator-treated patients.

Table 1. Overall Summary of Treatment Emergent Adverse Events—Eravacycline Phases 2 and 3 Clinical Studies

| Event | Eravacycline 1 mg/kg IV q12h, N = 576, n (%) | Comparators*, N = 547, n (%) |
|---|---|---|
| Any TEAEs | 217 (37.7) | 152 (27.8) |
| Nausea | 40 (6.9) | 5 (0.9) |
| Vomiting | 20 (3.5) | 13 (2.4) |
| Diarrhea | 12 (2.3) | 8 (1.5) |
| Inflammation plebitis | 13 (2.3) | 1 (0.2) |
| Pyrexia | 11 (1.9) | 11 (2.0) |
| Anemia | 7 (1.2) | 7 (1.2) |
| Treatment-related TEAEs | 71 (12.3) | 20 (3.7) |
| TEAEs leading to discontinuation from study drug | 9 (1.6) | 12 (2.2) |
| Serious TEAEs | 33 (5.7) | 33 (6.0) |
| TEAEs leading to death | 7 (1.2) | 7 (1.3) |

*Comparators include ertapenem 1 g IV q24h and meropenem 1 g IV q8h.
1977. Comparative Effectiveness of Linezolid vs. Trimethoprim–Sulfamethoxazole for Acute Bacterial Skin and Skin Structure Infections (ABSSSIs) at a Veterans Affairs Hospital

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Background. Linezolid (LZD) and trimethoprim–sulfamethoxazole (TMP-SMX) are both used in the treatment of acute bacterial skin and skin structure infection (ABSSSI) with differing adverse event profiles to guide usage, but their comparative efficacies in severe ABSSSI remain unclear.

Methods. This retrospective cohort study evaluated patients admitted to the VA St. Louis Health Care System for treatment of an ABSSSI between April 18, 2000 and December 31, 2014. The primary outcome was clinical failure, defined as a composite of an Emergency Department visit, clinic visit, inpatient admission, extension of antibiotics, change of antibiotic regimen for any reason, or the presence of an adverse reaction occurring in the 14 days after completion of the outpatient regimen. The secondary outcome evaluated inpatients were those who had clinical failure and were evaluated for factors contributing to clinical failure.

Results. A total of 1393 patients were included in the analysis; 51 treated with LZD and 88 treated with TMP-SMX. Length of hospital stay was greater in the LZD group (6.05 days vs. 3.69 days [P = 0.023]), as was antibiotic use during hospitalization (98% [49/50] vs. 86% [77/90]; P = 0.019). The mean day supply of antibiotic dispensed at discharge was 10.18 in the LZD group and 9.64 in the TMP-SMX group (P = 0.48). Twenty-two percent (113/513) of patients treated with LZD and 18% (168/88) of those treated with TMP-SMX (P = 0.878) experienced clinical failure. Only receipt of antibiotics for >24–48 hours during hospitalization met criteria for inclusion in the multivariate analysis, but was not significantly associated with clinical failure (0.367 [95% CI 0.083–1.65]; P = 0.187).

Conclusion. There was no difference in the rate of clinical failure between patients treated with LZD or TMP-SMX for severe ABSSSI.

Disclosures. All authors: No reported disclosures.

1978. Efficacy of Eravacycline in Secondary Bacteremia: A Post Hoc Analysis of Two Phase 3 studies of Complicated Intra-Abdominal Infection

Kenneth Lawrence, PharmD; Melanie Oleisky, PhD; Sergey Izmailyan, MS and Larry Tsai, MD; Tetraphase Pharmaceuticals, Watertown, Massachusetts

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Background. Eravacycline is a novel, fully synthetic fluorocycline antibiotic that was evaluated for the treatment of complicated intra-abdominal infections (cIAI) in two Phase 3 (IGNITE1 and IGNITE4) clinical trials. The objective of this analysis was to evaluate microbiological response at the test of cure (TOC) visit in patients with baseline bacteremia who received eravacycline vs. comparators (ertapenem and meropenem).

Methods. Pooled data from IGNITE1 and IGNITE4 studies were analyzed. All patients enrolled were randomized (1:1) to receive eravacycline (1 mg/kg IV q12h) or ertapenem 1 g IV q24h (IGNITE1 study) or meropenem 1g IV q8h (IGNITE4 study) for 4–14 days. Blood (aerobic and anaerobic bottles) and intra-abdominal samples were collected from all patients. Clinical outcome at the TOC visit (28 days after randomization) in the microbiological-intention to treat population (micro-ITT) was the primary efficacy endpoint.

Results. Four hundred fifteen patients were treated with eravacycline and 431 with comparators of which 39 (9.4%) and 40 (9.3%), respectively, had concurrent bacteremia. Demographic and baseline characteristics were similar among the groups. In the micro-ITT population, the pooled clinical response at the TOC visit for eravacycline vs. comparators was 88.7% and 89.3% (<0.7; 95% CI, –4.9, 3.6), respectively. The baseline pathogens associated with concurrent bacteremia and the microbiological eradication for selected pathogens are presented in Table 1.

Table 1. Microbiological Eradication at the Test of Cure Visit by Baseline Pathogen from Blood Specimen

| Pathogen     | Eravacycline, (N = 410), n (%) | Comparators*, (N = 431), n (%) |
|--------------|-------------------------------|-------------------------------|
| Gram-negative | 14/15 (93.3)                  | 14/15 (93.3)                  |
| E. coli      | 5/6 (83.3)                    | 6/7 (85.7)                    |
| Gram-positive | 15/15 (100)                   | 11/11 (100)                   |
| Streptococcus spp. | 8/8 (100)                  | 4/4 (100)                     |
| Enterococcus spp. | 2/2 (100)                    | 5/5 (100)                     |
| Aerobacter    | 9/9 (100)                     | 13/14 (92.9)                  |
| Bacteroides spp. | 6/6 (100)                    | 8/8 (100)                     |

*Meropenem and ertapenem.

Conclusion. Eravacycline demonstrated a similar microbiological eradication rate as comparator agents in patients with cIAI associated with secondary bacteremia.

Disclosures. K. Lawrence, Tetraphase Pharmaceuticals: Employee, Salary. M. Oleisky, Tetraphase Pharmaceuticals: Employee and Shareholder, Salary. S. Izmailyan, Tetraphase Pharmaceuticals: Employee, Salary. L. Tsai, Tetraphase Pharmaceuticals: Employee and Shareholder, Salary.

1979. Time to Viral Suppression Does Not Impact SVR in Patients Treated With Gliclazepr/Pibrtenasib for 8 Weeks

Christoph Sarrazin, MD; Tamm Tran, MD; Douglas Dylla, PhD; Jordan J. Feld, MD; Sangee Arora, MD; 1289 patients (63% [830] vs. 86% [779]); P = 0.019. The mean day supply of antibiotic dispensed at discharge was 10.18 in the LZD group and 9.64 in the TMP-SMX group (P = 0.48). Twenty-two percent (113/513) of patients treated with LZD and 18% (168/88) of those treated with TMP-SMX (P = 0.878) experienced clinical failure. Only receipt of antibiotics for >24–48 hours during hospitalization met criteria for inclusion in the multivariate analysis, but was not significantly associated with clinical failure (0.367 [95% CI 0.083–1.65]; P = 0.187).

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