1373. Activity of Ceftriaxone–Sulbactam–EDTA Against Multi-Drug-resistant *A. baumannii*, *P. aeruginosa* and Enterobacteriaceae Isolates (WHO Critical Priority Pathogens) Collected from Various Hospitals in India

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Background. Ceftriaxone–Sulbactam–EDTA (CSE) is the first cephalosporin–β-lactamase inhibitor combination with an antibiotic resistance breaker–disodium edetate, recently evaluated in a Phase 3 clinical trial for treatment of adults with complicated urinary tract infections (NCT03477422). The addition of Sulbactam and EDTA expands the spectrum of activity of Ceftriaxone to include extended-spectrum-β-lactamase (ESBL) and metallo-β-lactamase (MBL) producing bacteria. This study evaluated the *in vitro* activity of CSE against 3,150 isolates (716 (22.73%) *E. coli*; 435 (13.81%) *K. pneumoniae*; 1,075 (34.13%) *A. baumannii*; 924 (29.33%) *P. aeruginosa*) collected from 22 hospitals in India during 2013–2016.

Methods. A total of 3,150 nonduplicate Gram-negative clinical isolates were collected, and susceptibility testing was conducted using reference broth microdilution method for CSE and comparators. CLSI defined phenotypic methods were used for ESBL and MBL detection, and thereafter, all isolates were further characterized genotypically using single PCRs and a panel of primers for detection of most β-lactamase enzymes, including bla_{TEM}, bla_{SHV}, bla_{CTX-M}, bla_{AmpC}, bla_{OXA}, bla_{KPC}, bla_{VIM}, bla_{NDM}, and bla_{IMP}.

Results. Of the 3,150 isolates, 2,717 (86.25%) were β-lactamase producers, of which, 851 (31.32%) tested positive for ESBL, 1,591 (58.56%) tested positive for MBL, while 275 (10.12%) tested positive for both ESBL and MBL production during phenotypic evaluation. Once the genotype data were available, isolates were re-characterized as per the functional classification of β-lactamases into four distinct categories, including ESBL, AmpC, Carbapenemase and MBL. An astonishing 1,866 (59.23%) isolates harbored at least one MBL gene, of which, the prevalence was the highest in *A. baumannii* (78.6%), followed by *K. pneumoniae* (63%), *P. aeruginosa* (46.6%) and *E. coli* (44.1%). A summary of the results of susceptibility testing is shown in Figures 1, 2, and 3.

Conclusion. CSE showed a high overall susceptibility in ESBL- and MBL-producing bacteria and could provide a useful alternative to carbapenems and colistin in clinical settings.

Figure 1: MIC of Cefriaxone-Sulbactam-EDTA against 3150 isolates collected from across India between 2013-16

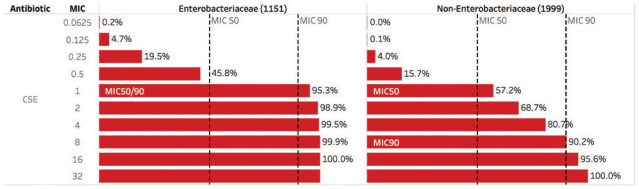
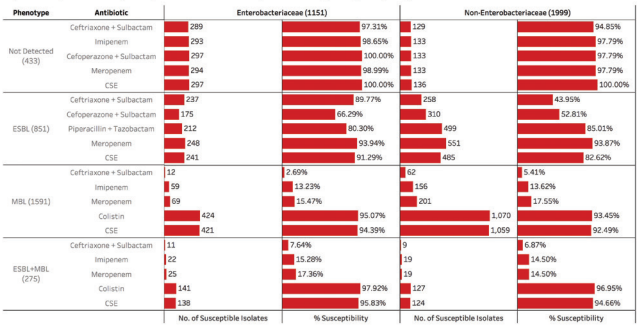
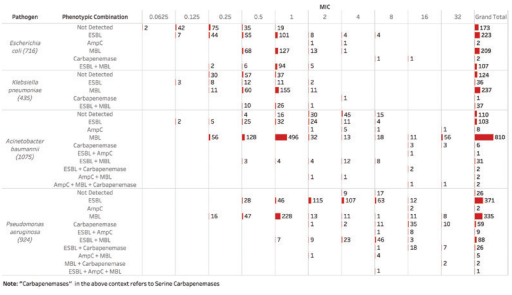


Figure 2: Comparative susceptibility of antibiotics in isolates, characterised phenotypically using Combined Disk Diffusion Methods



Note: Susceptibility has been interpreted using CLSI breakpoints. For Ceftriaxone-Sulbactam and CSE, Ceftriaxone breakpoints have been used to interpret susceptibility (except *P. aeruginosa* where susceptibility has been interpreted using *A. baumannii* breakpoints). For Colistin - MIC ≤2 mcg/ml; Cefoperazone-Sulbactam - MIC ≤16mcg/ml have been used to interpret susceptibility.

Figure 3: MIC distribution of Ceftriaxone-Sulbactam-EDTA in isolates, re-characterised as per functional classification of beta-lactamases



Note: "Carbapenemases" in the above context refers to Serine Carbapenemases

Disclosures. **R. Girotra**, Venus Medicine Research Centre: Employee, Salary. **A. Pyasi**, Venus Medicine Research Centre: Employee, Salary. **M. Chaudhary**, Venus Medicine Research Centre: Board Member and Shareholder, Salary. **M. A. Mir**, Venus Medicine Research Centre: Employee, Salary. **S. Chaudhary**, Venus Medicine Research Centre: Employee and Shareholder, Salary. **P. Mandale**, Venus Medicine Research Centre: Employee, Salary.

1374. Integrated Safety Summary of Omadacycline: A Novel Aminomethylcycline Antibiotic

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Background. Omadacycline (OMC) is a novel aminomethylcycline with activity against Gram-positive, many Gram-negative, anaerobic, and atypical pathogens. It is in clinical development as once-daily oral (PO) and intravenous (IV) monotherapy for acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP). Cumulative safety results from Phase 3 clinical trials are reported.

Methods. This pooled safety analysis is based on 2,150 subjects: OASIS-1 (N = 645), OASIS-2 (N = 735) in ABSSSI; OPTIC (N = 770) in CABP. Comparators were linezolid (LZD) 600 mg IV then PO in ABSSSI (n = 689); moxifloxacin (MOX) 400 mg IV then PO in CABP (n = 388). Safety parameters included treatment-emergent adverse events (TEAEs), laboratory evaluations, vital signs, and electrocardiogram (ECG) findings.

Results. A total of 1,073 subjects received OMC: 705 received OMC IV then PO (ABSSSI, n = 323; CABP, n = 382); 368 received OMC PO only for ABSSSI. Overall, 60.6% were male and 91.6% white; mean age ranges were 44.7–45.1 and 60.9–62.1 years in ABSSSI and CABP studies, respectively. TEAEs were observed in 47.5% (OMC), 41.2% (LZD), and 48.5% (MOX) of subjects, with gastrointestinal events the most common TEAEs. Serious TEAEs were low (3.6% OMC, 1.9% LZD, 6.7% MOX). Nausea (14.9% OMC, 8.7% LZD, 5.4% MOX) and vomiting (8.3% OMC, 3.9% LZD, 1.5% MOX) were the most frequently reported TEAEs. Diarrhea was observed in 2.4% OMC, 2.9% LZD, and 8.0% MOX subjects, with no cases of *Clostridium difficile* in OMC-treated subjects. Most TEAEs were mild to moderate and did not result in study drug discontinuation (3.1% OMC, 1.5% LZD, 7.0% MOX); 4 OMC, 1 LZD, and 0 MOX subjects discontinued for nausea and vomiting. Frequency of hepatic TEAEs was similar for OMC, LZD, and MOX: 4.3% OMC, 4.1% LZD, and 4.5% MOX subjects had post-baseline ALT >3× upper limit of normal. Vital signs and ECGs had comparable clinically notable values post-baseline in each treatment group. Known tetracycline class adverse events such as fungal infections were similar in all groups.

Conclusion. Pooled analyses demonstrate a favorable OMC safety profile, consistent with its tetracycline heritage. OMC was generally well tolerated in subjects with ABSSSI and CABP, with infrequent treatment discontinuations.

Disclosures. **T. M. File Jr.**, BioMerieux: Consultant, Consulting fee; Curetis: Consultant, Consulting fee; Melinta Therapeutics: Consultant, Consulting fee; Merck: Consultant, Consulting fee; Motif Bio: Consultant, Consulting fee; Nabriva Therapeutics: Consultant and Investigator, Consulting fee and Research grant; Paratek Pharmaceuticals: Consultant, Consulting fee; Pfizer: Consultant, Consulting fee. **T. Van Der Poll**, Paratek Pharmaceuticals: Consultant, Consulting fee. **P. McGovern**, Paratek Pharmaceuticals: Employee, Salary. **E. Tzanis**, Paratek Pharmaceuticals: Employee, Salary.

1375. *In vitro* Activity of Cefiderocol and Comparator Agents against Gram-Negative Isolates from Cancer Patients

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Background. Gram-negative bacilli (GNB) are now the predominant cause of bacterial infection in cancer patients (CP). Many GNB are problematic because they have become resistant to commonly used antibiotics. Cefiderocol (CFDC), a novel siderophore cephalosporin, is active against a wide spectrum of GNB. We evaluated its *in vitro* activity and that of eleven comparator agents against GNB isolated from CP.

Methods. A total of 341 recent GNB blood isolates from CP were tested using CLSI approved methods for MIC determination by broth microdilution. Comparator agents were amikacin (A), aztreonam (AZ), ceftazidime (CZ), ceftazidime/avibactam