

1984. Ceftriaxone-Sulbactam-EDTA vs. Meropenem: Analysis of Failed Patients With Assessment of MIC Increases and Changes in Genotypic Profile in PLEA (a Phase 3, Randomized, Double-Blind Clinical Trial in Adults With Complicated Urinary Tract Infections or Acute Pyelonephritis)

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Background. Ceftriaxone-sulbactam-EDTA (CSE) is a novel combination being developed to treat serious infections caused by Gram-negative bacteria. *In vitro* molecular biology studies have shown that the addition of EDTA in the combination helps to prevent horizontal gene transfer during conjugation by chelating the divalent magnesium ions (Mg²⁺) required for the activity of DNA relaxase enzyme. An assessment of acquisition of resistant genes and a concomitant increase in MIC for patients that failed therapy in the Phase 3 clinical trial (NCT03477422) was conducted.

Methods. MICs were conducted on baseline and post-treatment isolates recovered during treatment period. MICs were determined using CLSI reference methods and MIC changes from baseline were further assessed. Bacterial DNA was extracted by the alkaline lysis method. β -Lactamase (BL) genes were amplified in single PCRs using a panel of primers for detection of most β -lactamase enzymes, including extended-spectrum β -lactamases (ESBLs) (*bla*_{TEM}, *bla*_{SHV}, *bla*_{CTX-M}), metallo- β -lactamases (MBLs) (*bla*_{VIM}, *bla*_{NDM}, *bla*_{IMP}), carbapenemases (*bla*_{OXA}, *bla*_{KPC}) and class C cephalosporinases (*bla*_{AmpC}).

Results. Nine of 143 [2/74 (2.7%) in CSE; 7/69 (10.1%) in MR (meropenem)] patients had a microbiological failure at the TOC visit. Of these nine patients (all *E. coli*), a variation in the post-treatment genotypic profile was noted for four patients (44.4%) in the MR group and two of these patients also reported a ≥ 4 -fold increase in post-treatment MIC. Both patients harbored four distinct BL genes (*bla*_{TEM} + *bla*_{SHV} + *bla*_{CTX-M} + *bla*_{AmpC}) at baseline, and had acquired two additional genes (*bla*_{OXA}, *bla*_{KPC}), both carbapenemases, as a result of treatment failure (after 6 days and 8 days of IV therapy respectively) with MR. In the first case, MIC increased 16-fold (1 μ g/mL to 16 μ g/mL for MR and 2 μ g/mL to 32 μ g/mL for CSE), while in the second case, MIC increased 8-fold (1 μ g/mL to 8 μ g/mL for MR and 32-fold (1 μ g/mL to 32 μ g/mL) for CSE. No such increase in MIC or acquisition of resistant genes was noted in patients that failed therapy with CSE.

Conclusion. These findings highlight the need for an effective choice of empirical therapy as failed treatments could lead to selection for resistant genes, rendering once susceptible drug non-susceptible.

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

1985. Atypical Symptoms and High Mortality Associated With Serogroup B Meningococcal Disease in Cartagena Colombia 2012-2016

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Background. Meningococcal disease occurs in an endemic or epidemic form, such as meningitis or meningococemia, the latter being a fast and high disease, mainly in children. Atypical symptoms have been described by the serogroup W. The aim of this study was to determine the clinical and epidemiological characteristics of invasive meningococcal disease (IMD) by serogroup B and the factors associated with mortality in the Cartagena, Colombia between 2012 and 2016.

Methods. Cross-sectional study, carried out from 2012 to 2016 in patients diagnosed with meningococcal disease. Measures of central tendency and dispersion were calculated. A bivariate analysis was performed comparing deceased patients with survivors.

Results. From January 2012 to December 2016, a total of 41 cases were reported: one suspected, seven probable, and 33 confirmed cases (all serogroup B), which 73.2% were male, average age 17.9 \pm 19.16 years old. Mortality was 39% (16/41), 68.7% (11/16) did it in the first 24 hours. Atypical symptoms were 51.21% (21/41): vomiting 48.7%, myalgias in the lower extremities 36.5%, abdominal pain 19.5% and diarrhea 17.0%, necrotic lesions 12.1%, cyanosis 31.7%, cough 12.1% and rhinorrhea 14.6%. And among the typical symptoms: fever 90.2%, drowsiness 70.7%, purpuric rash 60.9%, headache 53.6%, seizure 14.6%, photophobia 4.8%, psychomotor agitation 21.9%, neck stiffness 29.2% and gait deficit 17.0%. When comparing deceased with surviving cases, significant differences were found in abdominal pain OR 6.0 [1.18-40.27], neck stiffness OR 0.08 [0.009-0.74], meningococemia OR 8.90, [1.66-47.75] and myocarditis OR 3.08 [1.93-490], leukocytosis OR 0.22 [IC95% 0.05-0.88], and PCR OR 0.24 [0.06-0.94]. The most prevalent serotype and sero-subtype was B: 10.15: nt (60.0%). Cluster A, with clonal complex ST-41/44 in 64.3%.

Conclusion. Atypical gastrointestinal manifestations, besides being described by serogroup W, may also be a form of presentation of serogroup B, related to a higher mortality.

Disclosures. All authors: No reported disclosures.

1986. Rapid Identification and Antimicrobial Susceptibility Testing Utilizing the Accelerate Pheno™ System for Gram-Negative Bloodstream Infections and Its Potential Clinical Impact

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Background. This study's aim was to compare pathogen identification (ID) and antimicrobial susceptibility testing (AST) result turnaround times of the Accelerate Pheno™ system (AXDX) against current standard methods (SOC). Secondly, we assessed whether its implementation for positive blood cultures (PBC) with monomicrobial Gram-negative bacilli could provide theoretical improvement in time to active and optimal antibiotic therapy.

Methods. Over 3 months, Gram-negative PBC from 114 patients, including 29 pediatric patients, were identified for the study. Blood cultures were tested on both the Verigene® and AXDX platforms in tandem after flagging positive on the BACTEC® FX system. Isolates were tested on the Bruker MALDI Biotyper® system for ID and VITEK® 2 system (GN73 cards) for AST. Patient charts were then retrospectively evaluated to calculate time to active and optimal therapy. On comparing time to results (ID and AST) for AXDX with SOC, timing calculations to mimic setup and reporting times for tests and results were included.

Results. From time of blood culture positivity, mean time to ID averaged 36.3 hours for MALDI-TOF MS, 4.5 hours for the Verigene® system and 3.6 hours for AXDX, while the mean time to AST averaged 35.8 hours for the VITEK® 2 system and 8.9 hours for AXDX. Thirty-nine percent (45/114) of patients were not on active therapy at time of positive blood culture. Of these, 29 were put on active therapy within a mean of 21 hours (range: 9.3 hours to 5.6 days), such that 25% of patients could have been put on active therapy sooner had AXDX AST results been available clinically for action by a physician or stewardship team. Similarly, 34 were put on optimal therapy within a mean of 1.3 days (range: 9.3 hours to 5.6 days). Thus, 30% of patients could have had therapy optimized earlier had AXDX AST results been available.

Conclusion. Overall, the Accelerate Pheno™ system is a reliable new diagnostic modality that has the potential to significantly reduce time to PBC ID and AST results, as well as time to active and optimal therapy, thus aiding in effective antimicrobial stewardship. Prospective studies evaluating the clinical impact of AXDX on patient outcomes are needed and planned.

Disclosures. J. Schneider, Accelerate Diagnostics: Investigator, kits and data management and Research support.

1987. Validation of a MALDI-TOF MS-Based Direct-on-Target Microdroplet Growth Assay (DOT-MGA) for Rapid Detection of Extended-Spectrum β -Lactamase (ESBL) and AmpC in Clinical Enterobacteriaceae Isolates

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Background. Most phenotypic methods routinely employed for the detection of ESBL and AmpC producing *Enterobacteriaceae* require 18 hours of incubation. Aiming to offer this clinically relevant information in a shorter time, we developed a MALDI-TOF MS-based direct-on-target microdroplet growth assay (DOT-MGA) as a one-step screening and confirmation panel in accordance with the EUCAST guidelines.

Methods. DOT-MGA was performed on 12 clinical *Enterobacteriaceae* strains displaying resistance against third-generation cephalosporins plus four control strains recommended by EUCAST for detection of ESBL production. Microdroplets (6 μ L) containing bacterial suspension and antibiotics (cefepodoxime, cefotaxime, ceftazidime, cefepime with or without clavulanic acid, and/or cloxacillin) in cation-adjusted Mueller-Hinton broth (CA-MHB) were spotted directly onto MBT Biotargets 96 (Bruker Daltonics, Germany). Targets were incubated for 4 hours at 36°C in plastic transport boxes in order to avoid evaporation. Subsequently, culture medium was removed and MALDI-TOF MS of the cells adhered to the target's surface was performed. The minimum inhibitory concentration (MIC) was considered to be the lowest concentration at which the MALDI Biotyper software (Bruker) provided no species identification. ESBL/AmpC production was defined as an 8-fold or greater decrease of