

P2780 Performance of amoxicillin/clavulanic acid disk diffusion against broth microdilution from bloodstream isolates non-susceptible to ceftriaxone

Andrew Henderson^{*1,2}, Paul Tambyah³, David Lye^{4,5,6}, Mesut Yilmaz⁷, Thamer Alenazi⁸, Matteo Bassetti⁹, Elda Righi⁹, Benjamin Rogers^{10,11}, Souha S. Kanj¹², Hasan Bhally¹³, Jon Iredell^{14,15}, Marc Mendelson¹⁶, David Looke^{1,17}, Spiros Miyakis^{18,19,20}, Genevieve Walls²¹, Amy Crowe²², Paul Ingram^{23,24,25}, Nick Daneman²⁶, Paul Griffin^{17,27,28}, Eugene Athan²⁹, Michelle Bauer², Kyra Cottrell², Ernest Tan², Leah Roberts³⁰, Scott Beatson³⁰, Anton Peleg^{31,32}, Tiffany Harris-Brown², David L. Paterson^{2,33}, Patrick Harris^{2,34}

¹ Infection Management Services, Princess Alexandra Hospital, ² Centre for Clinical Research, University of Queensland, ³ Department of Infectious Diseases, National University Hospital, ⁴ Yong Loo Lin School of Medicine, National University of Singapore, ⁵ Department of Infectious Diseases, Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital, ⁶ Lee Kong Chian School of Medicine, Nanyang Technological University, ⁷ Department of Infectious Diseases and Clinical Microbiology, Istanbul Medipol University, ⁸ King Saud Bin Abdulaziz University for Health Sciences and King Abdullah International Medical Research Center, ⁹ Infectious Diseases Clinic, Department of Medicine University of Udine and Santa Maria Misericordia Hospital, ¹⁰ Centre for Inflammatory Diseases, Monash University, ¹¹ Monash Infectious Diseases, Monash Health, ¹² Department of Internal Medicine, Division of Infectious Diseases, American University of Beirut Medical Center, ¹³ Department of Medicine and Infectious Diseases, North Shore Hospital, ¹⁴ Marie Bashir Institute for Infectious Disease and Biosecurity, University of Sydney, ¹⁵ Centre for Infectious Diseases and Microbiology, Westmead Hospital, ¹⁶ Division of Infectious Diseases & HIV Medicine, Groote Schuur Hospital, University of Cape Town, ¹⁷ University of Queensland, ¹⁸ School of Medicine, University of Wollongong, ¹⁹ Illawarra Health and Medical Research Institute, ²⁰ Department of Infectious Diseases, Wollongong Hospital, ²¹ Department of Infectious Diseases, Middlemore Hospital, ²² Department of Infectious Diseases, Department of Microbiology, St Vincent's Hospital, ²³ School of Pathology and Laboratory Medicine, The University of Western Australia, ²⁴ Department of Infectious Diseases, Fiona Stanley Hospital, ²⁵ Department of Microbiology, PathWest Laboratory Medicine, ²⁶ Sunnybrook Health Sciences Centre, University of Toronto, ²⁷ Department of Medicine and Infectious Diseases, Mater Hospital and Mater Medical Research Institute, ²⁸ QIMR Berghofer, ²⁹ Department of Infectious Diseases, Barwon Health and Deakin University, ³⁰ School of Chemistry and Molecular Biosciences, University of Queensland, ³¹ Infection & Immunity Program, Biomedicine Discovery Institute & Department of Microbiology, Monash University, ³² Department of Infectious Diseases, Alfred Hospital and Central Clinical School, Monash Health, ³³ Department of Infectious Diseases, Royal Brisbane and Women's Hospital, ³⁴ Department of Microbiology, Pathology Queensland

Background: Amoxicillin/clavulanic (AMC) acid is a beta-lactam/beta-lactamase inhibitor (BLBI) combination often utilised for treatment of Enterobacteriaceae. Clinical microbiology laboratories frequently utilise disk diffusion testing for determining susceptibility to BLBIs. In this study, we tested the performance of AMC disk diffusion against broth microdilution from bloodstream isolates collected from the MERINO study, an international randomised trial of patients enrolled with ceftriaxone non-susceptible *E. coli* and *K. pneumoniae*.

Materials/methods: MIC testing was performed by broth microdilution (BMD) using custom made Sensititre plates (Thermo Fisher) with an AMC range between 4 µg/ml and 256 µg/ml and performed according to EUCAST recommendations with a fixed concentration of 2 µg/ml of clavulanic acid. AMC disk diffusion was performed with

20/10 µg AMC disks (BD) on Mueller Hinton agar, as per EUCAST recommendations. Isolates were assessed as susceptible by BMD and disk diffusion based upon EUCAST v8.0 breakpoint tables for standard (≤ 8 µg/mL/ ≥ 19 mm) and uncomplicated UTI infections (≤ 32 µg/mL/ ≥ 16 mm).

Results: 307 isolates were included in this study, collected from initial blood cultures from enrolled patients in the MERINO trial. Susceptibility rates were significantly higher by disk testing than by BMD (42.7% vs 21.5%) at the standard breakpoint. At this breakpoint, the performance of disk testing demonstrated a significant very major error rate (VME; false susceptible) of 18.1% and major error rate (ME; false resistant) of 3.3%. When uncomplicated UTI breakpoints were applied, susceptibility again remained higher by disk diffusion to BMD (65.5% vs 53.1%). At this breakpoint, VME rates (11.1%) were lower, however, ME rates (6.6%) were higher than for standard breakpoints.

Conclusions: Significant error rates for AMC disk testing were noted comparative to BMD at both standard and uncomplicated UTI breakpoints. These error rates suggest clinicians should be cautious when interpreting AMC disk diffusion reporting of susceptibility in isolates non-susceptible to ceftriaxone.

