L0031 The effect of renal replacement therapy and antibiotic dose on antibiotic concentrations in critically ill patients: The SMARRT Study

Jason Roberts1,2, Gavin Joynt3, Anna Lee3, Gordon Choi4, Rinaldo Bellomo4, Salmaan Kanji5, M. Yugan Mudaliar6, Sandra Peake7, Dianne Stephens8, Fabio Taccone9, Marta Ulldemolins10, Miia Valkonen11, Clement Boidin12, Louise Cole13, Jan De Waele14, Christina König15, Alexander Brinkmann16, Renea Deans1, Melissa Lassig-Smith2, Jean-Yves Lefrant17, Marlies Ostermann18, Ignacio Martin-Loeches19, Stefan Kluge15, Michael Roberts1, Anka Roehr16, Claire Roger17, Mahipal Sinnolareddy20, John D. Turnidge21, Steven Wallis1, Suzanne Parker1, Sanjoy Paul22, Jeffrey Lipman1,2

1 The University of Queensland, Saint Lucia, Australia, 2 Royal Brisbane and Women’s Hospital, Herston, Australia, 3 Chinese University Of Hong Kong, Hong Kong, Hong Kong, 4 Austin Hospital, Heidelberg, Australia, 5 The Ottawa Hospital General Campus, Ottawa, Canada, 6 Westmead Hospital, Westmead, Australia, 7 The Queen Elizabeth Hospital, Woodville South, Australia, 8 Royal Darwin Hospital, Tiwi, Australia, 9 Hospital Erasme, Bruxelles, Belgium, 10 Hospital Parc Taulí de Sabadell, Sabadell, Spain, 11 University of Helsinki, Helsinki, Finland, 12 Hôpital Pierre Garraud - HCL, Lyon, France, 13 Nepean Hospital, Kingswood, Australia, 14 Ghent University Hospital, Gent, Belgium, 15 Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany, 16 General Hospital of Heidenheim, Heidenheim, Germany, 17 Centre Hospitalier Universitaire de Nîmes (CHU), Nîmes, France, 18 Guy’s & St Thomas’ N H S Foundation Trust, London, United Kingdom, 19 St. James’s Hospital, Dublin, Ireland, 20 University of South Australia City West Campus, Adelaide, Australia, 21 The University of Adelaide, Adelaide, Australia, 22 University of Melbourne, Parkville, Australia

Background: In critically ill patients treated with renal replacement therapy (RRT), we sought to test the hypothesis that there would be significant variability in RRT techniques, antibiotic dosing, and trough antibiotic concentrations which commonly fail to meet therapeutic targets.

Materials/methods: This was a prospective, observational, multi-national, pharmacokinetic study in 29 intensive care units. Patient demographic, RRT and clinical data were collected. Trough antibiotic concentrations of meropenem, piperacillin-tazobactam, vancomycin and linezolid were measured. We calculated estimated total renal clearance (eTRCL) as the sum of the total effluent rate during continuous RRT and measured creatinine clearance. We assessed the achievement of high and low therapeutic trough concentrations.

Results: Across 14 countries, we enrolled 384 patients and obtained 514 trough antibiotic concentrations. RRT prescribing and endogenous renal function varied widely with an overall median eTRCL of 50 mL/min (interquartile range [IQR] 35-66). There was also wide variability (4-8 fold) in antibiotic dosing regimens. Increasing eTRCL was associated with decreasing trough concentrations for piperacillin, tazobactam and vancomycin (p<0.05). The median (IQR) trough concentration for meropenem was 12.1 mg/L (7.9-18.8), piperacillin 78.6 mg/L (50.1-127.3), tazobactam 9.5 mg/L (6.3-14.2), vancomycin 14.3 mg/L (11.7-21.8), and linezolid 1.7 mg/L (1.5-5.8). Trough concentrations failed to meet higher targets in 36% and 26%, 72% and lower targets in 4%, 55% and 4% of patients for meropenem, piperacillin and vancomycin respectively.

Conclusions: In patients treated with RRT, highly varied RRT prescription and eTRCL and highly varied antibiotic dosing result in antibiotic concentrations that fail to meet therapeutic targets in many patients.