

**P2205 Ex vivo characterisation of effects of renal replacement therapy modalities and settings on pharmacokinetics of meropenem-vaborbactam**

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**Background:** Renal replacement therapy (RRT) is common in infected critical care patients with renal dysfunction. RRT modalities and settings may influence drug concentrations and lead to therapeutic failure or toxicity if sub-optimal dosing is used. Meropenem-vaborbactam (M-V) is a novel beta-lactamase inhibitor combination developed for gram negative infections, including CRE. The aim of this *ex vivo* study was to describe the effect of RRT on the pharmacokinetics of M-V.

**Materials/methods:** A heparinized human whole blood and Hartmann's solution was spiked with M-V to give three concentration mixtures, 5, 20 and 50 mg/L. Blood was circulated through a ST100 (AN 69 hollow fiber) filter on a Prismaflex machine. An adsorption study, without dialysis fluid or replacement fluid was used and effluent was returned to the blood, was performed to assess binding of drugs to the filter over 3 hrs. A control experiment where no RRT filter was present was also conducted. Clearance and sieving coefficient of meropenem and vaborbactam were investigated in continuous veno-venous hemofiltration (CVVH) mode with various blood flow (200 and 100 mL/min), ultrafiltrate flow (1, 2 and 4 L/h) and point of dilution (pre-filter and post-filter) settings over 2 hrs.

**Results:** Drug remaining after adsorption ( $93 \pm 12\%$  for meropenem,  $96 \pm 8\%$  for vaborbactam) was equivalent to control ( $92 \pm 14\%$  for meropenem,  $96 \pm 5\%$  for vaborbactam). Clearance of meropenem at a blood flow of 200 mL/min and replacement fluid flow of 2 L/h was  $1.73 \pm 0.31$  and  $2.02 \pm 0.17$  L/h for pre- and post-filter dilution, respectively. At the same settings, clearance of vaborbactam was  $1.44 \pm 0.29$  and  $1.74 \pm 0.20$  L/h for pre- and post-filter dilution, respectively. The sieving coefficient for meropenem was  $1.09 \pm 0.10$  and  $1.05 \pm 0.05$ , whilst for vaborbactam was  $0.95 \pm 0.14$  and  $0.93 \pm 0.14$ , for pre- and post-filter dilution respectively.

**Conclusions:** There was negligible adsorption of meropenem or vaborbactam to the filter. Clearance for vaborbactam was slightly lower than meropenem. Meropenem adsorption, clearance and sieving coefficient were similar to previously data. These data will be used to inform dosing of M-V in subjects requiring CRRT.