

**P1204**

**Paper Poster Session**

**PK/PD of agents against Gram-positives**

**Serum and cerebrospinal fluid concentrations of Vancomycin in neurosurgical critically ill patients with central nervous system infections**

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**Background:** Combination therapy with meropenem and vancomycin is recommended for hospital-acquired central nervous system (CNS) infections. The limited penetration of vancomycin into the cerebrospinal fluid (CSF) is well known. However, only limited data exist on the disposition of vancomycin in critically ill patients with CNS infections and non-inflamed meninges. The aim of this study was to describe concentrations of vancomycin in serum and CSF in critically ill patients with external CSF drainage and proven or suspected CNS infections.

**Material/methods:** This was an observational pharmacokinetic (PK) study in neurosurgical critically ill patients with proven or suspected CNS infection receiving vancomycin. Serial blood and CSF samples are taken and analysed by using an *in vitro* chemiluminescent micro particle immunoassay (ARCHITECT *i*Vancomycin assay, Abbott; measuring range: 0.24 mg/l – 100.00 mg/l). Pharmacokinetic parameters are analysed by a one compartment model. The primary pharmacokinetic/pharmacodynamic targets are the area under the concentration curve (AUC) divided by the minimum inhibitory concentration (MIC) value of 400 in serum and concentrations above the MIC of suspected pathogens throughout the entire dosing interval in CSF (100 % T>MIC). According to EUCAST 67 % of *staphylococci* display an MIC of 1 mg/l, 13 % display an MIC of ≤ 0.5 mg/l. Variables are described with median values [interquartile range].

**Results:** Ten patients (mean age 54, mean weight 73) were enrolled. A total of 110 serum samples and 106 CSF samples were analysed. The median of peak and trough concentration in serum was 24.97 [19.96–29.86] mg/l and 8.66 [6.60-10.99] mg/l, respectively. The median AUC<sub>24</sub> in serum was 394.77 [337.93 – 450.89] mg/l. The median of corresponding peak and trough concentration in CSF was 1.60 [0.24-2.11] mg/l and 1.12 [0.24-2.50] mg/l, respectively. In CSF, 31 % of the samples remained below the detection limit. Assuming an MIC of 0.5 mg/l all patients achieved an AUC/MIC value >400. Assuming an MIC of 1 mg/l 50 % of all sampling days achieved AUC/MIC > 400. In CSF, 56 % of all concentrations reached 1 mg/l and 32 % of all concentrations reached 2 mg/l.

**Conclusions:** Vancomycin demonstrated adequate CSF concentrations for high susceptible *staphylococci/methicillinresistant staphylococcus aureus*. With the high inter-individual PK variability observed, therapeutic drug monitoring in CSF might be an option to optimize vancomycin dosing in critically ill patients with CNS infections. Higher serum level targets or switching to alternative antibiotics should be considered, if CSF concentrations are lacking.