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Abstract (poster session)

%fT>MIC (minimum inhibitory concentration) predicts probability of clinical outcome in the treatment of nosocomial pneumonia by ceftobiprole

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Objectives: Ceftobiprole (BPR) is a novel cephalosporin with bactericidal activity against Gram-negative (GN) and Gram-positive (GP) bacteria, including MRSA. A randomized, double-blind phase 3 clinical trial (NCT00210964) was conducted comparing the efficacy of BPR with ceftazidime plus linezolid in patients with nosocomial pneumonia (NP). We explored the relationship of BPR exposure and clinical outcome in patients with NP, excluding ventilator associated pneumonia (VAP). Methods: A population pharmacokinetic (PK) model from 171 patients (Muller et al, ICAAC 2012) was used to determine individual exposures to ceftobiprole dosed 500mg BPR t.i.d. infused over 2h. The MICs used in the analyses were the highest MICs of any pathogens (GN and GP) cultured at baseline (BL) or at BL and/ or end of treatment (EOT). Clinical cure at Test-of-Cure (TOC)-visit in the clinical evaluable population was defined as resolution of symptoms or clinical improvement after at least 5 days of treatment that makes further therapy unnecessary. CART analysis and (multiple) logistic regression was performed using SAS (JMP) software. Results: Using CART analysis, %fT>MIC based on micro-organisms cultured at BL was correlated with clinical outcome with a split value of 88.7% (p=0.0082) . Multiple logistic regression showed that %fT>MIC was the most significant predictor of clinical cure. The final estimates for the intercept were 0.1167 (SE 0.4603), and for the %fT>MIC 0.0131 (SE 0.0053), p=0.014. The analysis based on MICs of micro-organisms cultured at BL and/or EOT showed similar results, with the CART analysis split value at 51.6 %fT>MIC (p=0.0019) and final estimates for the intercept of 0.1776 (SE 0.03667), and for the %fT>MIC of 0.0143 (SE 0.0047), p=0.002. Conclusion: This analysis showed that clinical outcome at the TOC-visit in NP patients, excluding VAP, was significantly associated with exposure to ceftobiprole during treatment. A high probability of clinical cure was attained at 88.7 %fT>MIC or higher for BL microorganisms only and 51.5% or higher for BL and or EOT. Comparable cure rates and microbiological eradication were obtained for ceftobiprole 500 mg tid and ceftazidime 2 g tid both infused over 2 h. Outcome of antimicrobial treatment in nosocomial pneumonia is dependent on PK/PD relationships