

R2545

Abstract (publication only)

**Evaluation of the effects of racial differences on the pharmacodynamics of doripenem in critically ill patients**

A. Farkas\* (Nyack, US)

**Objectives:** Doripenem (DOR) is a broad spectrum carbapenem antibiotic often used for the treatment of serious infections in critically ill patients. The objective of this study was to describe the effects of racial differences on the Probability of Target Attainment (PTA) of DOR at doubling MIC dilutions in critically ill patients.

**Methods:** Population pharmacokinetic (PK) data for DOR in critically ill patients was used in this analysis.

DOR serum concentrations were evaluated with Monte Carlo simulation in Caucasian, Black, Hispanic, and Asian patients (n=5000) for short and extended duration infusion regimens. Targeting the index of  $fT > MIC$  of 40%, success rates were established for conventional dosing regimens at the MICs of 0.125 to 8 mg/L, and at the renal function categories of 20 to 120 ml/min. **Results:** DOR 500 mg every 8 hours infused over 0.5 hours is expected to achieve at least 90% PTAs up to an MIC of 0.5 mg/L at the renal function of 50 to 120 ml/min, irrespective of the racial origin of the patient. In Caucasians, Blacks and Asians, the PTA at the MIC of 1 mg/L continues to reach > 90%, however, it is likely to be suboptimal for patients with Hispanic descent. Extending the infusion time will optimize the chance of therapeutic success for all races when the MIC is less than or equal to 2 mg/L. DOR 250 mg every 8 or 12 hours infused over 0.5 hour regimens should adequately reach MICs of 1 mg/L in all races at the renal function categories of 30-49 and 20-29 ml/min, respectively. Extending the infusion time shows adequate exposure for MICs as high as 2 mg/L, but above that all regimens would have PTAs lower than 90% in all patients with moderate to severe renal impairment. **Conclusions:** As a result of the effects of racial differences on the PK of DOR in critically ill patients, the use of DOR should be individualized to ensure optimal exposure when treating isolates with MICs of greater than 0.5 mg/L in Hispanic patients with normal renal function or mild renal impairment. For these patients, a 4 hour infusion regimen should be utilized to treat MICs of 1 mg/L. At this MIC and in normal to mild renal impairment, 0.5 hour infusion time and standard dosing regimens should be adequate to treat all other patients. To treat MICs of 2 mg/l across renal function categories the extended infusion regimen is recommended for all patients.