

Evaluation of Cefepime Pharmacokinetics in Critically Ill Medical and Surgical Patient Subsets

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1. Abstract of Proposal

Background/Rationale: Multi-drug resistant (MDR) Gram-negative pathogens are associated with significant mortality in critically ill patients. Prompt initiation of appropriately dosed, adequate empiric antibiotic therapy is imperative in patients with suspected/confirmed infection. Pharmacokinetic changes in critical illness, particularly critically ill multiple trauma patients and patients receiving high-flow continuous renal replacement therapy (CRRT), may impair the ability of usual antibiotic dosages to attain optimal pharmacodynamic targets.

Objectives/Aims: (1) To determine and compare prolonged-infusion cefepime pharmacokinetics in adult critically ill multiple trauma and medical patients with normal renal function and (2) to determine conventional dosage cefepime pharmacokinetics in critically ill medical and surgical patients receiving high-flow continuous venovenous hemodialysis (CVVHD) or hemofiltration (CVVH).

Methods: This prospective, single center, clinical pharmacokinetic study is comprised of two sub-studies: (1) measurement and comparison of cefepime pharmacokinetics between critically ill multiple trauma and medical patients with suspected ventilator-associated pneumonia and (2) measurement of cefepime pharmacokinetics and CRRT clearance in critically ill medical and surgical/trauma patients receiving high-flow (≥ 35 mL/kg/hr) CVVHD or CVVH. Cefepime dosages will be consistent with local standards of care: non-CRRT patients will receive cefepime 2 g IV infused over 6 hours every 12 hours; CRRT patients will receive cefepime 2 g IV infused over 30 minutes every 8 hours. A total of 24 patients (12 in each substudy) will be enrolled. Unbound cefepime serum concentrations will be assessed after the third or fourth dose at regimen-specific time points and measured using reverse-phase high-performance liquid chromatography (HPLC). Pharmacokinetic parameters from compartmental and noncompartmental analyses will be determined for all patients. These parameters will be compared between critically ill trauma and medical patients. CRRT-related and modality-specific cefepime pharmacokinetics and clearance will be described.