NKTR-061 (Inhaled Amikacin) BID Achieves High Epithelial Lining Fluid Concentrations in Pneumonic Portions of Lung

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Introduction

The use of systemic antibiotics to treat ventilated patients with Gram-negative pneumonia (GNP) is being increasingly evaluated. Despite advances in the treatment of GNP, mortality remains high, and antibiotic resistance is a growing concern. This study was designed to evaluate the safety, tolerability, and pharmacokinetics of aerosolized inhaled amikacin administered to intubated and mechanically ventilated patients with nosocomial pneumonia caused by Gram-negative organisms.

Objectives

- To determine the pharmacokinetic profile of aerosolized amikacin administered via the PDDS Clinical, as shown in Figure 1.
- To measure the concentration of amikacin in the epithelial lining fluid (ELF) of the lower respiratory tract of the infected lung in patients with pneumonia.
- To determine if aerosolized inhaled amikacin administered via the PDDS Clinical is associated with a reduction of antibiotic exposure, as evidenced in Figure 2.
- To determine if aerosolized inhaled amikacin administered via the PDDS Clinical is associated with improved pulmonary drug delivery, as shown in Figure 3.

Methods

- The use of aerosolized antibiotics, such as amikacin, as adjuncts to IV antibiotic therapy of ventilated patients with HAP, respectively, is a severe respiratory infection with an associated mortality in the range of 25% to 50% despite conventional therapy.

Results

- The mean and median concentrations of AMK in the first tracheal aspirate samples after dosing were 1,778.8 µg/mL and 1,188.0 µg/mL, respectively, with a range of 100 to 10,480 µg/mL.
- The mean and median creatinine levels of AMK in the first tracheal aspirate samples after dosing were 0.60 µg/mL and 0.79 µg/mL, respectively, with a range of 0.00 to 2.10 µg/mL.

Conclusions

- Delivery of aerosolized AMK using the PDDS Clinical achieved very high antibiotic concentrations in the tracheal aspirate and ELF, i.e., the lower respiratory tract, without significant side effects. A total of 64 unexpected adverse events (AEs) were reported for 24 patients; 6 patients had no reports of AEs. The research disclosed that in a study of 64 patients with nosocomial pneumonia caused by Gram-negative organisms, 8 patients had no reports of AEs. The research disclosed that in a study of 64 patients with nosocomial pneumonia caused by Gram-negative organisms, 8 patients had no reports of AEs.

- These results validate the use of aerosolized AMK administered via the PDDS Clinical for patients experiencing respiratory infections, particularly pulmonary drug delivery system (PDDS Clinical), in intubated and mechanically ventilated patients with nosocomial pneumonia caused by Gram-negative organisms.