Evidence of High Amikacin Lung Deposition in Mechanically Ventilated Patients (MVP) with Pneumonia and Healthy Subjects (HS) Dosed Using NKTR-061

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Abstract

The objective of this study was to characterize the pharmacokinetics (PK) of amikacin (AMK) administered using the PDDS Clinical handheld device in mechanically ventilated patients (MVP) with Gram-negative pneumonia and healthy subjects (HS).

Methods:

This was a multi-center, randomized, double-blind, placebo-controlled, Phase II, dose-ranging clinical study to select the appropriate dose for pivotal trials of aerosolized amikacin in MVP with Gram-negative pneumonia.

Results:

There were no serious adverse events reported and the study medication was generally well tolerated by all healthy and mechanically ventilated patients.

Conclusions:

The Cmax in TA and the serum on Day 3 in patients treated with the dosing regimen 400 mg q12h as well as the 400 mg q24h dosing regimen were not different than those observed in the healthy subject study.

No serious adverse events were reported and the study medication was generally well tolerated by all healthy and mechanically ventilated patients.

Keywords: mechanical ventilation, aerosolized antibiotics, amikacin

References:


Figure 2: Scintigraphy scan after inhalation of radio-labeled amikacin using PDDS Clinical handheld device in one representative healthy subject.

Table 2: Amikacin concentration vs. time in lung (mean ± SEM) and serum (via administration of placebo (PL) or 400 mg q12h) in healthy subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo</th>
<th>400 mg q12h</th>
<th>400 mg q24h</th>
<th>400 mg q48h</th>
<th>100 mg q12h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Cmax (µg/mL)</td>
<td>3.2 ± 0.5</td>
<td>32.0 ± 5.3</td>
<td>29.0 ± 4.7</td>
<td>15.0 ± 2.9</td>
<td>3.0 ± 0.5</td>
</tr>
<tr>
<td>Serum AUC (µg/mL•hour)</td>
<td>20.2 ± 5.6</td>
<td>94.8 ± 22.4</td>
<td>95.2 ± 21.8</td>
<td>52.0 ± 12.8</td>
<td>10.0 ± 2.0</td>
</tr>
</tbody>
</table>

Figure 3: Amikacin concentration vs. time in lung (mean ± SEM) and serum (via administration of placebo (PL) or 400 mg q12h) in healthy Subjects.

Materials and Methods

Healthy Volunteers

1. In this open-label, crossover study, healthy subjects received a single dose of aerosolized amikacin containing 100 mg (0.2 mL) administered using the PDDS Clinical handheld device with a mouthpiece followed by a 15-minute period of breathing. Blood samples were collected for serum analyses and were analyzed for the concentration of AMK.

2. Aerosolized antibiotics effectively deliver high concentrations of AMK to the lungs, with significant reductions in serum levels, and minimal systemic toxicity.

Amikacin administered via the PDDS Clinical may improve efficacy and reduce adverse events. Aerosolized amikacin administered via the PDDS Clinical may improve efficacy and reduce adverse events.

Introduction

Aerosol therapy has been used as an alternative to intravenous (IV) administration of antibiotics in patients with ventilator-associated pneumonia (VAP) and hospital-acquired pneumonia (HAP).

The administration of antibiotics in ventilated patients results in high concentrations of antibiotics in the lungs, with significant reductions in serum levels, and minimal systemic toxicity.

This study was intended to describe the PK of aerosolized AMK using the PDDS Clinical handheld device in mechanically ventilated patients (MVP) with Gram-negative pneumonia.

Conclusions:

Aerosolized antibiotics administered via the PDDS Clinical may improve efficacy and reduce adverse events.

Aerosolized antibiotics have been shown to be effective in the treatment of ventilator-associated pneumonia (VAP) and hospital-acquired pneumonia (HAP). The administration of antibiotics in ventilated patients results in high concentrations of antibiotics in the lungs, with significant reductions in serum levels, and minimal systemic toxicity.

This study was intended to describe the PK of aerosolized AMK using the PDDS Clinical handheld device in mechanically ventilated patients with Gram-negative pneumonia.

Methods:

This was a double-blind, placebo-controlled, Phase II, dose-ranging clinical study to select the appropriate dose for pivotal trials of aerosolized amikacin in patients with Gram-negative pneumonia.

Results:

There were no serious adverse events reported and the study medication was generally well tolerated by all healthy and mechanically ventilated patients.

Conclusions:

The Cmax in TA and the serum on Day 3 in patients treated with the dosing regimen 400 mg q12h as well as the 400 mg q24h dosing regimen were not different than those observed in the healthy subject study. No serious adverse events were reported and the study medication was generally well tolerated by all healthy and mechanically ventilated patients.