Background

- Peritoneal dialysis is currently used by 11% of the global dialysis population with end stage renal disease
- Bacterial peritonitis is a major complication of peritoneal dialysis and is the primary reason for switching from peritoneal dialysis to hemodialysis
- Dosing in patients with peritonitis during automated peritoneal dialysis (APD) is empiric and extrapolated from pharmacokinetic (PK) studies in patients on continuous ambulatory peritoneal dialysis (CAPD)
- It is unclear if this practice would result in vancomycin under-dosing or overdosing in patients on APD

Objectives

Primary Objective
- Characterize the pharmacokinetics of vancomycin in plasma, dialysate, and urine following a single intraperitoneal dose

Secondary Objective
- Explore the safety, tolerability, and feasibility in administering vancomycin during the long dwell period in patients on APD

Methods

Study Design
- Ongoing prospective, open-label, single-center, PK study in peritonitis-negative patients receiving automated peritoneal dialysis
- Single dose vancomycin (20 mg/kg) in 1L of icodextrin solution was administered through the peritoneum and allowed to dwell for a minimum of 15 hours
- Blood for PK was obtained at 0, 6, 12, 18, and 24 hours following the initial drug-dialysate dwell, prior and following each cycle exchange, and at 48, 72, 96, 120, 144, & 168 hours post-dose. Wasted dialysate and urine were obtained and analyzed for vancomycin.
- This study was approved by the Thomas Jefferson University IRB (ClinicalTrials.gov ID: NCT03685747)

Study Schematic

- 15-hour dwell
- 9 hour on-cycler
- Home dialysis
- Dwell time sampling
- End of dwell and post-RF sampling

Study Population

- **Inclusion:** Adult male or females between 18-85 years old and stabilized on a peritoneal dialysis regimen for >3 months prior to study start
- **Exclusion:** Active peritonitis infection, previous intraperitoneal antibiotics or intravenous vancomycin treatment within 2 months, hemoglobin <9 g/dL

Bioanalytical, Pharmacokinetic, and Statistical Analysis

- Plasma vancomycin concentrations were determined using the Roche Cobas c502 assay (Roche Diagnostics, Germany). Dialysate and urine vancomycin concentrations as alternative sample types was verified for accuracy. A non-compartmental analysis was conducted (Phoenix WinNonlin Version 8, Certara) to estimate the pharmacokinetic parameters. Parameters were summarized by means and standard deviations
- Plots were generated on SPSS version 26 (IBM Corp.)

Funding and Disclosures

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Results

Patient Demographics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Race</th>
<th>Sex</th>
<th>Weight (kg)</th>
<th>Time on peritoneal dialysis (months)</th>
<th>Vancomycin dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>Black</td>
<td>Female</td>
<td>99</td>
<td>12</td>
<td>2000</td>
</tr>
<tr>
<td>42</td>
<td>Asian</td>
<td>Male</td>
<td>73</td>
<td>9</td>
<td>1500</td>
</tr>
</tbody>
</table>

Pharmacokinetic Parameters

<table>
<thead>
<tr>
<th>T_max (hrs)</th>
<th>C_max (mg/L)</th>
<th>AUC_pieri (mL/min/hour)</th>
<th>AUC_30 (mL/min/hour)</th>
<th>CL/F (mL/min)</th>
<th>V/F (L)</th>
<th>T1/2 (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>13.8</td>
<td>34.4</td>
<td>4520</td>
<td>3089</td>
<td>7.3</td>
<td>62.7</td>
</tr>
<tr>
<td>Patient 2</td>
<td>14.9</td>
<td>25.5</td>
<td>4565</td>
<td>2636</td>
<td>5.7</td>
<td>62.8</td>
</tr>
</tbody>
</table>

Dialysate PK parameters following a single IP dose

<table>
<thead>
<tr>
<th>Dwell time (hrs)</th>
<th>Transfer T1/2 (hours)</th>
<th>CL_renal (mL/min)</th>
<th>CL_APD at EOD1 (mL/min)</th>
<th>CL_APD at EOD2 (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>2.2 ±0.2</td>
<td>8.5</td>
<td>10.8</td>
<td>11.0</td>
</tr>
<tr>
<td>Patient 2</td>
<td>2.2 ±0.1</td>
<td>6.0</td>
<td>9.6</td>
<td>8.8</td>
</tr>
</tbody>
</table>

Pharmacokinetic Results

**Figure 1. Vancomycin concentration-time profiles of two patients in A) plasma and B) dialysate**

**Figure 2. Relationship between drug bioavailability and dwell time**

**Figure 3. End of drug-free dwell concentrations in plasma and dialysate**

Conclusions

- Despite the small sample size, this pilot study suggests that the dwell-time has important implications for systemic vancomycin exposure
- Vancomycin pharmacokinetics- when given at doses recommended by the International Society of Peritoneal Dialysis- were not largely altered during rapid exchanges and was well tolerated with no adverse events
- Frequent intraperitoneal doses after the initial dwell may be needed to maintain concentrations in the peritoneum above the minimum inhibitory concentration for *S. aureus* during peritonitis peritoneal dialysis (APD)