Single Ascending Dose Study of Intraperitoneal Triferic® (Ferric Pyrophosphate Citrate) in Patients on Chronic Peritoneal Dialysis

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RESULTS

Triferic IV Administration
- The PK profile of Triferic 6.6 mg Fe administered IV over 4 hours was similar to that observed in HD patients (Fig 1).
  - T max increased by 99.4 ug/dL from baseline.
  - T 1/2 was 1.84 hours
- Triferic in PD Fluid
  - The PK profile of Triferic added to PD fluid for a 12 hour dwell is presented in Fig 2.
  - T max is approximately 6.0 hr for all dose levels.
  - Approximate dose proportional increase in C max.
  - Triferic in PD show both a diffusional and a lymphatic uptake.
  - Half-life of Triferic iron is approximately 8 hr due to the ongoing lymphatic absorption.
  - Serum Fe concentration returns to baseline by ~12 hours after dwell stopped.
- Non-compartmental PK parameters in Table 1.

Triferic and Hecapid-25
- Elevated hepcidin concentrations are not affected by Triferic iron IV or via PD.
- Safety Profile
  - Triferic is well tolerated when administered via PD.

SAFETY

Dose Cohort
- 2.5 mg Fe/L: 6 6 6 6 6 29
- 5.0 mg Fe/L: 16.7 16.7 (33.3) 16.7 (3.3)
- 7.5 mg Fe/L: 16.7 16.7 (3.3)
- 12.5 mg Fe/L: 16.7 (3.3)
- IV 6.6 mg Fe/4 hr:

N Patients 6 6 6 6 6 29

Triferic 6 mg Fe IV/Hr.

Adverse Discomfort
- 16.7 (1.34)
- 16.7 (1.34)

Constipation
- 16.7 (1.34)

Nausea
- Vomiting
- 16.7 (1.34)

Grain Pain
- Headache
- 16.7 (1.34)

Dysmenorrhea

Table 1: NC PK analysis for Triferic in PD Fluid (Baseline Corrected)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Fe mg/L</th>
<th>Cmax</th>
<th>Tmax (median)</th>
<th>T1/2 (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>23.6</td>
<td>15.9</td>
<td>6.0</td>
<td>NC</td>
</tr>
<tr>
<td>5.0</td>
<td>77.5</td>
<td>17.4</td>
<td>6.0</td>
<td>9.2</td>
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<tr>
<td>7.5</td>
<td>44.6</td>
<td>31.8</td>
<td>6.0</td>
<td>3.0</td>
</tr>
<tr>
<td>12.5</td>
<td>74.6</td>
<td>40.8</td>
<td>5.0</td>
<td>8.8</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- Triferic added to PDF shows a dose dependent increase in iron transport from PD to systemic circulation.
- Two components of transport
  - Diffusion (initial rapid increase in sFe)
  - Lymphatic Absorption (extended slow increase in C max)
- Longer 1% of PDF Triferic compared to Triferic IV reflects the increased duration of exposure and two components of absorption
- High variability in the dose of iron absorbed
- No correlation with PET status
- Iodocerin seems to result in slightly lower transport

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