Population Pharmacokinetics and Pharmacokinetics/Pharmacodynamics of Etravirine in HIV-positive Children Ages 1-<6 Years

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Conflict of Interest

None to disclose
Etravirine

◊ Etravirine is an NNRTI with a high genetic barrier to the development of drug resistance mutations (approved for >6 years)

◊ IMPAACT P1090 is a Phase I/II study to determine the PK profile, optimal dosage and safety of ETR in HIV-positive children ages 1 to < 6 years old

◊ Objective: Characterize the population PK and PK/PD of etravirine in children ages 1-<6 years and to evaluate potential sources of inter-individual variability

Methods

◊ ETR weight-band based dosing as part of combination regimen, including a ritonavir-boosted PI (N=25)

◊ Swallowed whole or dispersed in liquid

◊ Intensive PK Day 7-14
  ◊ If $\text{AUC}_{12h} < 2350 \text{ ng*hr/mL}$: dose increased and intensive PK repeated
## Historical Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 - &lt; 6 years</th>
<th>6 – 17 years</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC$_{12}$, ng*hr/mL</td>
<td>4483 (75)</td>
<td>5216 (83)</td>
<td>5,501 (83)</td>
</tr>
<tr>
<td>C$_{max}$, ng/mL</td>
<td>542 (69)</td>
<td>589 (82)</td>
<td>797 (84)</td>
</tr>
<tr>
<td>C$_{last}$, ng/ml</td>
<td>320 (93)</td>
<td>346 (99)</td>
<td>393 (96)</td>
</tr>
<tr>
<td>T$_{max}$, hr</td>
<td>4 (range 1-9)</td>
<td>4 (range 1-6)</td>
<td></td>
</tr>
<tr>
<td>CL/F, L/hr</td>
<td>32 [12%, 25-39]</td>
<td>46.3 [8%]</td>
<td>43.7 [3%]</td>
</tr>
<tr>
<td>Dosage Admin on CL/F</td>
<td>-0.72</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>K$_a$, hr$^{-1}$</td>
<td>0.47 [24%, 0.25-0.70]</td>
<td>1.07 [34%]</td>
<td>0.88 [46%]</td>
</tr>
</tbody>
</table>

### Pharmacokinetic Parameters

- **AUC by Week 24 viral load**

\[ P=0.66 \]
Conclusions

- Children receiving ETR exhibit considerable inter-individual variability, similar to adults.

- Apparent oral clearance was 50% lower in those who swallowed the tablet whole.
  - Lower bioavailability and/or incomplete absorption/dosing in children taking ETR dispersed.

- PK parameters were not associated with Week 24 HIV-1 RNA load.

- This model can aid in comparisons of ETR PK parameters versus those previously reported and in ETR dose selection in this population.
Acknowledgements

We thank all of the members of the IMPAACT P1090 team for their efforts and the outstanding clinical sites for their contributions and commitment to the trial. We owe a considerable debt of gratitude to the children and families who participated in this study.