Tenofovir PK in Adults with Renal Dysfunction on LPV/r and NNRTI-based ART

Tim R. Crossley1,2, Anchalee Avihingsanon3,4, Guttiga Halue5, Prattana Leenaniramkul6, Pra-ornsuda Sukrakhanchana6, Anthony T. Podany6, Courtney V. Fletcher6, Jourdain Goujon5,8, Virat Klinikbauya6 and Chureeratana Bowonwatungru6

1NHATHLID, Faculty of Associated Medical Sciences, Chiang Mai University, Chiang Mai, Thailand, 2Department of Immunology & Infectious Diseases, Boston, Harvard School of Public Health, MA, USA, 3NHETH-Netherlands Australia Thailand (NHET) Research Collaboration, Bangkok, Thailand, 4Division of Endocrinology and Immunology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, 5Thai Army Medical Research Institute, Bangkok, Thailand, 6Faculty of Pharmacy, Chiang Mai University, Chiang Mai, Thailand, 7Cardiology Research Center, Chiang Mai University, Chiang Mai, Thailand, 8Institute of Chemistry, Namur University, Namur, Belgium, 9Department of Medical Physics and Biomedical Engineering, School of Health Science, Chiang Mai University, Chiang Mai, Thailand

Background: The recommended tenofovir disoproxil fumarate (TDF) dose is 300 mg every 48 hours in adults with normal renal function despite reduced renal function (eGFR 30-60 mL/min). The objective of this study was to explore the impact of renal function on the pharmacokinetics of TDF in this population. Pharmacokinetic parameters were compared between participants with eGFR >60 mL/min (N=35), eGFR 30-60 mL/min (N=11), and eGFR <30 mL/min (N=14). The primary outcome measure was the area under the curve (AUC) of TDF over 48 hours. The data were collected during clinic visits and were compared using ANOVA with Bonferroni correction for multiple comparisons. The median (IQR) of AUC of TDF was 11,550 (6,740-20,840), 17,150 (10,500-29,000), and 31,900 (17,150-55,550) for the three groups, respectively (p<0.05).

Objective: To compare the plasma and intracellular pharmacokinetics (PK) of TDF in 300 mg every 48 hours in HIV-infected adults with moderate renal function impairment receiving LPV/r and NNRTI-based antiretroviral therapy.

Study Design & Methods

Study Design: Data were collected within a Phase I, non-randomized, open-label, pharmacokinetic study in HIV-infected adults [ClinicalTrials.gov: NCT01741992].

Study Population: 55 adults with moderate renal impairment (eGFR 30-60 mL/min) were enrolled in the study. The demographic characteristics and baseline characteristics of the study population are presented in Table 1.

Clinical Characteristics

Table 1: Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1 (n=10)</th>
<th>Group 2 (n=15)</th>
<th>Group 3 (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36 (27-45)</td>
<td>38 (29-45)</td>
<td>37 (28-45)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>6/4</td>
<td>8/7</td>
<td>9/11</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.7 (23.0-28.8)</td>
<td>25.5 (23.0-28.0)</td>
<td>25.5 (23.0-28.0)</td>
</tr>
<tr>
<td>eGFR (mL/min)</td>
<td>52 (40-60)</td>
<td>45 (30-60)</td>
<td>35 (20-60)</td>
</tr>
</tbody>
</table>

Intracellular Tenofovir-phosphate Concentrations

Figure 2: Intracellular tenofovir-phosphate (TDF-P)-D CP in patients with moderate renal dysfunction, as part of (a) NNRTI- vs (b) LPV/r-based treatment. Boxplot represents mean and interquartile range.

Conclusion/Discussion

We observed a significantly higher tenofovir exposure among patients with moderate renal dysfunction receiving lopinavir/ritonavir compared to those receiving an NNRTI.

Acknowledgements

The authors wish to thank the participants that participated in the protocol and the staff of the participating centers. Study was supported by the Governmental Pharmaceutical Organization, Thailand.

References