Renal Function after Kidney or Liver Transplant in HIV Infected Patients using Tenofovir

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On behalf of the investigators of Solid Organ Transplantation in HIV Multi-Site Study
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Background

- TDF is a reverse transcriptase inhibitor active against HIV and hepatitis B
- Potential nephrotoxin
  - Fanconi Syndrome
  - Other mechanisms?
- Additional risk factors for nephrotoxicity
  - Concomitant nephrotoxic medications
  - Pre-existing renal disease, HTN, DM
- *HIV infected transplant recipients using TDF are potentially at high risk of renal dysfunction*
Study Aims

• To describe TDF use among HIV-infected kidney and liver transplant recipients
• To compare renal function in HIV infected kidney or liver transplant recipients who do and do not use tenofovir
  • By organ
  • By calcineurin inhibitor
  • By time of initiation of tenofovir
Study Design

- **Subjects**: Multi-center observational cohort study of HIV-infected kidney or liver transplant recipients
- **Interventions**: Antiretroviral and immunosuppressant regimens individualized
- **Measurements**: Pre- and post-transplant serum creatinine and urinary protein, blood, glucose
  - Basic demographics
  - Rejection
Analysis

• Prevalence and timing of TDF use
  • Early use = within 14 days post-transplant
• Comparison of creatinine
  1. TDF initiated within 14 days post-transplant
  2. TDF initiated after 14 days post-transplant
  3. Other Antiretrovirals
     “TDF group” limited to time on TDF and “Other ARV group” limited to time not on TDF
• By organ
• By calcineurin inhibitor
## Demographics

<table>
<thead>
<tr>
<th></th>
<th>No TDF (n=56)</th>
<th>Early TDF (n=42)</th>
<th>Late TDF (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>47 (84%)</td>
<td>37 (88%)</td>
<td>13 (93%)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>22 (39%)</td>
<td>27 (64%)</td>
<td>13 (93%)</td>
</tr>
<tr>
<td>Age - median (range)</td>
<td>43 (9-71)</td>
<td>49 (30-71)</td>
<td>46 (33-60)</td>
</tr>
</tbody>
</table>

**Hepatitis B status**
- 14 liver/1 kidney recipient Hep BsAg+
- 12 liver/4 kidney Hep B core Ab +
## Organ and Follow-Up

<table>
<thead>
<tr>
<th>Organ</th>
<th>No TDF (n=56)</th>
<th>Early TDF (n=42)</th>
<th>Late TDF (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>41</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Liver</td>
<td>13</td>
<td>29</td>
<td>9</td>
</tr>
<tr>
<td>Combined</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

### Mean # days TDF (± SE)

<table>
<thead>
<tr>
<th>Organ</th>
<th>No TDF</th>
<th>Early TDF (± SE)</th>
<th>Late TDF (± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>NA</td>
<td>244 ± 75</td>
<td>449 ± 94</td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td>333 ± 52</td>
<td>415 ± 109</td>
</tr>
</tbody>
</table>

### Mean f/u (months)

<table>
<thead>
<tr>
<th>Mean f/u (months)</th>
<th>14</th>
<th>10</th>
<th>19*</th>
</tr>
</thead>
</table>
TDF Use

• 56 of 112 (50%) HIV-infected transplant recipients used any tenofovir
  • 16/57 (28%) kidney recipients
  • 40/55 (73%) liver or liver/kidney recipients
• 42 (75%) initiated TDF prior to transplant
• 14 (25%) initiated TDF post transplant
Renal function

- No significant differences in serum creatinine or urinary protein, blood, or glucose in patients using or not using tenofovir.
- Serum creatinine did not increase over 101 days (median, range 24-377) in 5 kidney and 8 liver patients who initiated tenofovir post transplant.
Serum Creatinine After Kidney Transplantation

TDF initiated within 14 days post-transplant

“TDF group” = time on TDF
“Other ARV group” = time not on TDF
Serum Creatinine After Liver Transplantation

TDF initiated within 14 days post-transplant

“TDF group” = time on TDF
“Other ARV group” = time not on TDF
Creatinine after Kidney Transplant by Calcineurin Inhibitor

Kidney Tac

Kidney CYA
Creatinine after Liver Transplant by Calcineurin Inhibitor

Liver Tac

Liver CYA

S. Creat mg/dl

Days

Other ARV
Tenofovir

S. Creat mg/dl

Days

Other ARV
Tenofovir
Limitations and Future Analytic Plans

- Size of cohort and duration of follow-up
- GFR better measure than serum creatinine
- Future linear regression models of post-transplant GFR will include potential confounders
  - Diabetes mellitus, HTN
  - Pre-existing renal function in liver recipients
  - Rejection
  - Other nephrotoxins
Conclusions

• Tenofovir did not adversely affect renal function following liver +/- kidney transplantation during study period
  • Probably reflects careful selection of TDF recipients and monitoring of renal function by study clinicians
• Long term observation is required to establish safety of tenofovir in HIV-infected transplant recipients with various risk factors for renal insufficiency
HIVTR Participants

- UCSF
- Beth Israel Deaconess
- Georgetown
- University of Pennsylvania
- University of Virginia
- Cedars-Sinai
- University of Maryland
- Drexel
- Tulane
- Emory
- Rush
- University of Pittsburgh
- Washington Hospital Center
- Mt. Sinai
- Columbia
- University of Chicago
- University of Cincinnati
- University of Miami
- Cleveland Clinic
- Johns Hopkins
- Northwestern
- The Emmes Corporation
### Tenofovir Discontinuation

<table>
<thead>
<tr>
<th></th>
<th>Continued</th>
<th>Discontinued</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early Initiation</strong></td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td><strong>Kidney</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Late Initiation</strong></td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>Kidney</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Early Initiation</strong></td>
<td>24</td>
<td>7</td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Late Initiation</strong></td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td></td>
<td></td>
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</tbody>
</table>