**Association of tenofovir level and discontinuation due to impaired renal function**

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**Background**

Tenofovir (TFV) preparations are nucleotide reverse transcriptase inhibitors with highly antiretroviral activity used as first-line treatment in HIV-1-infected patients. Long term TFV treatment, however, is associated with a risk of renal impairment1, especially cellular damage in renal tubules. Plasma trough concentrations of TFV are high in patients with renal impairment2), but the mechanism by which high trough concentration of TFV following its long-term administration affects renal function has not been clarified.

**Patients & Methods**

**Participants**

A regimen including TFV disoproxil fumarate (TDF) was administered to 136 HIV-1-infected patients aged ≥18 years treated at the National Hospital Organization Osaka National Hospital. The association between trough concentrations of TFV and discontinuation of its administration due to renal function-related adverse events within 288 weeks after the start of therapy was measured. TFV plasma trough concentrations were measured by high-performance liquid chromatography. Use of antiretroviral agents (n, %)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n, %</th>
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<tbody>
<tr>
<td>Atazanavir/ritonavir</td>
<td>14 (41%)</td>
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<tr>
<td>Lopinavir/ritonavir</td>
<td>8 (24%)</td>
</tr>
<tr>
<td>Darunavir or Fosamprenavir/ritonavir</td>
<td>10 (29%)</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>0 (0%)</td>
</tr>
</tbody>
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AIDS(n, %) 16 (47%) 37 (36%) 0.18
HBV infection (n, %) 1 (3%) 19 (19%) 0.017
HCV infection (n, %) 1 (3%) 4 (4%) 0.63
Treatment naïve(n, %) 31 (91%) 99 (97%) 0.16

**Results**

- **TDF was discontinued due to renal function-related adverse events** in 34 patients (25%), and the median time to discontinuation was 967 days (range: 183–1986 days).
- The median trough TFV concentration was significantly higher in discontinued patients (87.5 vs 73.0 ng/mL; p = 0.0033, Fig.1).
- Trough concentrations of TFV did not correlate with time to TDF discontinuation (p = 0.29, Fig.2).
- Trough TFV concentration was significantly correlated with TFV discontinuation due to renal function-related adverse events (p = 0.0022, Fig.4).
- Construction of a receiver operating characteristic (ROC) curve showed that the cut-off value of trough TFV concentration at TDF discontinuation was 98 ng/mL (area under the curve [AUC], 0.668; sensitivity, 0.471; specificity, 0.833).

**Conclusions**

Discontinuation of long-term TDF administration due to renal function-related adverse events is associated with high trough TFV concentrations in Japanese patients infected with HIV-1. This implied the importance of early after administration TFV concentration measurement for the risk assessment of renal dysfunction in long-term administration.

**References**