Background

• Treatment with tenofovir disoproxil fumarate (TDF) has been associated with impairment of renal function in HIV-1 infected patients and may cause proximal renal tubular abnormalities and/or decreases in estimated glomerular filtration rate (eGFR).

The TAFNES study was initiated in 2016 to evaluate the real world effectiveness and safety of TAF based regimens in people living with HIV (PLHIV).

Objective

• The objective of this analysis was to evaluate the effects of elvitegravir/cobicistat/FTAF (E/C/FTAF) on renal function among the PLHIV switching from elvitegravir/cobicistat/emtricitabine/TDF (E/C/FTDF).

Materials and Methods

• TAFNES is an ongoing prospective observational clinical cohort of PLHIV initiating or switching to TAF/TDF based regimens in routine care in Germany.

PLHIV switching from E/C/FTDF (with a minimum usage of 30 days) to E/C/FTAF, with eGFR data at the time of switch, in an interim data cut dated 1 August 2018 were included in the present analysis.

• Selection of E/C/FTAF was based on clinician discretion and was in accordance with SMPC in Germany. eGFR was calculated using the CKD-EPI equation.

• Univariate analyses were performed in the subset of patients that had eGFR data at all visits from time of switch to month 12 (time of switch, months 3, 6, and 12), whereas all patients switching from E/C/FTDF to E/C/FTAF were included in multivariate analyses.

• Change within subject over time in eGFR was evaluated univariately by Wilcoxon signed-rank test.

Multivariate mixed linear models were used to evaluate change over time in eGFR with adjustment of age, gender, HIV-RNA level at time of switch, CD4 T lymphocyte count at time of switch and duration of previous E/C/FTDF use.

Analyses were performed for all patients and for subgroups of patients with eGFR at time of switch < 90 and ≥ 90 ml/min/1.73m².

Results

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE PATIENTS

• A total of 84 PLHIV were included in the present analyses, and 66 out of them had eGFR data at all visits from time of switch to month 12.

• 92.9% of all patients switched were male and median (interquartile range) age at the time of switch was 40 (34 – 52) years (Table 1).

• 94.0% had HIV RNA <50 copies/mm³ at the time of switch and 70.2% of the PLHIV had CD4 T lymphocyte count ≥500 cells/mm³ (Table 1).

• Median (IQR) time on E/C/FTDF prior to switch was 24 (12-36) months (Table 1).

• Patients with baseline eGFR 90 mL/min/1.73m² were younger and had been significantly less time on E/C/FTDF than patients with baseline eGFR <90 mL/min/1.73m² (Table 1).

ESTIMATED GLOMERULAR FILTRATION RATES

Change over time (univariate analysis)

• Median eGFR increased significantly from time of switch to month 12 (from 88.0 mL/min/1.73m² at the time of switch to 94.4 mL/min/1.73m² at month 12) (Table 2).

• In the subgroup of patients with eGFR ≥ 90 mL/min/1.73m² at the time of switch to 97.1 mL/min/1.73m² at month 12 (Figure 2).

• In the subgroup of patients with eGFR ≥ 90 mL/min/1.73m², no significant change was observed over time and eGFR remained stable over the 12 months (Figure 2).

Table 1. Demographics and medical characteristics of the patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All switched (n=84)</th>
<th>eGFR at the time of switch subgroups</th>
<th>p values*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>90 mL/min/1.73m² (n=41)</td>
<td>&lt;90 mL/min/1.73m² (n=43)</td>
<td></td>
</tr>
<tr>
<td>Gender, male, n (%)</td>
<td>78 (92.9)</td>
<td>37 (86.0)</td>
<td>0.374</td>
</tr>
<tr>
<td>Age (years), median (IQR)</td>
<td>40 (34 – 52)</td>
<td>38 (33 – 45)</td>
<td>0.014</td>
</tr>
<tr>
<td>CD4 T-lymphocyte count, cells/mm³, median (IQR)</td>
<td>641 (476 – 888)</td>
<td>565 (472 – 851)</td>
<td>0.437</td>
</tr>
<tr>
<td>CD4 T-lymphocyte &lt;500 cells/mm³, n (%)</td>
<td>59 (70.2)</td>
<td>27 (63.0)</td>
<td>0.714</td>
</tr>
<tr>
<td>HIV RNA &lt;50 copies/mm³, n (%)</td>
<td>79 (94.4)</td>
<td>68 (92.9)</td>
<td>0.437</td>
</tr>
<tr>
<td>Previous E/C/FTDF usage duration, months, median (IQR)</td>
<td>24 (12 – 36)</td>
<td>24 (12 – 36)</td>
<td>0.034</td>
</tr>
<tr>
<td>At the time of diagnosis CD4 T-lymphocyte &gt;500 cells/mm³, n (%)</td>
<td>24 (28.6)</td>
<td>4 (13.2)</td>
<td>0.162</td>
</tr>
<tr>
<td>CD4 T-lymphocyte &gt;200 cells/mm³, n (%)</td>
<td>20 (23.8)</td>
<td>3 (11.1)</td>
<td>0.162</td>
</tr>
</tbody>
</table>

Results (cont’d)

eGFR stages

• The percentage of patients with normal eGFR increased from 42.4% at the time of switch to 62.1% at month 12 with an increase of 19.7% (Figure 1).

• The percentage of patients with moderately to severely decreased eGFR declined from 9.1% at the time of switch to 3.0% at month 12 with a decrease of 6.1% (Figure 1).

Figure 1. Stages of estimated glomerular filtration rates over time in patients with data from the time of switch to month 12

Figure 2. Adjusted predicted eGFR over time

Predicted values were calculated by using the following formulas and based on mean age (years) and mean duration of previous TDF usage (years) by subgroup

- eGFR = 121.2 + 0.5364 * (months on TAF) – 0.6742 * Age – 1.7212 * (TDF usage) (years)
- eGFR = 104.4 + 0.2058 * (months on TAF) – 0.0884 * Age + 0.0233 * (TDF usage) (years)
- eGFR = 100.4 + 0.0584 * (months on TAF) + 0.7516 * Age – 0.0374 * (TDF usage) (years)
- eGFR = 100.2 (no TAF or TDF usage) (years)
- eGFR: estimated glomerular filtration rate
- TDF: tenofovir disoproxil fumarate
- TAF: tenofovir alafenamide
- TAFNES: Tenofovir Alafenamide Nephrotoxicity Study

Conclusions

This clinical cohort demonstrated an improvement in eGFR in patients switching from E/C/FTDF to E/C/FTAF, with a significant increase in estimated glomerular filtration rate and an increase in the percentage of patients with normal renal function from time of switch to month 12.

References
