TDF/3TC/EFV regimen-related renal and neuropsychiatric toxicity in Vietnam HIV-infected patients

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Objectives

- TDF/3TC/EFV is recommended as a first-line regimen for naïve HIV-infected patients by WHO.
- Limited data on EFV-associated neuropsychiatric adverse effects and TDF-associated renal dysfunction in low body weight patients.

1. To determine the incidence of neuropsychiatric and renal adverse events of TDF/3TC/EFV regimen.
2. To identify possible risk factors associated with adverse effects
Methods

Study design: a prospective cohort study including HIV-infected patients in 10 clinics in 7 cities in Vietnam from 16/3/2015 to 15/7/2016

Inclusion:
- age $\geq 18$ years old
- antiretroviral naivety
- initiation of ARV between 16/3/2015 and 15/1/2016
- non-pregnant during monitoring period.

Exclusion:
- EFV cohort:
  - No follow-up visits.
- TDF cohort:
  - Missing baseline weight or serum creatinine
  - No data on follow-up serum creatinine results
Methods

Basic demographic data and baseline laboratory parameters were recorded within 90 days prior to initiation of ART.

Adverse effects were monitored and reported by trained healthcare professionals at clinics.
- EFV-related neuropsychiatric disorders: by interviewing patients
- TDF-related renal toxicity: defined as a 25% decline in CrCl from the baseline level by follow-up body weight and serum creatinine.
Methods

Statistical analysis

Statistical analyses were performed by the RStudio.

Risk factors identification: multivariate analyses by Bayesian Information Criterion (BIC) to find the most appropriate model

The Predictive Mean Matching (PMM) method was used to deal with missing values of continuous variates.
Results

Included subjects: **841**

- **EFV cohort**
  - Evaluated obs. **838**
  - No return: 3

- **TDF cohort**
  - Evaluated obs. **539**
  - Lack of baseline / follow up serum creatinine data: 302
## Results

### Baseline characteristics and laboratory investigations

<table>
<thead>
<tr>
<th></th>
<th>EFV cohort</th>
<th>TDF cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>838 (100.0)</td>
<td>539 (100.0)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>33 (29, 38)</td>
<td>34 (29, 39)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Male 561 (66.9)</td>
<td>Male 365 (67.7)</td>
</tr>
<tr>
<td></td>
<td>Female 277 (33.1)</td>
<td>Female 174 (32.3)</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>53 (48, 59)</td>
<td>53 (48, 59)</td>
</tr>
<tr>
<td><strong>CrCl</strong></td>
<td>86.0 (72.5-101.0)</td>
<td>86 (72-102)</td>
</tr>
<tr>
<td><strong>Follow-up time, months</strong></td>
<td>10.4 (7.9-12.8)</td>
<td>11.1 (8.7-13.0)</td>
</tr>
</tbody>
</table>
Results

Neuropsychiatric adverse events:
- 38.7% (324 patients) experienced psychiatric disorders
- 94.5% experienced AEs in the first month of treatment
- 76.9% experienced only mild or moderate symptoms
- Most common: dizziness, headache and fatigue (>50.3%)
Results

Renal dysfunction events

- Median (IQR) of monitoring: 11.1 (8.7-13.0) months.
- 78 (14.5%) patients had a 25% decrease in CrCl.

Serverity

- Normal: 76.92%
- 1 - 1.5 ULN: 19.23%
- 1.5 - 3.0 ULN: 3.85%

Adjusted HR TDF-related events with CI 95%
Results

Multivariate logistic analysis

- Risk of Adverse events
- Age
- Weight
- Creatinin
- Hb
- CD4
- Gender
- Clinical stage
- ALT

Processed missing values: ALT, CD4, Hb.
# Results

## Multivariate logistic analysis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>HR (CI 95%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EFV cohort</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (per 10kg)</td>
<td>0.822 (0.686– 0.959)</td>
<td>0.011</td>
</tr>
<tr>
<td>Hb (per 1g/dL)</td>
<td>1.111 (1.055-1.168)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>1.218 (1.076-1.363)</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>TDF cohort</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb (per 1g/dL)</td>
<td>0.846 (0.745 – 0.948)</td>
<td>0.003</td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>1.363 (1.062 – 1.672)</td>
<td>0.018</td>
</tr>
<tr>
<td>CrCl (per 10ml/min)</td>
<td>1.177 (1.140 – 1.214)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Conclusions

324 (38.7%) patients experiencing neuropsychiatric adverse events.

- Appear mainly in the first month of initiation (94.5%).
- Most of the adverse effects were mild; Dizziness, headache and fatigue was the most common

78 (14.5%) patients had renal dysfunction.

- creatinine level remain normal in 60 (76.9%)

Risk factors:

**Neuropsychiatric toxicity**
- higher age
- lower weight
- higher baseline hemoglobin

**Renal dysfunction**
- higher age
- higher baseline CrCL
- Lower baseline hemoglobin
Thank you, questions?