Detection of NNRTI resistance mutations after interrupting NNRTI-based regimens

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on behalf of UK HIV Drug Resistance Database & UK CHIC study.


BACKGROUND

There is evidence that NNRTI mutants emerge after interruption of suppressive NNRTI-based ART, due to the long half-life of NNRTIs. This has implications for both treatment options for people undergoing ART interruption and potential transmission of drug resistance.

The aim of this study was to quantify the extent to which NNRTI resistance mutations can be detected in the rebound viremia following interruption of suppressive NNRTI-based ART.

METHODS

The study population comprised patients from the UK HIV Drug Resistance Database and from the UK Collaborative HIV Cohort study (UK CHIC).

Figure 1 illustrates the eligibility criteria and the size of the population eligible for the analysis.

RESULTS

Among the 208 individuals with a resistance test performed after stopping suppressive NNRTI-based ART (see characteristics in Table 1), 12% (n=25, 95% CI: 8%-17%) had 31 NNRTI resistance mutations detected at the first resistance test following ART interruption.

In those with at least 1 NNRTI resistance mutation detected, the median time between TI and the resistance test was 12 months (IQR: 3-20 months).

The distribution of NNRTI resistance mutations, when detected after TI interruption is illustrated in Figure 2. K103N was the most prevalent mutation. There was no occurrence of K101P/H, V106M, Y181V, Y181C/H or G190S.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Male</th>
<th>≤ 50 copies/ml</th>
<th>Patients with a resistance test after TI (white off-ART)</th>
</tr>
</thead>
<tbody>
<tr>
<td>yes</td>
<td>136 (69%)</td>
<td>1001 (70%)</td>
</tr>
<tr>
<td>no</td>
<td>136 (65%)</td>
<td>1009 (70%)</td>
</tr>
</tbody>
</table>

Table 2. NNRTI resistance mutations

<table>
<thead>
<tr>
<th>ARV</th>
<th>All eligible patients (n=1,636)</th>
<th>Patients with a resistance test after TI (white off-ART)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVP</td>
<td>1,459 (89%)</td>
<td>994 (60%)</td>
</tr>
<tr>
<td>D4T/TDF</td>
<td>1,276 (78%)</td>
<td>829 (49%)</td>
</tr>
<tr>
<td>EFV</td>
<td>744 (45%)</td>
<td>453 (27%)</td>
</tr>
<tr>
<td>ABC</td>
<td>652 (40%)</td>
<td>406 (24%)</td>
</tr>
</tbody>
</table>

Sensitivity analysis

1. Patients who stopped their ART regimen while having a VL ≤ 50 copies/ml (n=1,241, 87%) with a resistance test after TI (172/412, 12%):

- 12% (20%; 95% CI: 7-17%) had NNRTI resistance

2. People who had a resistance test performed within 2 months since TI (n=55/208, 26%):

- 7% (4%; 95% CI: 3-19%) had NNRTI resistance

3. People who had a resistance test performed within 6 months after TI (n=94/208, 46%):

- 9% (8%; 95% CI: 4-17%) had NNRTI resistance

4. Simultaneous TI, with resistance test (n=188):

- 12% (23%; 95% CI: 7-17%) had NNRTI resistance

5. Staggered TI, with resistance test (n=20):

- 10% (2%; 95% CI: 3-12%) had NNRTI resistance

CONCLUSIONS

- To our knowledge this is the largest study to evaluate the detection of NNRTI resistance in the rebound viremia that follows interruption of a suppressive NNRTI-based regimen.

- It confirms that resistance is a relatively common phenomenon, occurring in 12% of patients tested.

- These estimates support the concept that interruption of EFV or NVP based ART carries a significant risk to the patient and informs models that incorporate HIV drug resistance emergence and transmission.