Effect of Switching to Integrase Inhibitor on the HIV Reservoir in Ileum Biopsies


Introduction

Antiretroviral therapy switching towards newer drugs is a potential strategy to impact the HIV reservoir.

A previous study suggested that switching to raltegravir might be associated with a decrease in total HIV-1 reservoir in blood after 48 weeks.

However, the effect of integrase inhibitors on the HIV reservoir in tissues remain unknown.

Thus, the aim of this study was to evaluate the effect of switching from protease inhibitor (PI)- to dolutegravir (DTG)-based cART regimen on the HIV reservoir size in blood and ileum biopsies.

Methods

Study

Substudy from INDOOR study (EUDRACT 2014-004331-39), phase IV, randomized and opened clinical trial.

Cohort: 44 ART-naive HIV-1 infected subjects were randomly included in:

- Switch group (n=22): PI-based regimen was switched to DTG-based regimen
- Control group (n=20): maintained PI-based regimen during the study

Sample collection

We collected 4-8 endoscopic ileum biopsies and blood samples at weeks 0 and 24 from 33 subjects:

- Switch group (n=13)
- Control group (n=20)

LPL-vDNA protocol: biopsy processing and proviral reservoir quantification (Fig. 2).

We performed a DTT/EDTA-based treatment for epithelial layer removal followed by disruption of the tissue in absence of an enzymatic method to obtain the lamina propria leukocytes (LPL) cell suspension, as we previously described2.

Total HIV DNA was measured by droplet digital PCR (ddPCR), as we previously described3,4, at weeks 0 and 24. Shortly, ddPCR from PBMC and LPL cell lysed extracts, to estimate the size of the proviral reservoir.

In addition, we performed a LPL-vDNA protocol: biopsy processing and proviral reservoir quantification (Fig. 2).

Figure 2. Diagram of LPL-vDNA protocol (Morón-López S. et al. 2017 PLoS One).

Results

We did not observe significant longitudinal changes in the total HIV reservoir size, either in CD4⁺ T cells or PBMC.

Table 1. Clinical characteristics of trial participants.

<table>
<thead>
<tr>
<th>HIV group risk, n(%)</th>
<th>Male</th>
<th>Female</th>
</tr>
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<tbody>
<tr>
<td>IDU</td>
<td>12(60)</td>
<td>8(40)</td>
</tr>
<tr>
<td>Unknown</td>
<td>12(58)</td>
<td>18(82)</td>
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<table>
<thead>
<tr>
<th>Total HIV reservoir size (median [IQR])</th>
<th>Swtch group</th>
<th>Control group</th>
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<tr>
<td>CD45⁺ T cells, cell/ul (median [IQR])</td>
<td>204 [95-259]</td>
<td>192 [72-249]</td>
</tr>
<tr>
<td>Time since current PI-based ART initiation, years (median [IQR])</td>
<td>19.9 [14.5-25.5]</td>
<td>41.7 [35.8-47.7]</td>
</tr>
<tr>
<td>Time since ART initiation, years (median [IQR])</td>
<td>12 [5.3-18]</td>
<td>670 [605-890]</td>
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</table>

The INDOOR study evaluated for the first time changes in the HIV reservoir size in ileum biopsies in individuals switched from PI- to DTG-based cART.

This treatment switch was safe and well tolerated, but had no impact on the HIV reservoir size, measured as total HIV DNA, in CD4⁺ T cells of ileum.

Conclusions

- The INDOOR study evaluated for the first time changes in the HIV reservoir size in ileum biopsies in individuals switched from PI- to DTG-based cART.
- This treatment switch was safe and well tolerated, but had no Impact on the HIV reservoir size, measured as total HIV DNA, in CD4⁺ T cells of ileum.

References


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Figure 3. Association of total HIV reservoir in ileum leukocytes (LPL) and PBMC from the switch group (n=13) and the control group (n=20).

Figure 4. Comparison of total HIV reservoir in ileum leukocytes (LPL) and PBMC from the switch group (n=13) and the control group (n=20).

Figure 5. Longitudinal follow up of total HIV reservoir in ileum leukocytes (LPL) and PBMC from the switch group (n=13) and the control group (n=20).

FUTURE WORK

- Evaluation of HIV persistence markers in peripheral CD4⁺ T cells and plasma.
- Evaluation of immune activation and exhaustion markers in PBMC, and inflammation markers in plasma.

Appendix:

- Antiretroviral therapy switching towards newer drugs is a potential strategy to impact the HIV reservoir.

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