Variation L at codon 214 of the HIV-1 reverse transcriptase is antagonist to thymidine analogue-containing CART regimens than variant 214F if TAM types are concomitantly detected

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BACKGROUND
Previous reports have shown that polymorphism 214L is found in around 20% of patients' virus populations with similar frequency of detection in antiretroviral-naive and treated patients. However, it was observed a positive association between polymorphism 214L and mutations of the thymidine analogue nucleoside reverse transcriptase inhibitors (TAMs) type 2 profile (e.g. 65R, 74V, 210W) and, vice versa, a negative association between polymorphism 214L and mutations of the TAMs profile (e.g. 215Y, 219Q). In vitro studies (Sturmer et al., AAC 2003;47:54-61) have shown that TAMs 1 are in salmon; TAMs 2 in cyan; NNRTI resistance mutations in blue; novel mutations/ patterns of mutations in the RT region.

RESULTS
The table below shows the proportion of 214L frequency in the classifiable patients' virus populations and in the variable 214F.

<table>
<thead>
<tr>
<th>Variant at codon 214 of RT</th>
<th>Pre-treated patients</th>
<th>All patients</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>214L</td>
<td>25%</td>
<td>21%</td>
<td>0.04</td>
</tr>
<tr>
<td>214F</td>
<td>8%</td>
<td>9%</td>
<td>0.82</td>
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</table>

In pre-treated patients, the median number of antiretrovirals previously used was 4 (range: 1-11). These included: zidovudine (26%), indinavir (12%), saquinavir (1%), ritonavir (39%), saquinavir SG (16%), enfuvirtide (0%), nevirapine (3%), indinavir (3%), amphotericin (2%), nevirapine (0%), tenofovir (2%), lopinavir (7%) and others (9%).

In order to test this hypothesis, we evaluated the virological response to thymidine analogue-containing CART regimens according to a number of mutations patterns including TAMs and the variant 214F at week 24.

CONCLUSIONS
Our study confirms that polymorphism 214L tends to cluster with mutations of TAM2 profile while it is rarely associated with mutations of the TAM1 profile. This could be due to the fact that the enzyme of virus populations carrying TAM1 profile is more likely to be detected if a mutation of the TAM1 profile is concomitantly detected; vice-versa it is less likely to be detected if a mutation of the TAM1 profile is detected. An agnostic interaction between polymorphism 214L and mutations 210W and 215Y was also found (Table 3). Results were similar when we repeated the analysis using only patients who had been exposed to ART before starting the thymidine analogue-containing regimen (Table 4).

The overall week 24 virological response from pre-therapy levels and the viral load reductions in sub-groups. A Kaplan-Meier approach was used to estimate the overall week 24 viral load change from pre-therapy levels and the viral load reductions in sub-groups.

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