HIV neutralizing antibody titer during structured treatment interruption of highly active antiretroviral therapy

In a recent article, McLinden et al. [1] analysed the impact of neutralizing antibodies (NtAb) on CD4 T-cell count and viral load in a cohort of 50 HIV-infected patients who underwent structured treatment interruption (STI). The authors examined the neutralizing capacity of individual patient plasma taken at the time of treatment interruption against a panel of four heterologous subtype B primary isolates; high-titer, heterologous HIV-1 NtAb response was associated with a reduction in HIV-1 viral load in individuals possessing a more extensive neutralization phenotype, whereas there appeared to be minimal impact on CD4 T-cell decline, and no association with slower disease progression.

We previously described a CD4-guided STI in 62 patients with sustained viroimmunological response to antiretroviral therapy (persistently CD4 >500 cells/μl and HIV-RNA <50 copies/ml) after 24 months of highly active antiretroviral therapy and no previous AIDS-defining illness [2]. The criteria for restart therapy included a CD4 cell count of 350 cells/μl or less, a plasma HIV-1 RNA level more than 5.50 log10 copies/ml, the voluntary decision of the participant and the development of an AIDS-defining illness or any acute severe clinical event during the study [2].

Among the 62 recruited patients during STI, we report longitudinal data on NtAb titer against an heterologous primary isolate (HIV-1c23d, a CCR5 tropic, antiretroviral mutations-free isolate from an antiretroviral-naive patient) in 56 patients and against the respective autologous primary isolate in nine patients. The titer of NtAb was determined by a microculture neutralization assay as previously described [3]. A significant increase (≥ four-fold geometric mean) in the NtAb titer during STI was reported only when the HIV autologous primary isolate was tested against own patient's sera (Table 1) (χ² test, P = 0.01). There was a concordance in the increasing NtAb titer during STI against both autologous and heterologous isolates in only one individual. In the six patients with increasing NtAb titer against heterologous and/or autologous primary isolates, no difference in term of clinical progression, nadir and baseline CD4 cell count, CD4 cell count at NtAb titration and of virological parameters was reported all over the STI. Similarly, no difference was reported in the R5 tropism of the primary isolate in the two groups. Nevertheless, the duration of STI was significantly longer in the patients with increasing NtAb titer compared to the patients with stable or decreasing NtAb (375 ± 252 days versus 179 ± 174 days, P = 0.01 at analysis of variance).

In conclusion, the weak NtAb impact on the clinical and immunological response during STI, reported in the recent article by McLinden et al. [1], could be underestimated in consideration of the virus neutralization assay that they used. The panel of four heterologous subtype B primary isolates should be integrated with the NtAb titer determination against the autologous primary isolate. This could provide additional complementary information on the pathways that the virus use to escape the autologous unpertective immunological response.

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Conflicts of interest

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References


Table 1. Neutralizing antibodies titer determination over time against heterologous and autologous primary isolates.

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<thead>
<tr>
<th></th>
<th>Increasing NtAb titer</th>
<th>Unchanged or reduced NtAb titer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous isolate</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Heterologous isolate</td>
<td>4</td>
<td>52</td>
</tr>
</tbody>
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NtAb, neutralizing antibodies.

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