HIV Controllers Maintain Viral Suppression despite Waning T Cell Responses on ART

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Abstract

Background: Robust HIV-specific T cell responses are a hallmark of HIV control (HC). We studied the impact of antiretroviral therapy (ART) on HIV-specific T cell responses and the ability of HC’s to maintain viral suppression after discontinuation of ART.

Methods: A5308 is a prospective, open-label study of raltegravir, emtricitabine and tenofovir disoproxil fumarate (RTV/ETV/TDF) in ART-naive or experienced (≤50 VL copies/mL) people, for 24 weeks of ART, and every 12 weeks thereafter. Outcomes were evaluated by repeated measures GEE models. Analyses included people from HC’s in the U.S. and Europe with or without LC-SCLP evaluations after ART discontinuation.

Results: The HC’s (n=120) underwent 30 cycles of ART and were analyzed (in 6 stages) ART higher rates of HIV-specific CD4+ and CD8+ T cell responses were associated with undetectable VL. During the entire study period, 5 ART cycles of ART were analyzed. At each timepoint, the proportion of people with ≥50% viral suppression was 60% to 65% at 24 weeks of ART. HIV-specific CD4+ T cells expressing IFN-γ ≥100 copies/mL were detected in 32% at baseline (84% confidence interval 28%, 37%, 44% to 55%, 50% to 61%, 57% to 72%, and 64% to 77%). CD8+ T cells expressing IFN-γ ≥100 copies/mL were detected in 31% at baseline (77% confidence interval 27%, 42%, 56% to 67%, 72% to 81%, and 76% to 84%). These data are consistent with results from previous studies. By 24 weeks of ART, ART-naive or experienced people who had ≥50% viral suppression had significantly higher levels of HIV-specific CD4+ and CD8+ T cell responses. These HIV-specific CD4+ and CD8+ T cell responses were detected in ≥70% of people with ≥50% viral suppression and ≥60% of people with ≥30% viral suppression. A trend toward the ability of ≥70% of people with ≥50% viral suppression and ≥60% of people with ≥30% viral suppression to maintain ≥70% viral suppression was observed.

Conclusions: ART significantly reduces both HIV-specific CD4+ and CD8+ T cell responses in HC’s. ART has not adversely affect control status as HIV controllers maintained a low viral load after ART discontinuation.

Background

HIV controllers (HCs) are able to suppress plasma viremia spontaneously, i.e. in the absence of ART, and robust HIV-specific T cell responses are characteristics of HCs.

Current guidelines recommend ART in all people after diagnosis of HIV infection, including in HCs.

Objectives

1. Analyze changes in CD4+ and CD8+ T cell responses on RTV/ETV/TDF in ART-naive HCs.
2. Determine whether HCs are able to control viral replication after cessation of ART.

Methods

Study Design

A5308 is a prospective, open-label study of RTV/ETV/TDF in ART-naive HCs.

HIV-specific T cell responses were monitored in ART-naive HCs. The study population included people with or without baseline LC-SCLP evaluations. ART was started at 0 weeks of ART, and every 12 weeks thereafter. Outcomes were evaluated by repeated measures GEE models. Analyses included people from HC’s in the U.S. and Europe with or without LC-SCLP evaluations after ART discontinuation.

Results

HC’s (n=120) underwent 30 cycles of ART and were analyzed (in 6 stages) ART higher rates of HIV-specific CD4+ and CD8+ T cell responses were associated with undetectable VL. During the entire study period, 5 ART cycles of ART were analyzed. At each timepoint, the proportion of people with ≥50% viral suppression was 60% to 65% at 24 weeks of ART. HIV-specific CD4+ T cells expressing IFN-γ ≥100 copies/mL were detected in 32% at baseline (84% confidence interval 28%, 37%, 44% to 55%, 50% to 61%, 57% to 72%, and 64% to 77%). CD8+ T cells expressing IFN-γ ≥100 copies/mL were detected in 31% at baseline (77% confidence interval 27%, 42%, 56% to 67%, 72% to 81%, and 76% to 84%). These data are consistent with results from previous studies. By 24 weeks of ART, ART-naive or experienced people who had ≥50% viral suppression had significantly higher levels of HIV-specific CD4+ and CD8+ T cell responses. These HIV-specific CD4+ and CD8+ T cell responses were detected in ≥70% of people with ≥50% viral suppression and ≥60% of people with ≥30% viral suppression. A trend toward the ability of ≥70% of people with ≥50% viral suppression and ≥60% of people with ≥30% viral suppression to maintain ≥70% viral suppression was observed.

Conclusions: ART significantly reduces both HIV-specific CD4+ and CD8+ T cell responses in HC’s. ART has not adversely affect control status as HIV controllers maintained a low viral load after ART discontinuation.

Results

Study A

In the first 6 cycles of RTV/ETV/TDF, people in ART had ≥50% viral suppression and ≥60% of people had ≥70% viral suppression. The proportion of people with ≥50% viral suppression and ≥60% of people with ≥70% viral suppression remained stable throughout the study. The proportion of people with ≥50% viral suppression and ≥60% of people with ≥70% viral suppression remained stable throughout the study.

Study B

Overall, 30 cycles of ART were used. The proportion of people with ≥50% viral suppression and ≥60% of people with ≥70% viral suppression remained stable throughout the study. The proportion of people with ≥50% viral suppression and ≥60% of people with ≥70% viral suppression remained stable throughout the study.

Study C

Overall, 30 cycles of ART were used. The proportion of people with ≥50% viral suppression and ≥60% of people with ≥70% viral suppression remained stable throughout the study. The proportion of people with ≥50% viral suppression and ≥60% of people with ≥70% viral suppression remained stable throughout the study.

Table 1: Participant Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>AS686</th>
<th>Participants from SCOPE (N=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>43%</td>
<td>5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>41</td>
<td>54</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td>4%</td>
<td>54</td>
</tr>
<tr>
<td>Hispanic (%)</td>
<td>17%</td>
<td>54</td>
</tr>
<tr>
<td>HIV suppression at entry</td>
<td>37%</td>
<td>54</td>
</tr>
<tr>
<td>HIV suppression at week 24</td>
<td>37%</td>
<td>54</td>
</tr>
<tr>
<td>HIV suppression at week 36</td>
<td>37%</td>
<td>54</td>
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*Note: *p* value greater than 0.05 in AS686 and ≤0.05 in SCOPE

Table 2: Changes in CD4+ and CD8+ T Cell Responses on Antiretroviral Therapy

<table>
<thead>
<tr>
<th>Artifical Intelligence (AI)</th>
<th>HIV Controllers (HCs)</th>
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<tr>
<td>CD4+ and CD8+ T cell responses in HC’s are Waning During ART (Figure 2)</td>
<td>Thirty-five HC’s in A5308 completed 24 weeks of RTV/ETV/TDF treatment</td>
<td>After 24-48 weeks of ART, significant decreases in a broad range of HIV-specific CD4+ and CD8+ T cell responses were observed.</td>
<td>CD4+ and T cell responses at baseline after 24 weeks of ART.</td>
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<td><em>p</em> values from repeated measures GEE models are shown.</td>
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Acknowledgments

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