**Characterization of the HIV-1 Transcription Profile after Romidepsin Therapy in vivo**

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**Introduction**

Antiretroviral therapy (ART) cannot eliminate the HIV genomes integrated in latently infected cells, which are a major barrier to cure HIV [1-3]. One strategy to eradicate HIV consists of reactivating viral transcription with latency-reversing agents (LRAs), such as histone deacetylase inhibitors (HDACi).

A recent clinical trial, REDUC part B, analyzed the administration of the therapeutic HIV vaccine Vacc-4x and rhuGM-CSF as local adjuvant, in combination with the latency-reversing agents (LRAs), such as histone deacetylase inhibitors (HDACi). This approach showed an increase in unspliced cell-associated HIV vaccine Vacc-4x and rhuGM-CSF as local adjuvant, in combination with the latency-reversing agents (LRAs), such as histone deacetylase inhibitors (HDACi). However, the mechanism by which romidepsin reverses HIV latency in vivo remains unclear.

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**Results**

Romidepsin increases read-through, total, elongated, and polyadenylated but not multiply-spliced transcripts

Detection of different TAR sequences after romidepsin

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**Conclusions**

1. After romidepsin infusions, we observed:
   - Reactivation of transcriptionally silent proviruses (Fig. 5).
   - An increase in HIV transcriptional initiation and especially elongation, but not completion or multiple splicing (Fig. 3-4).
   - An inverse correlation between time to rebound after AT1 and levels of both total HIV DNA and elongated HIV RNA (Fig. 5).

2. Romidepsin may play a role in strategies to reverse latency, but new approaches are needed to increase HIV transcriptional completion and multiple splicing, which are likely necessary for productive infection and immune recognition/killing of HIV-infected cells.

3. Therapies that increase HIV transcription but do not lead to lethal infections may actually shorten time to rebound after ART.

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**Limitations**

1. The parent study had sequential study interventions (vaccination and then romidepsin), and we did not have access to samples between vaccination and romidepsin.
2. Samples were available from only 9 of 17 total participants, of whom 2 had an increase in viral load after romidepsin.
3. The presence of novel subtypes may have affected viral levels and detection frequencies.

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**References**


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