Functional T-Cell Responses and Prolonged HIV Control After Treatment Interruption

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AIM

This study aimed to investigate the association between pre-ATI HIV-specific T cell functionality and viral rebound following an analytical HIV treatment interruption.

METHODS

We pooled data from six different HIV cure trials (n=91) and analyzed pre-ATI blood samples using Nef, Gag and Pol-specific IFN-γ and granzyme B ELISpot and lymphocyte proliferation assay.

Outcome definitions

- Time to detectable viremia: Days from ART interruption to first measurement of >50 copies of HIV RNA per mL.
- Time to loss of virologic control: Days from ART interruption to two consecutive measurements of >1000 copies of HIV RNA per mL or ART restart.

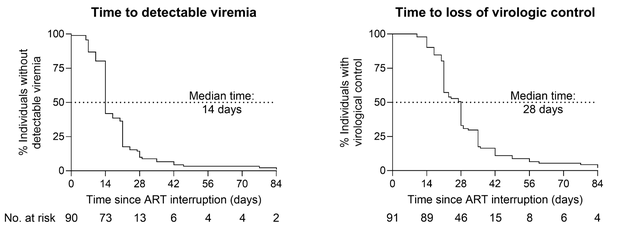


Figure 1, Kaplan-Meier curves showing percent individuals without detectable viremia and virological control, resp.

Participant characteristics		
Age at inclusion, years	45	(22–68)
Female	9	(10%)
Race and ethnicity		
Asian	3	(3%)
Black or African	11	(12%)
White	74	(81%)
Other or more than 1 race	2	(2%)
Unknown	1	(1%)
Intervention		
ART only	14	(15%)
HDACi	37	(41%)
TLR9 agonist	19	(21%)
bNAb during ART	10	(11%)
bNAb resistant at ART initiation	5	(5%)
bNAb sensitive at ART initiation	6	(7%)
Time from diagnosis to ART, years	1	(0–25)
Time from ART to baseline, years	6	(1–24)

High Gag-specific IFN-γ ELISpot and CD8⁺ T-cell proliferation responses prior to HIV treatment interruption are associated with prolonged virological control

RESULTS

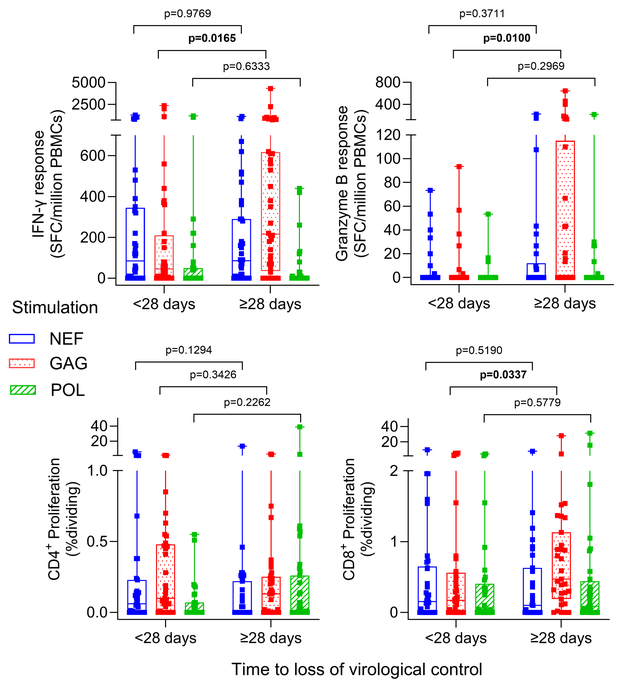


Figure 2, peptide-specific IFN-γ and granzyme B response and CD4⁺ and CD8⁺ T cell proliferative responses stratified based on median time to loss of virological control. Box-and-whisker plots show median values (center line), 25th to 75th percentiles (box outline), and the range of values (whiskers). P values were calculated using Mann-Whitney test.

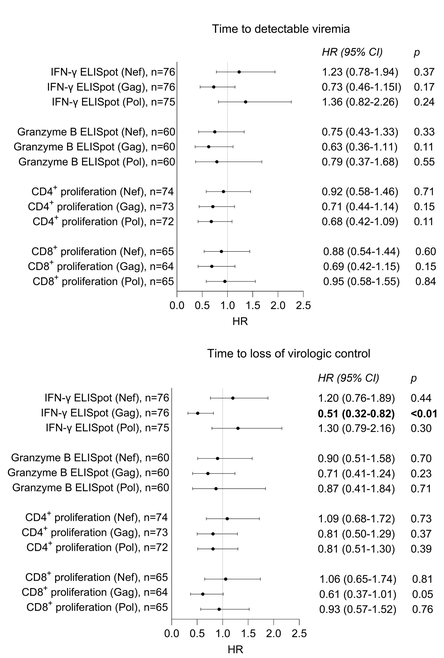


Figure 3, forest plot showing univariable cox proportional hazards regression for time to detectable viremia and time to loss of virologic control. Lymphocyte proliferation and ELISpot results are stratified into above-median or below-median (ref.).

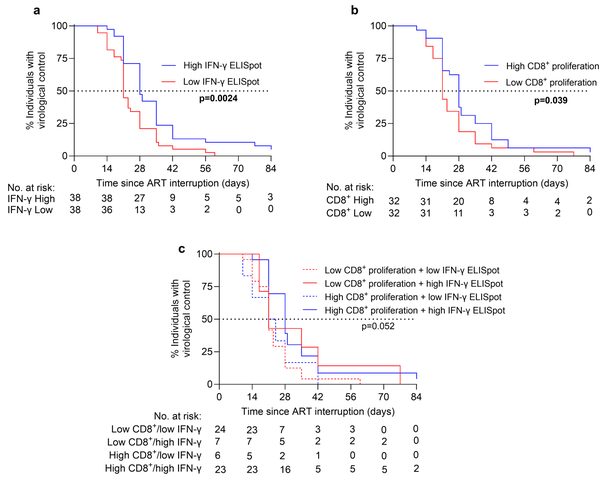


Figure 4, Kaplan-Meier curves comparing high (≥median) and low (<median) Gag-specific IFN-γ and CD8⁺ proliferative responders time to loss of virological control individually and in combination. P values were calculated using logrank test.

CONCLUSIONS

This study shows that Gag-specific IFN-γ response and CD8⁺ proliferation is associated with virologic control, but not initial viremia following HIV treatment interruption. These findings can potentially aid in development of future interventions targeting immunological HIV control, as well as understanding the immunological mechanisms underlying post-treatment control.

PLAIN LANGUAGE SUMMARY

People with stronger HIV-specific CD8⁺ T-cell responses before stopping treatment were more likely to keep the virus under control afterward, suggesting that these immune signals could help identify who might safely pause HIV therapy in cure-related studies.

CONTACT INFORMATION/ACKNOWLEDGEMENTS



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