HIV RESERVOIR REDUCTION IN PWH RECEIVING ART AND DASATINIB

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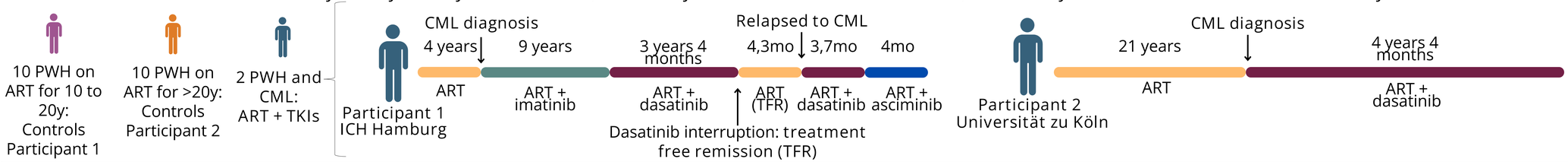
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BACKGROUND

- Tyrosine Kinase Inhibitors (TKIs) interfere with formation and replenishment of HIV reservoir by preserving SAMHD1 antiviral activity in CD4+ T cells, inducing the proliferation of cytotoxic cells populations and interfering with homeostatic proliferation and TCR-mediated activation of CD4+ T cells.
- We analyzed the reservoir composition and competency in two people with HIV (PWH) on antiretrovirals (ART) over 4 years of treatment with dasatinib.

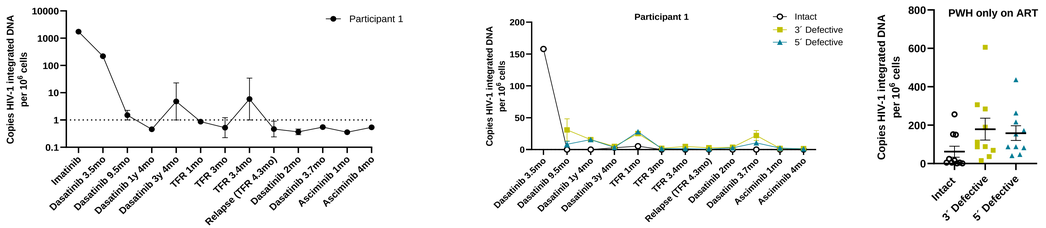
MATERIAL AND METHODS

Two Caucasian males with HIV-1 infection and CML were recruited. Blood samples were drawn periodically since 2019. Integrated provirus was measured in PBMCs by Alu-PCR and intact and defective proviruses by IPDA. Provirus reactivation was measured by flow cytometry in CD4+ T cells, after 5-day activation with CD3/CD28 + IL-2, followed by 16-18h activation with PMA + Ionomycin.

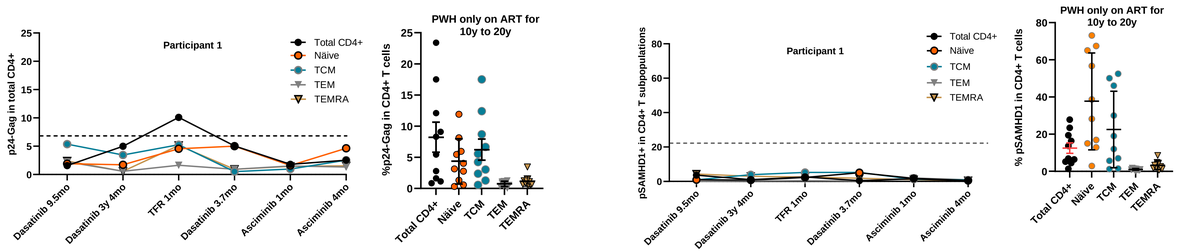


RESULTS

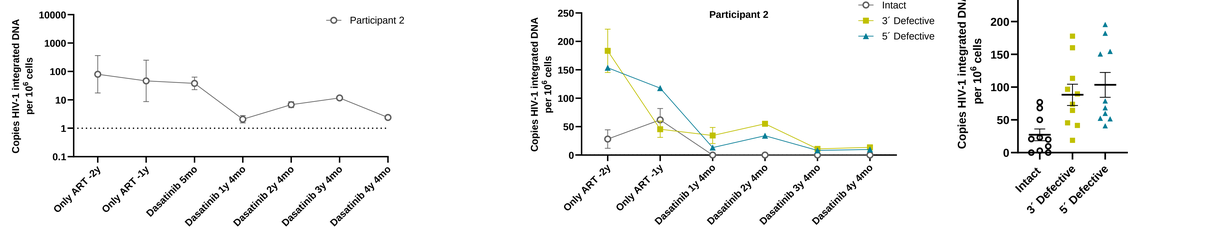
- First participant (ITK2-004): 50 years-old male with HIV for 17 years with CML for 13 years. HIV-1 DNA copies per 10^6 PBMCs was 1724.0 on imatinib. Dasatinib treatment reduced copies of integrated provirus: intact provirus undetectable after 9.5mo of dasatinib.



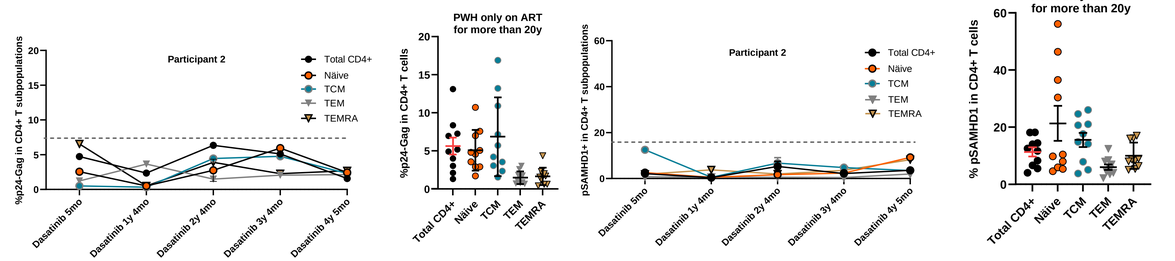
- Proviral reactivation was reduced compared to PWH only on ART, except during TFR of dasatinib. SAMHD1 phosphorylation was inhibited during all dasatinib treatment, TFR and asciminib.



- Second participant (ITK2-006): 62 years-old male on ART for 25 years and dasatinib for 4 years. Dasatinib treatment reduced copies of integrated provirus. Intact provirus was undetectable after 1y 4mo of dasatinib treatment. 5´-defective provirus also decreased during dasatinib treatment.



- Dasatinib treatment reduced proviral reactivation in all CD4+ T subpopulations compared to PWH only on ART. SAMHD1 remained in its active form during all dasatinib treatment.



CONCLUSIONS

- Dasatinib treatment changed the reservoir landscape towards a more favorable scenario in which there was a reduction in intact proviruses.
- Detectable p24-gag during proviral reactivation may proceed from defective proviruses.

ACKNOWLEDGEMENTS

To all the participants