PWH on ART and tyrosine kinase inhibitors show high cytotoxic activity against HIV-1-infected cells

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OBJECTIVE

- To evaluate if **PWH** with chronic myeloid leukemia (CML) on treatment with antiretrovirals (ART) and **tyrosine kinase inhibitors (TKI)** develop cell populations with high antiviral capacity that may explain the **reduced reservoir size** observed in these individuals.

RESULTS

Table 1. Clinical characteristics of participants. All participants were on standard ART.

	ART	ART+TKI
	n=18	n=6
Gender (male/female); n (%)	14/4 (78/22)	6/0 (100/0)
Age at sampling (years); median (IQR)	51 (41-59)	58 (54-66)
Age at diagnosis of HIV infection (years); median (IQR)	32 (25-37)	39 (32-45)
Time of infection with HIV (years); median (IQR)	19 (13-24)	22 (15-30)
Nadir CD4 (cells/mm³); median (IQR)	336 (167-420)	97 (63-382)
CD4 count (cells/mm³); median (IQR)	1,030 (737-1,231)	370 (186-843)
CD4/CD8 ratio; median (IQR)	1.0 (0.7-1.5)	0.6 (0.3-1.5)
Age at diagnosis of CML (years); median (IQR)	-	47 (42-63)
Time with CML at sampling (years); median (IQR)	-	11 (3-12)
Molecular response to CML (log); median (IQR)	-	5.0 (4.1-5.1)
Current TKI; n (%)		
Imatinib	-	3 (50)
Dasatinib	-	3 (50)
Previous TKI; n (%)		
None	-	4 (67)
Imatinib	-	2 (33)
Time of treatment with current TKI (years); median (IQR)	-	3.3 (1.7-9.6)

Reduced reservoir size in PWH treated with ART and TKI may be related to high levels of cytotoxic cells with antiviral activity

METHODS

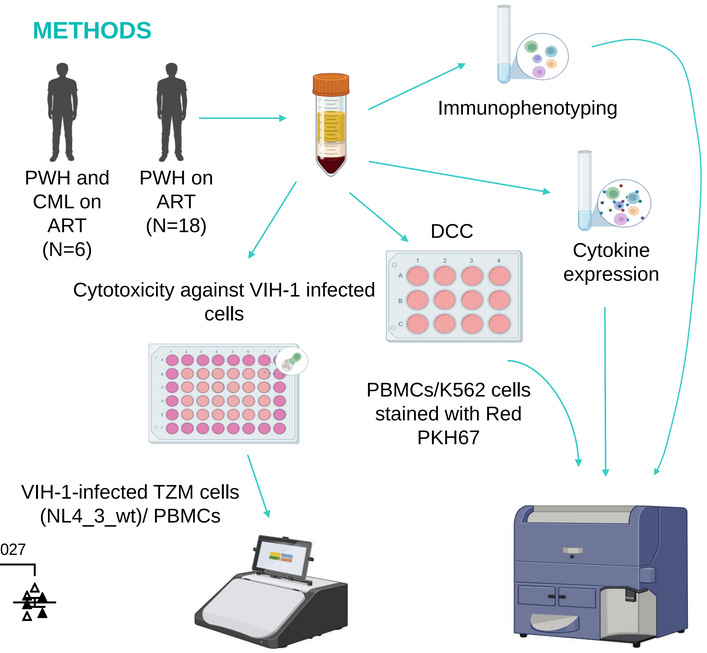


Figure 1. PBMCs from PWH on ART+TKI showed higher cytotoxicity against NK-specific (p=0.0050) and HIV-1-infected target cells (p=0.0462) than controls.

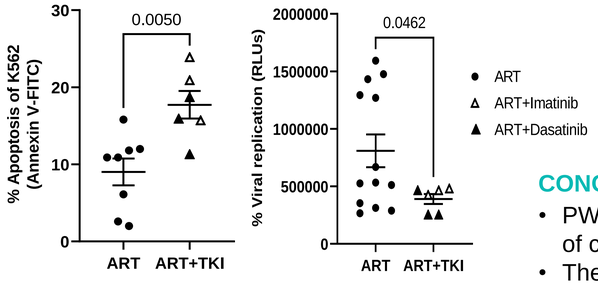


Figure 2. PWH on ART+TKI had higher levels of NK cells (p=0.0179) with higher expression of maturation / memory marker CD57 (p=0.0027).

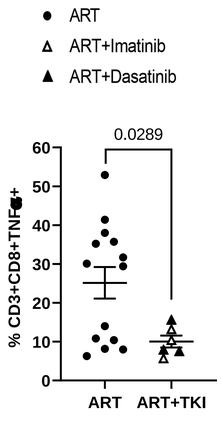
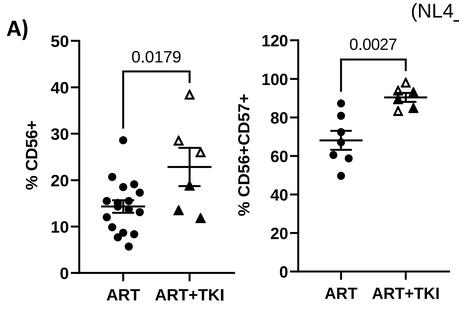


Figure 3. A) PWH on ART+TKI showed increased levels of CD8 (p=0.0325) with higher degranulation capacity (CD107a+; p=0.0402) and increased release of GZB (p=0.0007).
CD8 from PWH on ART+TKI released lower levels of TNFα (p=0.0289), which is essential in HIV-1-associated chronic inflammation. B) No changes were observed in the release of IFNγ.



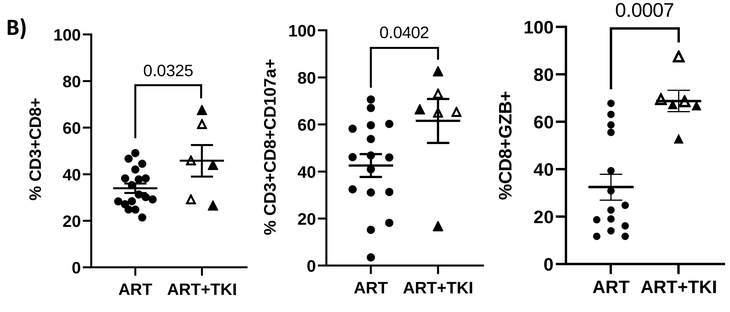
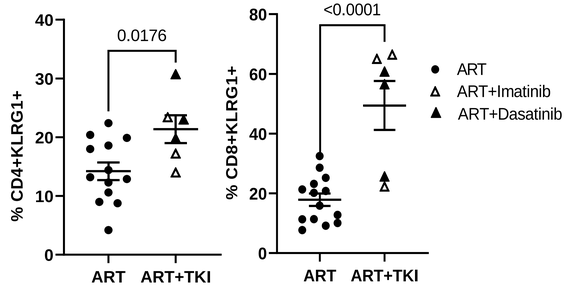


Figure 4. No differences were found in the expression of immunosenescence/exhaustion markers (PD-1, TIGIT, CD57, TIM3) in CD4 and CD8 except for KLRG1 that was increased in PWH on ART+TKI (p=0.0176 and p<0.0001, respectively)



CONCLUSIONS

- PWH on ART+TKI show low HIV-1 reservoir size, which may be partly related to higher levels of cytotoxic cells with antiviral activity.
- These cell populations may have been stimulated by the presence of cancerous cells, so these results have to be confirmed in clinical trials with PWH without CML.

ADDITIONAL KEY INFORMATION

Thanks to all participants!