LONG-TERM PROTECTION OF CD4+ T CELLS AGAINST HIV BY ONE-YEAR TREATMENT WITH PONATINIB

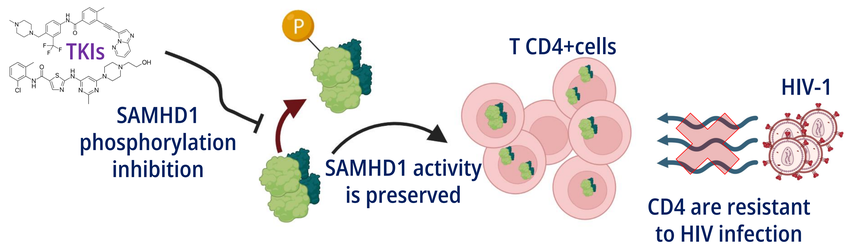
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BACKGROUND

- Tyrosine Kinase Inhibitors (TKIs) interfere with the formation and replenishment of HIV reservoir by preserving SAMHD1 antiviral activity in CD4+ T cells.
- We evaluated if treatment with ponatinib may also protect CD4+ T cells from HIV during treatment and if this protection was maintained after treatment interruption.



METHODS

- 9 Chronic Myeloid Leukemia (CML) participants of Phase II clinical trial NCT04043676 were recruited. Imatinib treatment was interrupted and they received one-year consolidation treatment with 15mg/day of ponatinib. Primary endpoint of this trial was to evaluate relapse after ponatinib discontinuation.
- Blood samples were taken before starting ponatinib (t=-12 months), after one year treatment (t=0) and 3,6 and 12 months after interruption.
- PBMCs were activated with PHA/IL-2 for 48h, then infected with NL4-3_wt for 72h.
- HIV p24, SAMHD1 phosphorylation and distribution of memory CD4 subpopulations were analyzed by flow cytometry.

One-year treatment with a reduced dose of **ponatinib** induced a sustained interference with **SAMHD1 phosphorylation** in all CD4+ T cell subpopulations, protecting them from HIV infection.
This **protective effect** was maintained for **one year after treatment discontinuation** in individuals with chronic myeloid leukemia who did not relapse in absence of treatment.

CONCLUSIONS

- One-year treatment with ponatinib preserved SAMHD1 antiviral activity in CD4 by a potent sustained cytostatic effect.
- HIV infection was impaired in all CD4 subsets after one-year treatment with ponatinib, and this effect was maintained for 12 months during TFR in Non-relapsed participants.
- Transient use of TKIs may be considered as a potential strategy to advance towards an HIV cure.

ADDITIONAL KEY INFORMATION

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RESULTS

***Table 1**: characteristics of study participants.*

	CML participants n (%)	Gender Male, n (%)	Years on treatment with TKIs, median (IQR)
Completed treatment and did not relapse	5 (41.7)	4 (80)	14 (5.5-15.5)
Completed treatment and relapsed	4 (33.3)	2 (50)	14 (11.7-17.0)
Drop-out due to toxicity	3 (25.0)	3 (100)	-

***Figure 1**: one-year treatment with ponatinib reduced 8.8-fold HIV infection in CD4+ T cells. This protection was maintained after 12 months of Treatment-free remission in Non-relapsed (p=0.0039) . pSAMHD1 levels in CD8+ T cells were not significantly modified*

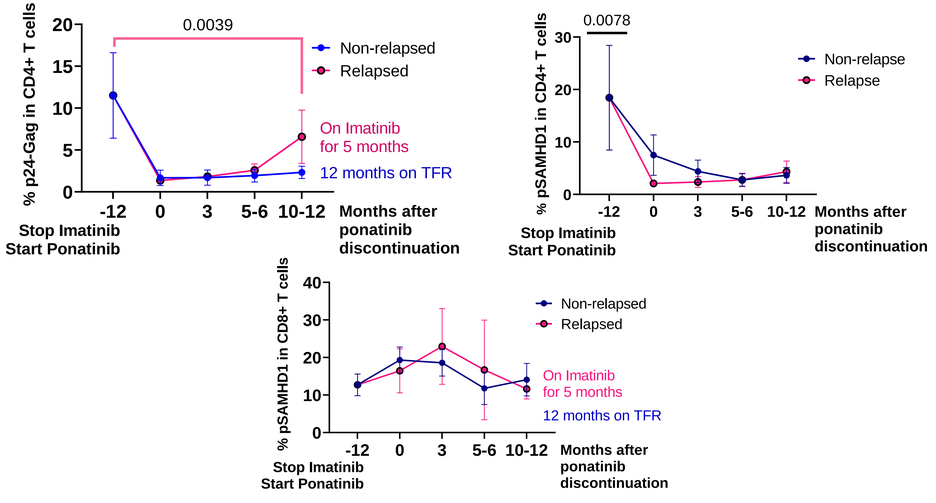


***Figure 2**: p24 production was increased 6.1-(p=0.0159), 8.6-(p=0.0159) and 5.0-fold(p=0.0317) in CD4 naive, CD4 T Central Memory (TCM) and Terminally Differentiated Effector Memory (TEMRA) of Relapsed after CML relapse and imatinib reintroduction.*

