Dasatinib Enhances Antiviral Function and Limits HIV-1 Infection in Macrophages from ART-Treated PWH

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BACKGROUND

Dasatinib, a proposed senolytic drug and HIV-1 latency promoter, may affect long-lived macrophage reservoirs that maintain viral persistence in tissues despite suppressive ART.

Objective:

In this substudy of BCN04, we evaluated if low-dose dasatinib (70mg/day for 24 weeks) alters the functionality and susceptibility to HIV-1 infection of monocyte-derived macrophages (MDMs) in ART-suppressed PWH.

RESULTS

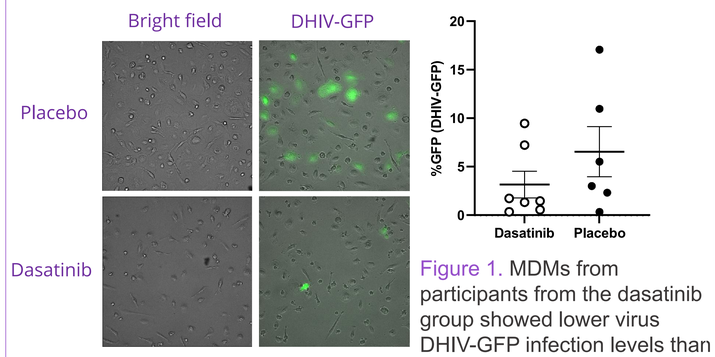


Figure 1. MDMs from participants from the dasatinib group showed lower virus DHIV-GFP infection levels than placebo.

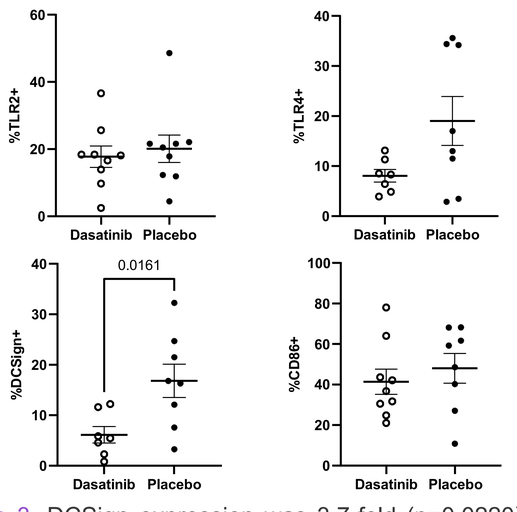


Figure 3. DCSign expression was 3.7-fold (p=0.0220) lower in participants from the dasatinib group. No changes were observed in IFNγ and TNFα expression.

Dasatinib reprograms macrophages toward a less permissive and less inflammatory state, potentially strengthening intrinsic HIV-1 restriction and constraining persistent reservoirs

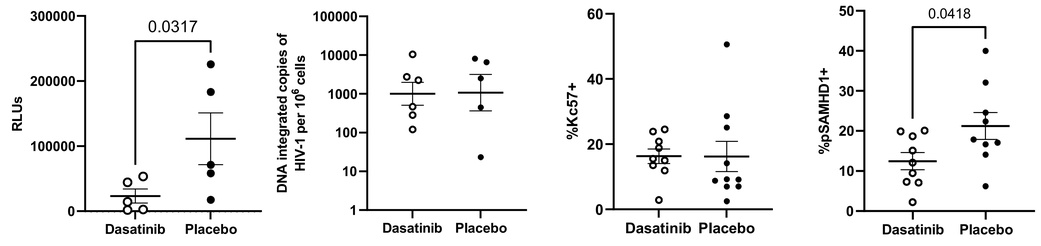


Figure 2. JR-FL_renilla infection was 4.8-fold (p=0.0317) lower in participants from the dasatinib group, correlating with 2.2-fold (p=0.0242) reduced expression of pSAMHD1. No changes were observed in proviral integration levels.

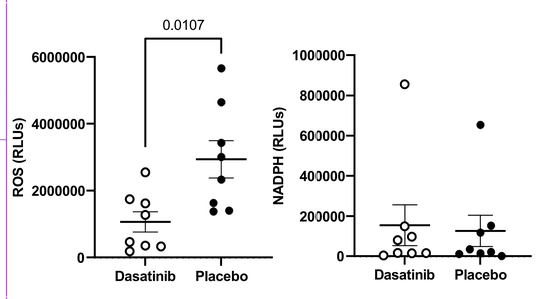


Figure 4. ROS levels were reduced 3.4-fold (p=0.0200) in participants from the dasatinib group, but NADPH levels remained unchanged.

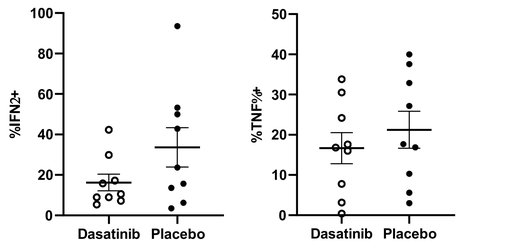
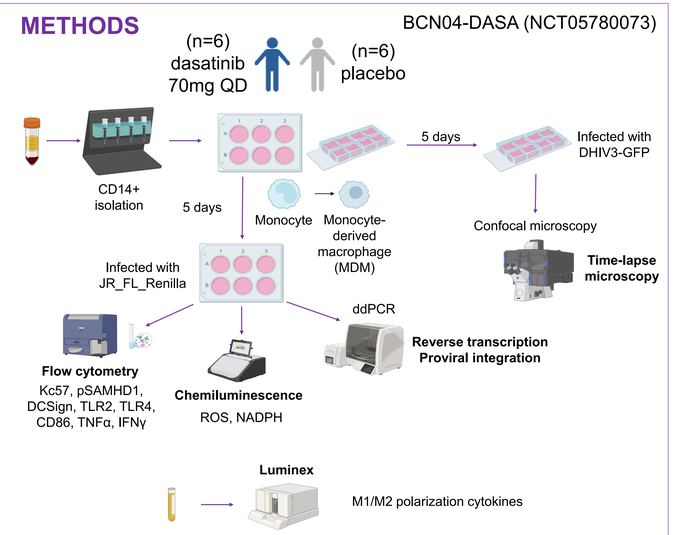


Figure 5. No changes were observed in IFNγ and TNFα expression and no significant changes were observed in cytokines expression related to M1/M2 polarization.

METHODS



CONCLUSIONS

- Low-dose dasatinib modulates MDMs in ART-suppressed PWH by reducing HIV-1 susceptibility, associated with decreased pSAMHD1 and DC-SIGN expression, suggesting enhanced intrinsic viral restriction.
- The concurrent reduction in ROS without changes in lipid oxidation and phagocytic activity indicate a shift toward a more functional, controlled metabolic state, consistent with an anti-inflammatory profile.
- Together, dasatinib may enhance antiviral defenses of macrophages while limiting inflammation, supporting its potential to constrain long-lived HIV-1 reservoirs.

PLAIN LANGUAGE SUMMARY

In a cohort of people with HIV, treated with ART and low-dose dasatinib, we evaluated if their macrophages showed an altered functionality. Dasatinib reduced inflammation while boosting antiviral factors, which means it could help diminish the HIV-1 viral reservoir in these cells.

AKNOWLEDGEMENTS

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