Immunophenotypic and T-cell Senescence Profile Modifications After Spontaneous HCV Clearance or After DAAs Treatment in People Living with HIV

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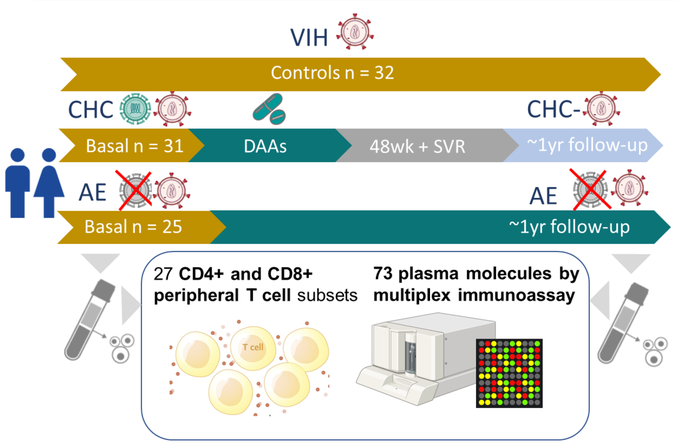
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BACKGROUND

Acquisition of HCV is frequent among people with HIV (PWHIV), an event that profoundly modifies natural history of both infections. Our goal was to analyze whether HCV clearance by direct-acting antivirals (DAAs) after chronic infection can partially restore both molecular and cellular immune profile to levels similar to those found in PWHIV. In addition, we explored whether changes over time in these patients were similar to those found in patients who cleared HCV spontaneously after acute infection.

METHODS



Differences in cell populations and plasma molecules were assessed by generalized linear models adjusted for the most significant clinical variables and multiple comparisons (p-value corrected by Benjamin-Hochberg – q<0.15).



CONCLUSIONS

- PWHIV who spontaneously cleared HCV showed elevated levels of effector cells despite increased expression of control molecules and cellular depletion markers compared to baseline samples. This may indicate possible accelerated aging driven by acute HCV infection.
- CHC PWHIV showed significant improvement in chronic inflammation and checkpoint upregulation 48 weeks after achieving a sustained virologic response (SVR) with DAA compared to the immune profile before treatment.

RESULTS

In AE at follow-up, there's a shift toward an aged immune system, characterized by a decrease in CD4+ and an increase in CD8+, as well as an increase in CD4+ senescence. There is also an alteration in the levels of several subpopulations, highlighting a decrease in CD4+ and CD8+ Naive, CD4+ CM and several regulatory and follicular subpopulations. In CHC we observed a generalized decrease in activation levels in both CD4+ and CD8+ subpopulations after HCV elimination, and again a decrease in regulatory T cells. Also, an increase in CD8+ CM and EM1 senescent populations.

In AE at follow-up, we observed a generalized increase in molecules associated with aging, especially in the SASP phenotype and immune checkpoint molecules, where we highlight IDO, LAG-3, perforin and arginase, which are related to cardiovascular diseases and cancer. In CHC, the elimination of HCV induces a reduction of numerous cellular checkpoint molecules, where LAG-3, IDO, and Cadherin-E – an additional molecule linked to cancer – appears.

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