Predictors of CD4/CD8 T-cell Inversion After 96 Weeks of ART Initiated During Acute HIV

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BACKGROUND

- Nearly 1 in every 2 persons with HIV (PWH) do not achieve CD4/CD8 T-cell ratio normalization (ratio>1.0) after sustained use of antiretroviral therapy (ART).
- Recent findings from RV254/SEARCH 010 revealed that mental health and immune factors were important determinants of CD4/CD8 ratio after ART.
- This study examined a larger array of potential predictors of persistent CD4/CD8 T-cell inversion, including multimodal indices of brain structure/function quantified using 3T MRI before ART initiation.

METHODS

- Archival data from RV254/SEARCH 010 were examined for individuals who completed 3T MRI (volumetrics, diffusion tensor imaging (DTI), and resting state connectivity) at enrollment into the cohort and completed follow-up visits through week 96.
- Gradient boosted multivariate (GBM) regression with repeated cross validation was utilized to identify a combination of variables that predict CD4/CD8 T-cell ratio status at week 96 from baseline neuroimaging, demographic, immune, viral, cognitive, and mental/behavioral health indices.

RESULTS

- 74 Thai males with an average duration of HIV infection of 19.5 (7.2) days were included in the analysis. Study participants were of 27.4 (6.0) years of age and had a median viral load (log_{10}) of 6.01 (IQR 5.43-6.79) copies/mL, CD4+ T-cell count of 330, CD8+ T-cell count of 526, and a CD4/CD8 T-cell ratio of 0.64.
- After 96 weeks of ART, all study participants were virally suppressed. 34 individuals had a CD4/CD8 T-cell ratio <1.0.
- The GBM analysis identified 10 baseline features that predicted CD4/CD8 T-cell ratio inversion at 96 weeks (average model performance of .72). The algorithm included larger volumes in 6 brain regions (medial superior frontal gyrus, superior temporal gyrus, rectus gyrus, nucleus accumbens, cerebellar lobes IV-V, pallidum), lower connectivity between the salience and visuospatial networks, lower high-density lipoprotein (HDL) levels, lower radial diffusivity in the external capsule, and higher IL-1α.

Among PWH who initiated ART during acute infection, larger regional brain volumes, altered brain connectivity, dyslipidemia, and systemic inflammation prior to ART predict CD4/CD8 T-cell ratio inversion after 96 weeks of ART.

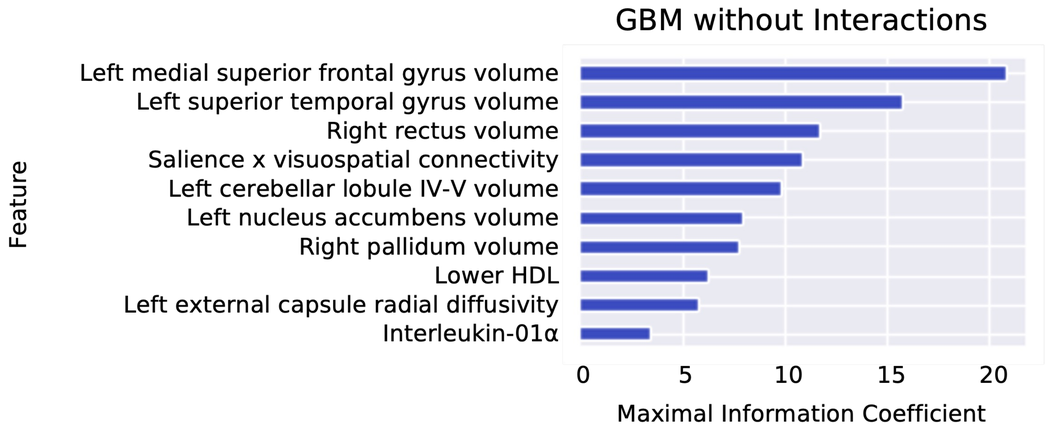

Figure. Variables that contributed to the GBM classifier. Larger regional brain volumes, lower resting state connectivity in the salience and visuospatial networks, higher plasma levels of IL-1α, and HDL levels < 40 predicted CD4/CD8 T-cell inversion at week 96. Blue bars represent the relative importance of each variable to the classification algorithm.

CONCLUSIONS

- Perturbations in brain structure and function, possibly reflecting early inflammatory mechanisms, dyslipidemia, and inflammation prior to ART initiated during acute infection predict CD4/CD8 T-cell outcomes after 96 weeks of ART.
- Further investigation of potential causal pathways is needed to identify modifiable mechanisms and potential therapeutic opportunities.

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DISCLAIMER

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