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Vaccination with dendritic cells loaded with HIV-1 lipopeptides elicits broad T cell immunity and control of viral load in HIV infected patients

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Background

The DALIA trial tested the hypothesis that immunization with HIV peptide loaded Dendritic Cells (DC) may improve HIV immune responses and help to contain viral replication.

Methods

19 pts with CD4 >500 cells/m3 and HIV RNA <50 cp/ml under HAART received at W0, 4, 8 and 12 ex-vivo generated IFN-α DC loaded with HIV-1 lipopeptides. Analytical treatment interruption (ATI) was conducted from W24. HAART resumption regardless of the reason and CD4 <350 cells/mm3 (or <25%) were considered as end points. HIV-specific immunity was evaluated at baseline, W16, and W48 using: i) ex vivo IFN-γ ELISPOT; ii) intra cellular staining; iii) multiplex analysis. PBMCs were stimulated with HIV peptide pools. Student t-test and Wilcoxon signed-rank tests were used with estimation of the False Discovery Rates (FDR) for controlling test multiplicity.

Results

Vaccine regimen was well tolerated. Following ATI, all pts experienced a viral rebound in 14 days in median (IQR 8-27). Median highest observed VL (peak) was 5 (4.28-5.23) log10 cp/ml. Three patients resumed HAART and eight had CD4 <350 cells/mm3. Median (IQR) SFU/106 PBMC rose from 186 (140-670) at baseline to 761 (470-1154) and 1878 (1102-4443) at W16 and 48, respectively. At the same time points the breadth of the response (nb of peptide pools) increased from 1 (1-3) to 4 (2-5) (P=.009) and 6 (3-7) (P=.008). % of polyfunctional CD4+ (> 2 cytokines among: IFN-γ,TNF-α,IL-2) increased from 0.026% (w-4) to 0.32% (w16) (P=.002). Respective % of CD8+ were 0.26% and 0.35% (P=.005). Production of IL-2, IFN-g, IL-21, IL-13, IL-17 increased significantly at W16 (FDR<.05). An inverse correlation was found between the peak of VL and % of polyfunctional CD4+ (r=-0.63, FDR=.007), production of IL-2 (r=-0.67, FDR=.006), IFN-g (r=-0.58, FDR=.01), IL-21 (r=-0.66, FDR=0.006) and IL-13 (r=-0.78, FDR=.001).

Conclusion

DC vaccination elicited polyfunctional HIV-specific responses associated with a reduced peak viral load following ATI.

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