

309 Maraviroc Intensification in HIV-Infected Patients Induces Increased CCR5 Expression On T Cells

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Background: Our group showed that Maraviroc (MVC) intensification over 24 weeks (W) in immunological non responders over the last two years (CD4<350 cells/mm³, CD4 slope <50 cells/mm³/year and HIV-RNA<50 copies/ml) enhanced CD4 cell slopes and significantly decreased CD8+ T cell activation#. We analyzed whether these effects were associated with modulation of CCR5 expression on various T cell subsets, frequencies of virus-specific T cells and levels of CCR5 ligands.

Methodology: 31 patients were monitored at baseline, after 24W of MVC intensification and at W28 (4W post-intensification). We evaluated CCR5 modulation on different T-cell subsets (Naïve (N), Central-Memory (CM), Effector-Memory (EM), Effector (E) and on CD4 T cells expressing CXCR3, CCR4 or CCR6, as well as on activated CD4+ and CD8+ T cells in parallel to plasma CCR5 ligands (MIP-1A, MIP-1B and RANTES) levels. T cells specific for HIV-1 gag and CMV antigens were quantified using IFN- γ ELISpot assay.

Results: During MVC intensification, a decrease in activated CD8+DR+CD38+ T cells is observed (-26%; p=0.001). We also observe to a significant increase of CCR5 on CD4+ (+6%; <0.001) and CD8+ T cells (+15%; p<0.001), mainly on CD8+ TEM (+14%; p=0.003) and on activated CD8+DR+38+ T cells (+10%; p=0.00014). MVC intensification also resulted in significant increase in CCR5 expression on CD4+CXCR3-CCR4+CCR6+ T cells defining Th17 cells (+4%; p=0.003). This increased CCR5 expression paralleled an increase in MIP-1B plasma levels (+57pg/ml; p=<0.001). At W28, 4 weeks after stopping MVC both CCR5 expression and MIP-1B levels were reversed. No significant changes were observed in frequencies of CMV- or HIV-specific T cells.

Conclusions: The blockade of CCR5 receptor-ligand interaction by MVC not only reduced CD8+ T-cell activation but also increased CCR5 expression mainly on effector-memory and activated T cells, paralleling the increase in plasma levels of MIP-1B the CCR5 ligand. These changes during MVC intensification might reflect a preferential decrease of activated T cells that do not display CCR5 and the redistribution of CCR5+ activated differentiated T cells in association with the positive effect on CD4 counts in immunological non responders.

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