Retrovirology

BioMed Central

Poster presentation

P18-13 LB. Immunogenicity of an autologous dendritic cell anti-HIV therapy in HIV-1 infected individuals

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from AIDS Vaccine 2009
Paris, France. 19-22 October 2009

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P412 doi:10.1186/1742-4690-6-S3-P412

This abstract is available from: http://www.retrovirology.com/content/6/S3/P412

Background

The immunogenicity of an autologous dendritic cell (DC) anti-HIV therapy, AGS-004, was evaluated in a multicenter Phase 2 trial. The treatment regiment consisted of four intradermal doses, administered monthly in combination with anti-retroviral therapy (ART) followed by a well-controlled structured treatment interruption (STI). The immunotherapy consisted of monocyte-derived DC co-electroporated with CD40L in vitro transcribed (IVT) RNA along with amplified IVT RNA encoding for 4 HIV-1 antigens (GAG, NEF, REV and VPR).

Methods

Cellular immunity was determined simultaneously by lymphocyte proliferation (CFSE) and cytokine production (ICS)) multi-parameter flow cytometry assays using peripheral blood mononuclear cells from vaccinated individuals stimulated in vitro with DC electroporated with either all 4 or the individual HIV RNA. The two assays were performed according to applicable GCLP guidelines.

Results

Among 28 subjects recruited until now, there were 8 subjects that had already undergone an initial cycle of this immunotherapy (CAN-HIV-1 pilot study). All other subjects that were naïve to this immunotherapy successfully completed the immune monitoring phase of the protocol and were on a treatment interruption of varying lengths. We performed an analysis of anti-HIV-specific response by evaluating the proliferation, IFNg production and the functionality in CD8+ and CD4+ T cells stimulated with autologous Gag, Nef, Rev and Vpr. Interestingly, the absolute number of proliferating CD8+ T-cells and those producing IFNg in response to GAG-peptides showed an impressive increase after the first vaccination and following ART interruption. Preliminary results of these roll-over subjects indicate an increase in HIV-specific CD8+ T-lymphocyte polyfunctional populations following immunotherapy which is accentuated after ART treatment interruption. These populations have mainly a CD27+CD8+CD45RA- phenotype.

Conclusion

This immunotherapeutic approach may overcome the lack of polyvalent specificity of the immune response for autologous HIV-1 antigens that has been one of the reasons for the failure of prior immunotherapies that use consensus HIV-1 sequences.