

## HPV vaccination in ARV-treated HIV-infected adolescents and young adults induces strong HPV-specific cell-mediated immune responses

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**Background:** Human Papilloma Virus (HPV)-associated ano-genital infections represent the most common sexually transmitted disease in the general population. The incidence of HPV-associated cancers has been increasing in HIV-infected patients. HPV vaccination may be an important approach to reduce the risk of HPV-associated cancers in HIV-infected patients and a combined strategy of screening and HPV vaccination may guarantee a more adequate prevention of HPV-associated lesions. Immunogenicity of HPV vaccines in HIV-infected patients is still not adequately evaluated. We analysed safety, immunogenicity and efficacy of a quadrivalent HPV vaccine in HIV-infected patients without baseline molecular evidence of vaccine-type HPV infection focusing on HPV-specific cell mediated immunity (CMI).

**Methods:** 31 ARV-treated HIV-infected adolescents (age range 28-14 years, mostly with undetectable viremia and effective CD4 recovery) and 25 sex- and age-matched HIV-seronegative healthy controls were enrolled in the study. Quadrivalent HPV-16/18/6/11 VLP vaccine (Gardasil®) was administered at baseline, 2 months and 6 months. Safety was evaluated in terms of rate and severity of vaccine-related adverse events. Immune activation (CD4/CD25/HLADRII, CD8/CD25/HLADRII), naïve and memory T-cell patterns and HPV-specific immune responses (CD4/IFN- $\gamma$ /IL-2, CD8/IFN- $\gamma$ /TNF- $\gamma$ , CD8/Perforin/GranzymeB) were evaluated at baseline and after vaccine administrations.

**Results:** Results obtained after the first immunization in HIV-infected individuals show: 1) no changes in CD4 counts, percentage of CD4 cells and HIV viral load; 2) a significant increase in naïve CD8 T-cells, activated CD8 T-cells and in central memory CD4 and CD8 T-cells; 3) a significant reduction in terminally differentiated CD8 T-cells; and 4) a significant augmentation of unstimulated and HPV-specific IL2+/CD4+, IFN- $\gamma$ + /CD4+, IFN- $\gamma$ + /CD8+ and TNF- $\alpha$ + /CD8+ T-cells. No differences were observed in Perforin- or Granzyme B-secreting CD8 T-cells. Similar results were obtained in healthy controls.

**Conclusions:** Quadrivalent HPV-16/18/6/11 VLP vaccine induces strong HPV-specific cell-mediated immune responses in ARV-treated HIV-infected individuals that are comparable to those observed in HIV-seronegative controls. HPV-specific CMI is likely an important component of the protective effect of this vaccine, data herein indicating that this component is not impaired in ARV-treated HIV infected individuals.

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