

## **TheraVac-01: Evaluation of safety and immunogenicity of the HIV-1 vaccine NYVAC-B in chronic HIV-1 infected patients successfully treated with HAART.**

P-A Bart<sup>1</sup>, A Harari<sup>1</sup>, J Vermeulen<sup>2</sup>, F Bellutti Enders<sup>1</sup>, E Castro<sup>1</sup>, M Cavassini<sup>1</sup>, F Wit<sup>2</sup>, B Autran<sup>3</sup>, J Lange<sup>2</sup> and G Pantaleo<sup>1</sup>

1 Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; 2 Academic Medical Center and IATEC, Amsterdam, the Netherlands; 3 Faculté de Médecine Pierre et Marie Curie, Paris, France.

The candidate HIV-1 therapeutic vaccine NYVAC-B evaluated in this study is a recombinant attenuated vaccinia vaccine containing HIV-1 clade B *env* gene and *gag-pol-nef* polygene. Objectives are to evaluate the safety of NYVAC-B and to characterize HIV-1-specific immune responses.

Ten HAART-treated HIV-1 infected patients (clade B), with HIV-1-RNA (pVL) <50 copies/mL prior to inclusion, were injected with NYVAC-B IM on week (W) 0 and 4. Vaccination was followed by 2h of direct observation, and visits on day 1, W1, 2, 3, 4, 6, 8, 12, 24, 36 and 48. Safety parameters (vaccination-related local and systemic reactions, clinical and laboratory parameters, pVL and CD4/CD8 T-cell counts) were evaluated at every visit. HIV-1 specific immune responses were assessed on cryopreserved PBMC by IFN $\gamma$  ELISpot and ICS at W0, 2, 4, 6, 8, 12, 24, 36 and 48 using pools of HIV-1 overlapping peptides encompassing *gag-pol-nef* and *env* regions, and with 193 HIV-derived optimal epitopes (W48).

After both vaccinations only grade 1 or 2 local injection-related adverse events (AE) were observed (no serious AE related to the vaccine). CD4 counts and pVL remained very stable over time. Global HIV-1-specific cellular responses increased in all patients (median 2.4-fold increase). This was mostly due to an expansion of pre-existing but also to the generation of new CD4 and CD8 T-cell responses. Furthermore, 38 (including 18 gag epitopes) HIV-1-specific CD8 T-cell responses against optimal epitopes were identified in 6 subjects prior immunization. These responses were significantly increased in magnitude ( $P<0.01$ ) and were more polyfunctional ( $P<0.01$ ) at W48.

The recombinant HIV-1 vaccine NYVAC-B is safe and well tolerated. Furthermore it significantly increases the magnitude and the polyfunctional profile of HIV-1-specific CD4 and CD8 T-cell responses. The clinical significance of these enhanced T-cell responses will be evaluated in a larger phase-2 study.