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VAC-3S, a safe Immunotherapeutic HIV Vaccine decreased total HIV DNA and increased CD4/CD8 ratio: Phase I Final Results

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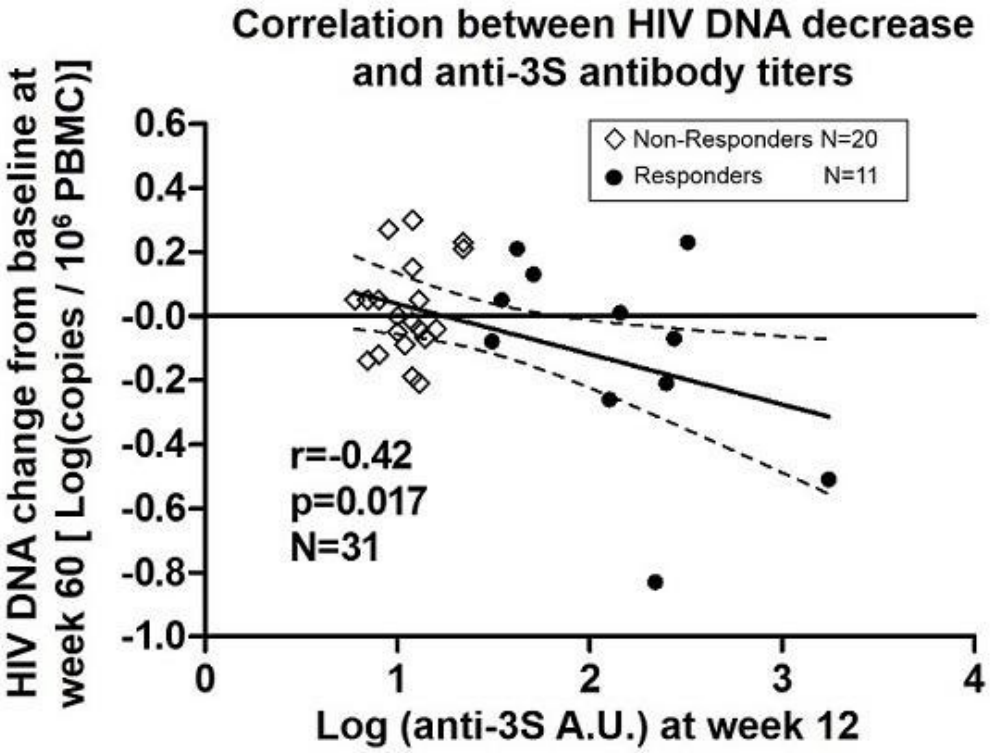
Background: VAC-3S is an immunotherapy targeting the conserved 3S motif of HIV-1 gp41. On non-infected CD4+ T cells (CD4), anti-3S antibodies prevent the surface expression of NKp44L, ligand of NKp44 expressed on activated Natural Killer cells. Anti-3S antibodies exert in vitro anti-CD4 apoptotic effects and are associated with protection of CD4 and low inflammation/activation biomarkers in SHIV-infected macaques. In patients, natural anti-3S antibodies are associated with slower disease progression.

Methods: IVVAC-3S/PI was a prospective, randomized, placebo-controlled, double-blind, dose-escalation study, to assess safety and immunogenicity of 3 VAC-3S intramuscular administrations (weeks 0, 4, 8) at 0.1, 1, 10 and 20µg and 1 booster (week 32) in 1 and 10µg arms, in patients receiving ART with CD4>200cells/mm3 and virologically controlled. Analysis included safety, anti-3S antibodies (ELISA), CD4/CD8 ratio, T lymphocyte activation/differentiation, total HIV DNA and inflammation biomarkers. Responders were defined as anti-3S antibodies above 30 arbitrary units (AU) at week 12.

Results: 33 HIV-1-infected patients (29 men) were enrolled. Age, median [range]: 47 years [32;54], CD4: 710cells/mm3 [311;1187]. 89 expected AE for 113 vaccinations : 99% of grade 1-2, 1 cephalia, 1 tenosynovitis grade 3 in 20µg arm, 1 myalgia grade 3, 1 TLF increase grade 4 in placebos, no related SAE nor viral rebound were reported. A dose-response (p=0.003) was shown with 3 responders among 6 patients in 1µg, 3/6 in 10µg and 5/6 in 20µg arms (responders, N=11). Booster injections were immunogenic. Responders showed a transient CD4/CD8 ratio increase of 0.08 [0.01;0.15] at week 24 (p=0.002). Among all patients, a sustained negative correlation was obtained between differences from baseline in log(HIV DNA copies/106 PBMC) and anti-3S titers at weeks 12 (p=0.027), 36 (p=0.107), 60 (p=0.017, see figure) and 84 (p=0.026).

Among responders, these DNA levels decreased at week 60 and week 84 of -0.07 [-0.83;0.23] (p=0.091) and of -0.15 [-0.41;-0.01] (p=0.015) respectively. No group or dose difference was shown in activation, differentiation and inflammation markers. Functions of anti-3S antibodies are under investigation.



[VAC-3S decreased total HIV DNA]

Conclusions: VAC-3S is a safe and immunogenic HIV immunotherapy at higher tested doses. The induction of anti-3S antibodies was associated with increased CD4/CD8 ratio and decreased total HIV blood reservoir.