Novel therapeutic approaches (including gene therapy)

PE66

VAC-3S immunotherapeutic HIV vaccine combined with ART is immunogenic and safe. Phase II initial analysis of the IPROTECT1 multicenter European study

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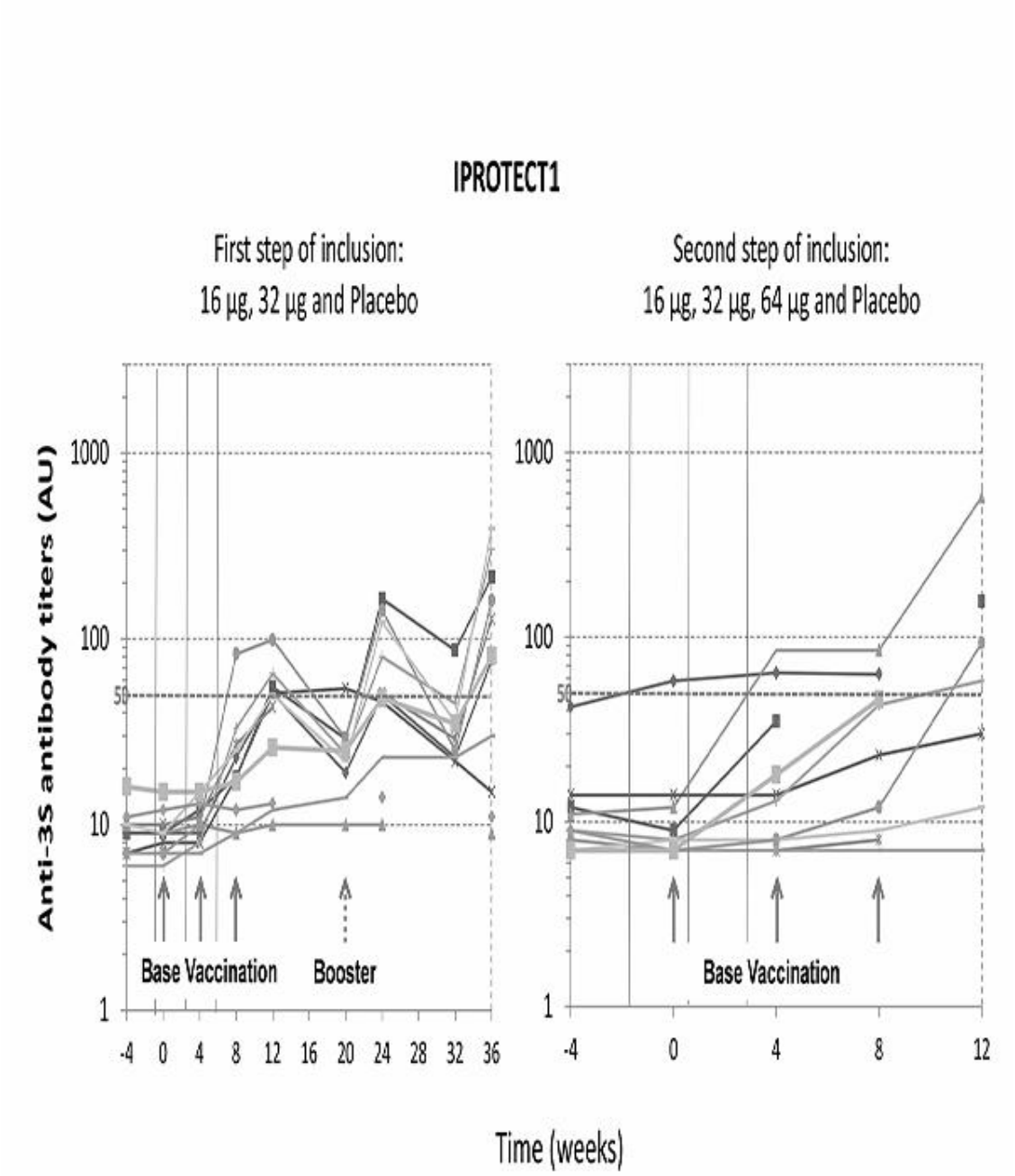
Background: VAC-3S is a novel vaccine directed to the highly conserved gp41, 3S motif of HIV-1. Anti-3S antibodies (Abs) block 3S binding to gC1qR, prevents CD4 surface expression of NKp44L, the natural ligand of NKp44 expressed on activated Natural Killer cells. Anti-3S Abs have anti-CD4 apoptotic effects, in vitro. High 3S Abs are associated with low inflammation biomarkers in SHIV-infected macaques. Anti-3S Abs have been shown to be negatively correlated with HIV DNA. We hypothesize that VAC-3S enables re-establishment of CD4/CD8 homeostasis hence can comprise the immunological component of an HIV functional cure approach.

Methods: Prospective, randomized, placebo-controlled, double-blind, 3-step study in Europe, assessing immunotherapeutic properties of VAC-3S at 16, 32, 64 mg with 3 IM base immunizations at 4 wk intervals and 3 maintenance boosters in the 16, 32 mg arms. Ninety HIV ART suppressed pts with 200-350 & 350-500 CD4 c/mm3 planned. Endpoints include: anti-3S Abs (ELISA), T lymphocyte activation/differentiation, HIV DNA, inflammatory biomarkers. Planned analysis after 50% inclusions in first 2-steps.

Results: In these first two steps, 56 pts (47 male / 9 female), randomized, and completed vaccinations. Pts are 62% Caucasian, 30% African heritage. Median age 46 years (23-59); BMI 23 kg/m2 (16-33), HIV duration 60 months (1-346); baseline CD4 count 365 cells/mm3 (200-596); nadir CD4 167 cells/mm3 (31-410). One serious Adverse Event (AE) prior to vaccination, one viral rebound post-ART non-adherence. One hundred twenty AEs reported after a total 182 vaccinations, were local (erythema, induration, sensitivity, pain), or systemic (headache, myalgia, vertigo). AEs were mild in 53% pts, moderate in 39% pts, severe in 6% pts. Figure 1 shows immunogenicity. Median CD4/CD8 ratios, at baseline, were 0.48 (0.20-1.46) and 0.66 (0.23-2.90) in the low and high CD4 strata, respectively. At the 12-weeks post-vaccination point CD4/CD8 ratio was 0.49 (0.21-1.120) in the low and 0.57 (0.34-2.82) in the high CD4 strata.



[Figure 1 VAC-3S Immunogenicity Results]

Conclusions: VAC-3S is a novel mechanism immunotherapeutic HIV vaccine. Phase II preliminary results, confirms phase I safety, as well as, immunogenicity for all new dose levels assessed. Scheduled long term evaluation includes CD4/CD8 homeostasis, HIV DNA and biomarkers of chronic inflammation.