A PLACEBO-CONTROLLED ATI TRIAL OF HTI VACCINES IN EARLY TREATED HIV INFECTION

Abstract Number:

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Authors:

Lucia Bailon[1], Anuska Llano[2], Samandhy Cedeño[2], Miriam B. Lopez[1], Yovaninna Alarcón-Soto[1], Pep Coll[2], Àngel Rivero[3], Anne R. Leselbaum[4], Ian McGowan[5], Devi SenGupta[6], Bonaventura Clotet[2], Christian Brander[2], Jose Molto[1], Beatriz Mothe[2], for AELIX-002 Trial Group

Institutions:

[1]Fundació Lluita Contra la Sida, Badalona, Spain, [2]IrsiCaixa Institute for AIDS Research, Badalona, Spain, [3]Projecte dels NOMS-Hispanosida, BCN Checkpoint, Barcelona, Spain, [4]AELIX Therapeutics S.L., Barcelona, Spain, [5]University of Pittsburgh, Pittsburgh, PA, USA, [6]Gilead Sciences, Inc, Foster City, CA, USA

Background:

HTI is a novel HIV vaccine immunogen designed at redirecting cellular immune responses to HIV targets associated with viral control.

Methods:

The AELIX-002 trial (NCT03204617) was a randomized, single-center, placebo-controlled trial to evaluate the safety, immunogenicity and antiviral effect of DNA.HTI (D), MVA.HTI (M) and ChAdOx1.HTI (C) vaccines after discontinuation of ART in early-treated people living with HIV (PLWH). 45 participants were randomized (2:1) to receive heterologous prime-boost vaccination regimens consisting of DDDMM followed by CCM, or matched placebo (P). During a 24-week analytical treatment interruption (ATI), plasma viral load (pVL) was monitored weekly and ART was resumed if pVL >100,000 copies/mL, or >10,000 copies/mL over 8 weeks, and/or CD4<350.

Results:

A total of 45 participants received DDDMM (n=30) or PPPPP (n=15). Of the 45 participants, 41 further completed the CCM (n=26) or PPP (n=15) regimen and entered the ATI. Immunizations were well tolerated, with no SAEs, and were immunogenic in 97% of vaccine recipients (defined by a >2-fold increase in HTI-specific T cell responses compared to baseline). Median (range) increase in total frequencies of HTI-specific T cells from baseline was 1,499 (120 to 3,150) SFC/million PBMC. At time of ATI start, 71% (0 to 100) of the total anti-HIV-1 T-cell response was HTI-specific. For participants without any potentially beneficial HLA class I alleles (32 of the 41), 8 (40%) of the vaccinees and 1 (8%) of the placebo recipients were able to remain off ART for 22 weeks (Δ 32%, 80%CI [7.6; 55.7]); with pVL <2,000 copies/mL being observed in 5 and 1 vaccine and placebo recipients, respectively. Magnitude of HTI-specific responses at the time of ATI start positively correlated with time off ART in vaccinees (Rho 0.65, p <0.01). Decay in total or intact HIV proviral DNA from baseline to ATI was similar between vaccine and placebo arms.

Conclusion:

HTI vaccines were safe and highly immunogenic in early-treated PLWH with a prolonged time off ART seen in vaccinees with non-beneficial HLA class I alleles. Time off ART positively correlated with vaccine-induced HTI-specific T cell responses at ATI start. Multivariate analysis for other correlates of response is ongoing. These encouraging data strongly support the use of HTI-based vaccines as the backbone of combination cure regimens such as with the TLR7 agonist vesatolimod, which is currently being evaluated in the AELIX-003 study (NCT04364035).

Basic Science:

(E) HIV Reservoirs, Latency, and Curative Strategies Including Therapeutic Vaccines and Gene Therapy