PE46

Safety and immunogenicity of ChAd.HIVconsv and MVA.HIVconsv therapeutic vaccines in a cohort of early treated HIV-1 infected individuals

Mothe B.[1,2,3], Manzardo C.[4], Coll P.[1,2], Cobarsi P.[2], Sanchez-Bernabeu A.[1], Escrig R.[2], Perez-Alvarez N.[2,5], Miró J.M.[4], Dorrell L.[6], Clotet B.[1,2,3], Hanke T.[7], Brander C.[1,3,8], BCN01 Study Group

[1]IrsiCaixa AIDS Research Institute - HIVACAT, Badalona, Spain, [2]Fundació Lluita contra la Sida, Hospital Germans Trias i Pujol, Badalona, Spain, [3]UVic-UCC, Vic, Spain, [4]Hospital Clínic-IDIBAPS, Barcelona, Spain, [5]Technical University of Catalonia, Barcelona, Spain, [6]John Radcliffe Hospital, Oxford, United Kingdom, [7]The Jenner Institute, Oxford, United Kingdom, [8]ICREA, Barcelona, Spain

Background: T-cell vaccines targeting the most conserved regions of the HIV-1 proteome may be required for the elimination of the latent viral reservoir. HIVconsv vaccines vectored by chimpanzee adenovirus (ChAdV63) and modified vaccinia virus Ankara (MVA) have shown to induce high levels of effector T cells in healthy individuals (HIVCORE02 trial). BCN01 (NCT01712425) is a phase I study to evaluate the safety and immunogenicity of ChAdV63 and MVA.HIV-consv vaccines in early-treated HIV-1 infected individuals

Methods: 24 individuals identified with recent HIV infection (< 6m from acquisition) who initiated Tenofovir/Emtricitabine/Raltegravir within 1 week after diagnosis, received an intramuscular ChAdV63.HIVconsv (5x1010vp) vaccination after 6 months under cART. Participants were given an MVA.HIVconsv booster immunization (2x108pfu) 24 or 8 weeks afterwards and were followed for 6 months. Local and systemic events were recorded for a minimum of 7 days following each immunization. Immunogenicity to the vaccine insert and the rest of the HIV-1 proteome was assessed by IFNg ELISPOT.

Results: Local and systemic events after vaccination occurred in 22/24 individuals, mostly severity grade 1-2 and transiently (48 hours). Local pain was more often reported with MVA than ChAdV63 vaccination. Responses to conserved regions before cART initiation were only observed in 4 individuals and diminished significantly after achieving viral supression. All participants significantly increased T-cell responses that targeted the vaccine insert, with a peak 1-4 weeks after MVA vaccination (median of 1,015 SFC/106 PBMC, range 140-6,805, p=0.0003, Wilcoxon t-test compared to baseline). Over vaccination period, no unspecific expansion of T cells targeting HIV-1 regions outside HIVconsv insert or CEF was noted, allowing for an optimal focusing of T-cell responses on conserved regions (48% of total HIV immune response being HIVconsv-specific 4 weeks after MVA vaccination). Among vaccinees, no significant differences in peak immunogenicity was observed between short and long prime/boost regimen.

Conclusions: ChAd.HIVconsv and MVA.HIVconsv was a safe strategy to shift pre-existing immune response towards conserved, vaccine-encoded regions of HIV in a cohort of early-treated individuals and may set the stage for successful subsequent of cure strategies.

Under embargo until 14.30 on 22 July 2015