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

B. Mothe1, C. Manzardo1, P. Coll1, P. Cobarsi1, A. Sanchez1, R. Escrig1, N. Perez-Alvarez2,4, JM. Miró3, L. Dorrell5, B. Clotet1, T. Hanke6 and C. Brander1,7 for the BCN01 study group

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-infected individuals.

Methods

24 individuals identified with recent HIV infection (<6 months from acquisition. Table 1 for population characteristics) who initiated Tenofovir/Emtricitabine/Raltegravir within 1 week after diagnosis, received an intramuscular ChAdV63.HIVconsv (5×10⁶vp) vaccination after 6 months under cART. Participants were given an MVA.HIVconsv booster immunization (2×10⁷pfu) 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. Immune responses to the vaccine insert and the rest of the HIV-1 proteome were assessed by IFNγ 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 suppression.

All participants significantly increased T-cell responses that targeted the vaccine insert over vaccination schedule, with a peak HIVconsv-specific response at 1 or 4 weeks after MVA vaccination (median of 938 SFC/10⁶ PBMC, range 73-6,805, p=0.0001, Wilcoxon t-test, Fig 2).

No significant differences in peak immunogenicity or 24 weeks after last vaccination was observed between short and long prime/boost regimen.

Conserved regions of Pol-RT were the most immunogenic out of the 14 regions included in the HIVconsv immunogen (Fig 3).

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). (Fig 4)

Conclusions and Future work

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.

All individuals have been rolled-over and after 3 years of viral suppression will be invited to participate in the BCN02-Romi trial (2016) where booster vaccinations with MVA.HIVconsv will be administered in combination with a latency reversal agent (Romidepsin). A monitored antiretroviral pause will be performed to test the efficacy of the ‘Kick & kill’ strategy.