119LB. VIRAL CONTROL INDUCED BY HIVCONSV VACCINES & ROMIDEPSIN IN EARLY TREATED INDIVIDUALS

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Background:
The combined use of therapeutic vaccination and specific drugs that can reactivate latent reservoir virus (Kick and kill strategies) hold the promise to achieve a functional cure for HIV infection. The recently completed BCN01 vaccine trial (NCT01712425) consisted in a ChAd.HIVconsv and MVA.HIVconsv prime/boost vaccination in early treated individuals (<6 months from HIV acquisition) and was able to redirect CTL responses towards highly conserved regions of HIV-1. Likewise, romidepsin (RMD) has been shown in earlier studies to induce HIV-1 transcription demonstrating that significant reversal of HIV-1 latency is possible so that a combination of these two approaches may help achieve the goal of a functional cure of HIV.

Methods:
BCN02-Romi (NCT02616874) is an ongoing single-arm proof-of-concept study enrolling 15 individuals rolled-over from BCN01 trial. After 3 years under viral suppression, all participants were immunized with MVA.HIVconsv (2x10E8 pfu), followed by three weekly-doses of romidepsin (RMD, 5 mg/m2 BSA), and by a second MVA.HIVconsv vaccination. Participants underwent a monitored antiretroviral pause (MAP) and treatment was resumed if plasma viral load (pVL) increased >2,000 copies/ml.

Results:
15 participants completed all immunizations and RMD infusions, with pVL >20 copies/ml being detected during the intervention in all of them. After the first MVA.HIVconsv vaccination, HIVconsv-specific T cell responses raised to a median peak magnitude of 965 IFNg SFC/10E6 (range 400-3,340, in cryopreserved-and-thawed PBMC), which was significantly higher (p=0.0353) than peak responses during BCN01. Responses transiently decreased by 35% in magnitude after RMD in 10 individuals. However, all but two participants were able to maintain or increase HIV-consv specific responses after the 2nd vaccination relative to pre-RMD, and were therefore invited to start the MAP. To date, 11 patients have interrupted treatment: 7 had to resume cART within the first 4 wk of MAP while 4 participants remain off cART after 7, 12, 14 and 22 weeks (36% of viremic controllers)

Conclusion:
Therapeutic vaccination targeting conserved regions of HIV-1 combined with HIV latency reactivation strategies may facilitate clearance of the viral reservoir in early-treated individuals. This is the first reported immune intervention demonstrating a manipulation of the CTL immunodominance pattern and a durable viremic control of HIV-1 infection in a large proportion of participants.