2015 Towards an HIV Cure Symposium
Abstract Book | Poster Exhibition

Curative interventions (including those aimed at reservoir depletion)

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Reduction in total HIV-1 proviral DNA following re-boost immunizations using the peptide-based therapeutic vaccine candidate, Vacc-4x, during ART

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Background: This study (2012/1 - NCT01712256) investigated the impact of booster immunizations on sustaining vaccine effect in a therapeutic HIV vaccine setting. The effect of two Vacc-4x booster immunizations on total proviral DNA during ART, and on viral load (VL) set-point following a new ART interruption were determined.

Methods: At weeks (w) 0 and 2, eligible study participants from the clinical study (2007/1 - NCT00659789) were given intradermal (i.d.) Vacc-4x booster immunizations (1.2mg) on ART with GM-CSF (60µg) i.d. as a local adjuvant. At w12, ART was interrupted for up to 16 weeks (w28). Study participants were thereafter followed on ART until w36. Total proviral DNA was measured at w0,4,16,28 and 36 using real-time PCR (Taqman) targeting the gag gene. VL set-point was defined as the mean of the last two VL values prior to ART resumption. All study participants provided signed informed consent. The per protocol population (PP) included participants with no major deviations that would challenge the validity of the data.

Results: This open, multicenter, clinical study conducted from 12.2012 to 01.2014 enrolled 33 participants from 9 clinical trial sites within the US and Europe. In the PP, a statistically significant reduction in total proviral DNA (49%) between w0 and w4 was observed (Wilcoxon signed rank p-value 0.030, n=26) which could suggest immune-based killing of infected cells while on ART. The duration of ART prior to the first reboost immunization was mean 36 months (n=22) (min 26; max 47 months). The VL set-point in this study (2012/1) had a geometric mean (GM) value of 26279 copies/ml and was significantly lower than the pre-ART VL set-point (GM VL 74048 copies/ml) (p=0.021, n=13). The VL set-point in this 2012/1 study (GM VL 18162 copies/ml) was reduced compared to the 2007/1 study VL set-point (GM VL 22035 copies/ml), however the difference was not statistical significant, paired t-test p-value 0.453 (n=18).

Conclusions: Vacc-4x booster immunizations safely restored virus control to the VL set-point established following primary Vacc-4x therapeutic vaccination. The reduction in total proviral DNA supports the potential for Vacc-4x therapeutic vaccination to impact on HIV reservoirs during ART and to contribute to HIV cure strategies.

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