ABSTRACT INTL AIDS CONFERENCE 2014

Title: Baseline antibody levels to C5/gp41$^{732-744}$: A potential prognostic marker for viral load outcome following immunization with the peptide-based therapeutic HIV vaccine, Vacc-4x.

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Background:
Antibody responses to C5/gp41$^{732-744}$ regions of HIV envelope glycoproteins have previously been correlated with low/moderate viral load (VL) and slowed disease progression. An earlier phase II study of the therapeutic HIV vaccine, Vacc-4x, showed a log 0.40 (60%) reduction in median VL setpoint in Vacc-4x subjects interrupting ART for 6 months, compared to their preART median VL set point (n= 45; p=0.0001). There was no corresponding reduction in median VL setpoint for placebo subjects (n=18; p=0.983, log 0.02 reduction). This study sought to determine the influence of baseline anti-C5/gp41$^{732-744}$ antibody levels on VL outcome for the Vacc-4x group in this study.
Methods:
The phase II study (NCT00659789) enrolled 137 subjects and took place between July 2008 and June 2010 in Spain, Italy, USA, UK, and Germany in accordance with the Declaration of Helsinki and with informed consent. Baseline sera were available for 57 subjects who remained off ART for 6 months and where preART values were available (Vacc-4x n=39 and placebo n=18). In an exploratory, ad hoc, subset analysis, antibody responses to C5/gp41$^{732-744}$ were measured using an ELISA assay. The Wilcoxon Signed Rank Sum Test was used to analyze change in median VL setpoint from median preART VL setpoint values.
Results:
Vacc-4x subjects with baseline anti-C5/gp41$^{732-744}$ antibody levels above 4µg/ml had a statistically significant reduction in median VL setpoint of log 0.94 (88%) compared to their median pre-ART VL setpoint (p=0.005, n=12). Vacc-4x subjects with anti-C5/gp41$^{732-744}$ antibodies below 4µg/ml had a median VL reduction of only log 0.20 or 37% (p=0.019, n=27) compared to their median pre-ART VL setpoint. Preliminary analyses indicate these observations were independent of HLA type.
Changes from median preART VL setpoint for placebo subjects was not statistically significant, neither for subjects having levels above 4µg/ml (p=0.875; n=4, log 0.21 increase) nor antibody levels below 4µg/ml (p=0.903; n=14, log 0.05 reduction).
Conclusions:
Anti-C5/gp41$^{732-744}$ antibody levels above 4µg/ml influenced VL outcome in Vacc-4x subjects compared to their median preART VL setpoint values. The presence of these antibodies at baseline may thereby represent a potential prognostic marker for Vacc-4x treatment effect. This will need to be confirmed in future Vacc-4x clinical trials.