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EFFICACY ASSESSMENT OF THE PROCLEIX® dHIV-1 ASSAY IN A PHASE 3 VACCINE CLINICAL TRIAL

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Background:

Licensed Procleix® HIV-1/HCV Multiplex (Mx) Assay and discriminatory HIV-1 (dHIV) and HCV (dHCV) Assays are Transcription Mediated Amplification tests that detect HIV-1 and HCV RNA from blood/plasma donations intended for transfusion or manufacture. Donations are tested for HIV-1/HCV RNA in Minipools (MP) of 16-24 samples. Individual Mx reactive (Rx) samples are tested with dHIV-1 and dHCV to resolve the Mx reactivity. We performed dHIV-1 testing on high risk subject samples that were HIV negative as determined by the algorithm for EIA non-reactive (NR) or EIA Rx but, Western Blot (WB) any less than 2 bands Rx excluding the gp120 and gp160 bands. The study objective was to detect the earliest date HIV-1 infection in VAX004 HIV-1 EIA positive, immunoblot confirmed subjects. The objective was to use the dHIV-1 assay as a tool for look back procedures, estimating annual incidence of HIV infection, and assessment of the any possible differential impact of placebo and gp120 vaccine on the time window when an infected subject is seronegative, but dHIV-1 positive.

Methods

A total of 576 samples obtained from HIV-1 infected subjects from the VAX004 Phase III U.S. North America/Europe. trial were supplied. Serum samples' draw date was prior to date of first HIV-1 EIA positive and HIV-1 immunoblot confirmation of infection. The treated status (Vaccinated or Placebo) as well as ID and draw date of subject samples remained blinded. Procleix dHIV-1 was used to determine a qualitative positive/negative (presence or absence) of HIV-1 RNA in VAX004 HIV-1 Day 0 seronegative subject samples..

Results:

The 576 samples were tested across 9 valid dHIV-1 assays. There were 453 (79%) NR and 123 (21%) Rx samples. The mean NR signal to cut-off (S/CO) was 0.08 (95% CI: 0.076-0.82), while the Rx mean S/CO was 24.2 (95% CI: 23.4 -24.8). The separation between positive and negative was significant, $p < 0.001$. The Procleix dHIV-1 results showed an increased level of sensitivity beyond serological and WB results. It allowed for reclassification of 21% vaccine subjects' seronegative samples that were thought to be infectious. These true RNA Positive/Seronegative Subjects either had their date of infection revised, or were excluded from the efficacy analysis (12 subjects whose Day 0 specimen was HIV positive), thereby increasing the resolution power in analyzing the differences of placebo versus vaccine.

Conclusions:

These results demonstrate that this assay is useful for detection of HIV infection in the setting of vaccination, which may be important for donor screening in the future if widespread HIV vaccination is implemented.