Safety and Immune Responses to a DNA-Based Human Immunodeficiency Virus (HIV) Type I Env/Rev Vaccine in HIV-Infected Recipients: Follow-up Data

To the Editor—We recently reported the safety and immunologic response to a DNA vaccine containing env/rev in a group of untreated healthy human immunodeficiency virus (HIV)–infected subjects with CD4 lymphocyte counts >500 cells/μL [1]. No significant adverse experiences occurred, with some evidence for antibody responses and occasional cell-mediated immune responses. We now report an additional cohort immunized with a 300-μg dose by jet injection (JI) or by needle (N), follow-up safety data over >2.5 years for the whole cohort, and results of boosting with 1 mg of vaccine.

The safety profile for the vaccine continues to be excellent. No participant experienced a significant adverse response requiring interruption or withdrawal from study. Anti-DNA antibody was detected in 1 subject with a borderline antinuclear antibody level before vaccination, and 2 others had transient chemistry abnormalities immediately before boosting, with resolution 2 weeks later. Local mild-to-moderate reactions were noted with 9 of 17 JI injections, compared with 4 of 54 with N injections.

We compared the immune responses to primary vaccine series (300 μg × 3) administered by JI versus N, measured at entry, week 21 (1 week after 3d dose), and week 36 (4 months after 3d dose). Responses were defined as in our original paper [1]. No subject in either 300-μg group had a >20% increase or decrease in CD4 lymphocyte count, compared with the value at entry. No subject had a >0.5 log change in viral titer in plasma, compared with the value at entry. For lymphoproliferative response, we defined response as stimulation index (SI) >4 above baseline value. Four subjects in the JI group were studied: 1/4 responded to gp120 and rev antigens; 1/4 responded only above baseline value. Four subjects in the JI group were studied: 1/4 responded to gp120 and rev antigens; 1/4 responded only to rev. Three patients in the N group were studied: 3/3 responded to gp120; none responded to rev.

We defined an antibody response as a geometric mean titer ≥2× the baseline value. After JI, 0/5 responded, whereas 3/5 immunized by N responded. For immune responses to 1 mg boosting, we compared values at time of boost (≥6 months after primary immunization series) with those 2 and 4 weeks later. Five of the 12 subjects available for boosting had begun antiretroviral therapy. No subject had a ≥20% increase or decrease in CD4 lymphocyte count, compared with the value at boost. For HIV quantitation in plasma, no subject had a ≥0.5 log change in viral titer, compared with titer at boost. When stimulated with gp160, none of 12 subjects showed a rise in SI (range, 0.8–5.1 before boost and 0.8–4.5 after boost); SIs increased in 3 of 12 subjects in response to rev (range, 0.5–5 before and 0.7–6.1 after). The responders were not receiving antiretroviral therapy. Three of 10 assessable subjects had a ≥2-fold geometric mean titer rise, compared with levels at boost; none had been receiving antiretroviral therapy.

There were no clear differences in CD4 cell count, viral load, or immunologic responses between patients immunized by JI and those immunized by N, although more lymphoproliferative activity (LPA) and antibody increases were seen in the N-injected cohort. Boosting of all cohorts (30 μg–100 μg–, and both 300–μg groups) with 1 mg of the construct resulted in occasional LPA and antibody responses (without regard to whether they had initiated antiretroviral therapy) and no significant changes in CD4 cell counts or viral loads. Adverse experiences were minor, although more local tenderness was seen after JI. No subject withdrew because of toxicity. Safety monitoring for follow-up safety data over >2.5 years did not reveal any adverse events that were interpreted as related to the vaccine.

The study began in 1994, before the dynamic daily turnover in CD4 lymphocyte counts and viral load was recognized [2, 3]. It is now theorized that viral replication and CD4 turnover must be suppressed to elicit a potentially protective immune response to HIV vaccine [4, 5]. We are currently conducting such a trial, using env/rev- and gag/pol-containing constructs in patients whose viral production is maximally suppressed with highly active antiretroviral therapy [6].

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