

## LONG-TERM EFFECTS OF THERAPEUTIC VACCINATION WITH RGP 120

Therapeutic vaccination could be a valuable attribution to HIV treatment. Although therapeutic vaccinations with rgp (recombinant glycoproteine) vaccines have shown to induce an immune response, no clear effect on clinical endpoints has been found [1,2]. To our knowledge data on long-term effects of therapeutic vaccination studies are not available. At the Municipal Health Service of Amsterdam long-term effects of a phase 1, rgp 120 therapeutic vaccination study (conducted in 1993-1994 and sponsored by Genentech) were evaluated. In 1993 fifteen males and three females were included. MN rgp 120/HIV-1 [3] was given alone (600 µg, n = 6) or concurrently (300 µg of each, n = 6) with III B rgp 120/HIV-1. Six subjects received a placebo. Vaccination was given at weeks 0, 4, 8, 12, 16, 20 and 32 to HIV-1 infected subjects with a known date of seroconversion and a CD4 T cell count > 400 cells/mm<sup>3</sup>. Participants were anti-retroviral therapy naive, infected by a NSI HIV variant and comparable in age, sex, riskgroup, duration of HIV infection, and viral load. However, despite randomization, the mean number of CD4 T cells was higher in the placebo group (645/ mm<sup>3</sup>) then in the group that received MN rgp 120 (495 / mm<sup>3</sup>). All participants received 7 vaccinations.

In order to explore long-term effects the two groups of vaccinees were combined (n = 12). Nineteen subjects, matching the inclusion criteria of the Phase 1 study and selected from the same time period, were added to the placebo group (n = 25). Increasing the number of controls made the mean CD4 T cell count comparable between groups. The mean follow-up was 47 months for vaccinees and 54 months for controls. Using Cox regression analysis we studied progression to AIDS, death, CD4 T cell counts < 200 cells/ mm<sup>3</sup> and NSI/SI switch. Although small numbers limited our analysis, we did not find any differences in progression to endpoints. We studied the rate of CD4 T cell decline before and after the start of vaccination using piece-wise linear regression analysis with correction for repeated measurements within one person. The mean CD4 T cell decline per year before vaccination was 74 cells/mm<sup>3</sup> for vaccinees and 65 cells/mm<sup>3</sup> for controls (p= 0,67). After the start of vaccination the mean CD4 T cell decline per year was 20 cells/mm<sup>3</sup> for vaccinees and 17 cells/mm<sup>3</sup> for controls (p= 0,58). Within both groups there was no significant change in CD4 T cell decline before and after vaccination (fig.1). Fifty percent of the vaccinees and ten percent of the controls received anti-retroviral medication ((non-)nucleoside reverse transcriptase inhibitors, with or without protease inhibitors) at some point during the follow-up study. Despite this difference CD4 T cell decline was comparable between groups. This does not suggest an additional effect of therapeutic vaccination on anti-retroviral therapy.

This long-term follow-up study of therapeutic vaccination with a rgp 120 vaccine showed neither a positive nor a negative effect of vaccination on CD4 T cell decline. We found no evidence for a difference in progression to clinical endpoints between groups. The results of this exploring study do not suggest an additional effect of vaccination on anti-retroviral therapy.

#### REFERENCES:

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Predicted mean CD4+ decline before and after vaccination with rgp 120

