VAC-3S immunotherapeutic HIV vaccine combined with ART is Immunogenic and Safe. Phase II Initial Analysis of the IPROTECT Multicenter European Study.

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METHODS
Prospective, randomized, placebo-controlled, double-blind, 3-step study in Europe, assessing immunotherapeutic properties of VAC-3S at 16, 32, 64 µg with 3 IM base immunizations at 4 weeks intervals and 3 maintenance boosters in the 16, 32 µg arms. Ninety HIV-1 infected patients with 200-349 and 350-500 CD4 cells/mm3 planned, 40 % and 60 % of the patients respectively. Primary endpoint is immunogenicity measured by total anti-3S Ig at week 12 measured by ELISA. Secondary endpoints include: T lymphocyte activation/differentiation, HIV DNA, inflammatory biomarkers.

Figure 2: Study Plan

Figure 3: Sample size / Randomisation. The total sample size of the study to evaluate the null hypothesis for the primary endpoint is estimated at 90 patients assuming an overall type I error of 2.5 %, one-sided test, with the power of at least 80 %. The assumptions regarding humoral responses are 0% in the placebo group, 52 % in the 16 µg group, 62 % in the 32 µg group and 72 % in the 64 µg group.

IMMUNOREACTIVITY

Weeks

First step of inclusion: 6 patients; 32 µg
3 patients: 16 µg
2 patients: placebo

Second step of inclusion: 6 patients; 64 µg
3 patients: 16 or 32 µg
2 patients: placebo

Third step of inclusion: 55 patients: 16 µg, 32 µg, 64 µg or placebo

Figure 4: Immunogenicity. The first step of inclusion permitted to evaluate the safety of the 32 µg dose, the second step of inclusion of the 64 µg dose. During these two steps, the minimum required interval between two inclussions was of 60 days. The third step of inclusion enrolled the remnant of the patient population without timing limitation between inclussions. Total Anti-3S Ig were measured by ELISA. Arbitrary Units are reported as a log10 scale for each patient. Blue vertical bars: VAC-3S/placebo administration. Temporary threshold of 30 AU above which immunological and virological effects were demonstrated during the phase Ila is represented by the grey area. Results are blinded.

REFERENCES

Acknowledgements

All related (possibly related, probably related and related) Treatment Emergent Adverse Events are reported by severity for 86 patients who received 291 VAC-3S/placebo Administrations corresponding to a total of 542 injections (an administration = 1 injection in each arm for methodology constraints).

CONCLUSION

VAC-3S is confirmed safe and immunogenic in HIV-infected patients with CD4 counts between 200 and 500 CD4+ T cells/mm3. The current schedule of administration permits sustained levels of anti-3S antibodies. Further analysis will be conducted in order to confirm biological effects on T cell homeostasis and HIV reservoir observed during the phase Ila.

SAFETY

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Table 1: Demography. 86 patients were enrolled in the study in 13 investigational centers in France, Spain and Germany: 36 patients in the low CD4 strata and 50 patients in the high CD4 strata; 16 women and 68 men.

An event was considered serious if: a) it was life threatening; b) required hospitalization or prolongation of existing hospitalization; c) resulted in persistent or significant disability or incapacity. All related events (possibly related, probably related and related) were reported by severity.

Figure 4: Immunogenicity. The first step of inclusion permitted to evaluate the safety of the 32 µg dose, the second step of inclusion of the 64 µg dose. During these two steps, the minimum required interval between two inclussions was of 60 days. The third step of inclusion enrolled the remnant of the patient population without timing limitation between inclussions. Total Anti-3S Ig were measured by ELISA. Arbitrary Units are reported as a log10 scale for each patient. Blue vertical bars: VAC-3S/placebo administration. Temporary threshold of 30 AU above which immunological and virological effects were demonstrated during the phase Ila is represented by the grey area. Results are blinded.

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