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A first-in-human phase I/II trial demonstrates the safety and the immunogenicity of a lentiviralbased therapeutic HIV vaccine eliciting potent polyfunctional multispecific CD8 and CD4 Tcell responses in HIV-infected individuals

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Background: One approach to reach the functional cure in HIVinfected individuals is the development of Tcell immunebased strategies able to contain viral replication while preserving CD4+ T cells. We assessed the safety and efficacy of a therapeutic antiHIV1 primeboost vaccine regimen based on intramuscular injection of two integrative lentiviral vectors (ClinicalTrials.govIdentifier: NCT02054286).

Methods: The randomized, placebocontrolled trial enrolled 38 HIVinfected individuals on suppressive ART and aimed at comparing the safety, tolerability and immunogenicity of the therapeutic vaccine candidate at 3 incremental doses (5.106, 5.107 or 5.108 TU) versus placebo.

The vaccination regimen consisted of two intramuscular injections 8 weeks apart with nonreplicative and self inactivating lentiviral vectors encoding for immunogenic regions of the HIV GAG, POL and NEF proteins under the regulation of the ß2microglobulin human promoter.

Vaccineinduced HIVspecific Tcell in peripheral blood were characterized by intracellular cytokine staining in all participants, placebo included, before and after ART interruption and up to 24 weeks after the first injection.

Results: With the lack of any serious adverse events in all 38 participants and no safety concerns related to the treatment, the clinical data confirmed safety and tolerance of the lentiviralbased therapeutic vaccine.

Analysis of the immunological data demonstrated the ability of the vaccine to elicit multispecific and polyfunctional cellular immune responses in vaccinated subjects. The vaccine candidate was highly immunogenic at all doses when compared to the placebo group: i) 93% of the vaccinated subjects showed vaccine specific CD4+ and CD8+ Tcell responses compared to 66,6% of the placebo group; ii) a high frequency, from 0.097 to 0.874%, of functional Tcells able to produce at least 2 or 3 cytokines among IFNγ, TNFα and IL2 was evidenced; iii) a dose effect was observed when comparing the 3 groups, with greater magnitude with the highest dose; iv) sustainable responses were characterized up to 24 weeks.

Conclusions: This firstinhuman study demonstrates the safety, tolerability and immunogenicity of a lentiviralbased therapeutic vaccine regimen.

We are currently evaluating the impact of ART interruption of vaccination on CD4 Tcell levels, plasma viral load and viral reservoirs of the induced immune response to optimize the design of the planned Phase II.

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