

Preclinical evaluation of an mRNA HIV vaccine combining rationally selected antigenic sequences and adjuvant signals (HTI-TriMix): Erratum Phase I clinical trial of an intranodally administered mRNA-based therapeutic vaccine against HIV-1 infection: Erratum

The authors of these papers [1,2] inform the readers that the study product iHIVARNA-01 had an error – the RNA sequence contained by mistake a second start codon in front of the HTI immunogen coding sequence.

This error is likely to influence the expression of the HTI protein from the mRNA vaccine. The degree to which this impacted the expression of HTI remains unclear. The results of the preclinical study showed an induction of an immunogen specific T-cell response in mice which could not be correlated with known HTI expression, as the expression level of the HTI protein had not been assessed. Similarly, in the clinical studies, the level of expression of the immunogen was not quantified.

The approval of the trial application for iHIVARNA-01 was based on the outcomes of in-vivo potency assays developed to analyse the functionality of the HIVACAT construct, and an in-vitro DC assay of the erroneous and correct HIVACAT/HTI mRNA.

The in-vivo assay showed a positive immune read out after intranodal immunization of mice with the HIVACAT (HTI) mRNA combined with murine TriMix. In addition, a comparison between the HIVACAT and HIVACAT-DCL construct – the latter with only one start codon and codifying for HIVACAT T immunogen – revealed no significant differences in the in-vivo potency assay.

The in-vitro DC assays tested the erroneous and correct HIVACAT/HTI mRNA. The correct HIVACAT/HTI mRNA also encoded a cytoplasmic region of human DC-LAMP sequence to improve the antigen presentation via MHC class II. Our preliminary results showed that both versions had quite similar effects on DC maturation and induced T-cell proliferation and Th1 cytokine at almost the same levels.

However, in summary as the level of expression of HTI was not measured it is unknown how the product error could have affected the results in this clinical study.

References

1. Guardo AC, Joe PT, Miralles L, Bargalló ME, Mothe B, Krasniqi A, *et al.* **Preclinical evaluation of an mRNA HIV vaccine combining rationally selected antigenic sequences and adjuvant signals (HTI-TriMix).** *AIDS* 2017; **31**:321–332.
2. Leal L, Guardo AC, Morón-López S, Salgado M, Mothe B, Heirman C, *et al.* **Phase I clinical trial of an intranodally administered mRNA-based therapeutic vaccine against HIV-1 infection.** *AIDS* 2018; **32**:2533–2545.