Retrovirology



Poster presentation



# P18-07. *Ex vivo* production of autologous HIV-1 to be used as immunogen in autologous dendritic cell-based therapeutic vaccine (clinical trial DCV02)

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## Background

The use of inactivated autologous HIV-1 from infected patients as an antigen formulation for a therapeutic vaccine involves the isolation and propagation of HIV in cell-culture conditions fulfilling the clinical grade Good Manufacturing Practice (GMP), and the development of analysis systems to detect adventitious agents. In this study we present the development of heat inactivated autologous HIV-1 produced *Ex vivo* to be used as immunogen in human therapeutic vaccine (Clinical Trial DCV02).

## Methods

Autologous HIV-1 was isolated from 14 infected subjects (4.2 log HIV-1 cp RNA/mL plasma), by co-culture of the CD4-enriched PBMCs from these infected patients with CD4-enriched PBMCs pre-activated from healthy donors, during 21 days in X-Vivo 20 media, 10% of AB human serum and IL-2. Cell-culture supernatants were concentrated by ultrafiltration. Viral productions were analyzed by ELISA p24Ag-HIV-1 and RNA cp/mL in the final product. Adventitious agents were analyzed by cell culture in PBMCs, MRC-5 and VERO cell lines, microbiology cultures, gram and mycoplasma tests. The HIV-1 protease (PR) sequence was also analyzed.

## Results

To obtain de immunogen from 14 patients it was necessary to perform 21 cell-cultures to produce the immunogen in optimal cGMP conditions. From each patient, a median of 80 mL of cell culture supernatant with a median of 8,8 log HIV-1 cp RNA/mL were heat inactivated and concentrated until a volume of 1 mL of final product with 9.8 log HIV-1 cp RNA/mL. No differences were found between HIV-1 PR sequences of cell culture and plasma. Heat inactivation reached an infectivity reduction median of 5.5 Log in 11 days PBMCs cell cultures.

## Conclusion

*Ex vivo* isolation and production of autologous HIV-1 by cell co-culture fulfilling clinical grade GMP for therapeutic vaccine is feasible, but requires a concerted effort to guarantee the quality and safety of the final product.