PHASE 2 CLINICAL TRIAL OF VEDOLIZUMAB AND ART IN SUBJECTS WITH NO PREVIOUS ART

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CROI Conference on Retroviruses and Opportunistic Infections

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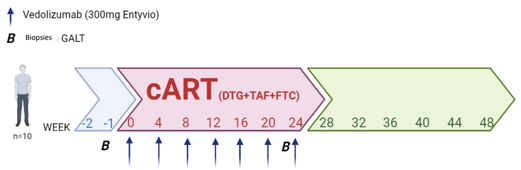
INTRODUCTION

Complete HIV remission off treatment has not been possible. The aim of this study was to evaluate the safety and efficacy of Vedolizumab (anti-α4β7 mAb) combined with ART to achieve permanent virological remission in ART naïve subjects after ART interruption.

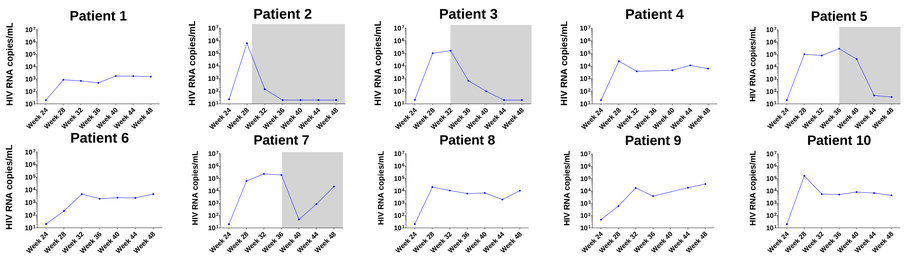
MATERIALS AND METHODS

Open-label, single-arm phase 2 clinical trial. Ten patients were enrolled with CD4-T cells count of > 350 cells/µl and viral load >10.000 copies/ml. The time of infection was 75 [40-82] days. Patients started ART together with Vedolizumab infusions (300mg) at week 0, 4, 8, 12, 16, 20 and 24 weeks. At this time point ART and Vedolizumab treatment were interrupted. Biopsies were obtained from ileum and caecum at baseline (BL) and week 24. Subjects were monitored monthly by measuring CD4+T-cell counts, plasma viremia, Vedolizumab levels, HIV reservoir and flow cytometry to measure α4β7 levels and immune check point molecules among other markers. Criteria to restart ART were CD4 T-cells below 350 cell/µl or viral load >10^5 HIV-RNA copies/ml in two consecutive measurements.



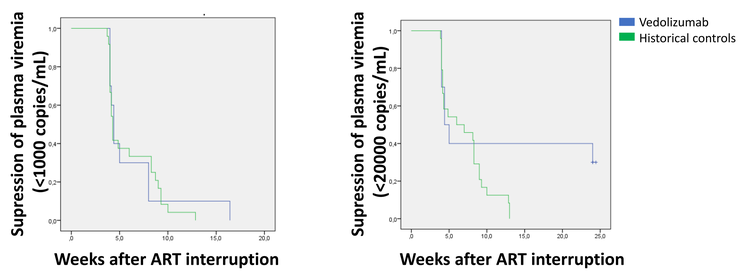
RESULTS

1_ Four patients restarted ART due to an increase of viral load (>10^5 HIV-RNA copies/ml). The other six patients did not show criteria to restart ART and completed the follow up with of 1590, 6250, 10000, 36450 and 4300 HIV-RNA copies/ml.

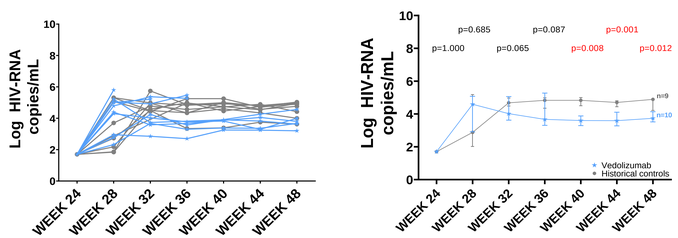


2_ No differences on either time to restart ART or time to first plasma viremia of >1000 HIV-RNA copies/ml when compared to historical controls of ART interruption (n=24) were observed (A). Nevertheless, Vedolizumab trial group present a viral load set point significant lower to the historical control group (B).

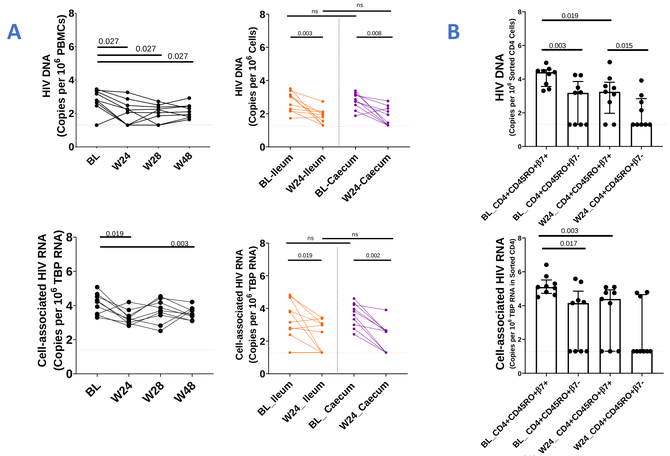
A



B



3_ We observed a decrease in HIV-DNA (p=0.027) and cell-associated HIV RNA on peripheral PBMCs (p=0.003), ileum and caecum cells over the follow up(A). The decrease on PBMCs was prominent in sorted CD4+CD45RO+ β7+ cells (B). Patients who restart ART presented higher levels of HIV reservoir on PBMCs (C).



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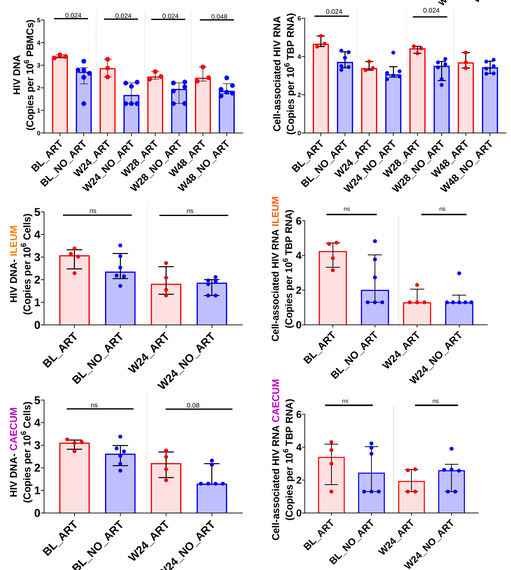
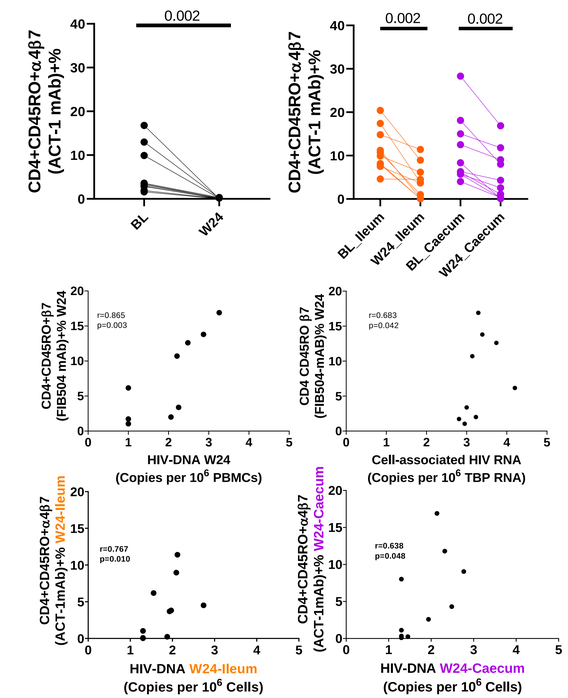
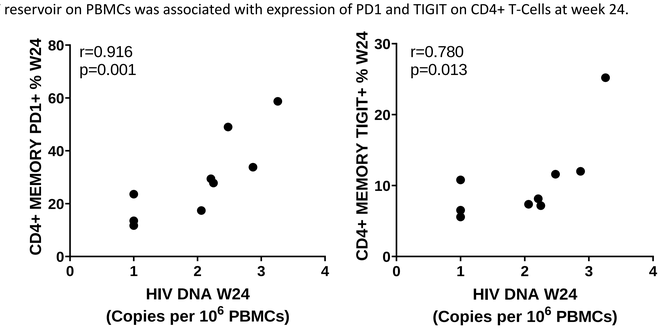


4_ At W24, α4β7 was completely blocked by Vedolizumab on peripheral CD4+ T-Cells, unlike on gut (A). HIV reservoir was associated with expression levels of α4β7 integrin (B).



5_ HIV reservoir on PBMCs was associated with expression of PD1 and TIGIT on CD4+ T-Cells at week 24.



DISCUSSION

Vedolizumab was safe and well tolerated. No dramatic virological remission after ART interruption was found in naïve subjects. Reservoir establishment in PBMCs, IL and CC was associated with α4β7 and immune check point molecules expression.

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