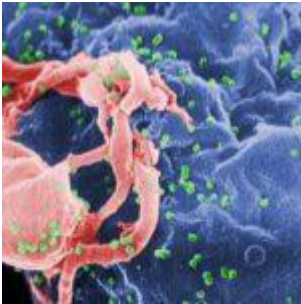


# Rethinking HIV remission strategies: end of the road for anti- $\alpha 4\beta 7$ ?



An immunological therapeutic alternative to HIV antiretroviral treatment (ART) is one of the goals of the HIV community. Vedolizumab, a monoclonal anti- $\alpha 4\beta 7$  antibody, is an example of such a potential immunotherapeutic.  $\alpha 4\beta 7$  is an integrin that facilitates T cell homing to gut-associated lymphoid tissue and has been shown to contribute to HIV pathogenesis. HIV binds to  $\alpha 4\beta 7$  which then triggers T cells to develop virological synapses, facilitating cell to cell transmission of the virus. Therefore targeting  $\alpha 4\beta 7$  could potentially reduce cell to cell transmission and control viral replication.

We have reported summaries of studies that have tested the effect therapeutic effect of anti- $\alpha 4\beta 7$  in non-human primates. The first study [Byrareddy et al., 2016](#) ([HIV R4P Highlights:  \$\alpha 4\beta 7\$  antibody and ART: a novel HIV therapy](#)) demonstrated the ability of anti- $\alpha 4\beta 7$  in preventing viral rebound in the absence of ART. This promising result provided sufficient motivation to conduct a phase 1 clinical trial, which began in 2016. In the phase 1 trial., Sneller et al., recruited 20 HIV infected individual with ART-induced viral suppression. Participants then received 9 doses of vedolizumab in a 30 week window period, during which ART was interrupted after the 7th dose. Treatment resulted in down-regulation of  $\alpha 4\beta 7$  on CD4 T cells and an increase in CD4 T cell count, both of which

rebounded to baseline levels post-treatment. Researchers showed that vedolizumab had no effect on HIV replication when ART was interrupted, demonstrated by viral rebound in all 19 individuals who completed the study.

Sneller *et al.*, showed in a phase 1 trial that vedolizumab is safe to use in HIV infected individuals, but unfortunately is unable to prevent viral rebound in the absence of ART. Results from this study, are in line with [recently published studies - Mascio \*et al.\*, 2019; Abbink \*et al.\* 2019, Iwamoto \*et al.\*, 2019- which attempted but were unable to confirm Byrareddy \*et al.\*, findings](#). Importantly, these results highlight the importance of confirmatory animal studies before embarking on clinical studies and trials.

\*\*It should be noted that phase 1 trials are not designed to demonstrate an effect of the intervention, but to demonstrate the **safety profile of the** intervention.

Journal Article: Sneller *et al.*, 2019. [An open-label phase 1 clinical trial of the anti- \$\alpha\$ 4 \$\beta\$ 7 monoclonal antibody vedolizumab in HIV-infected individuals](#). Science Translation Medicine.