LATE BREAKERS

TUAA0202LB

A randomised controlled trial comparing the impact of antiretroviral therapy (ART) with a "Kick-and-Kill" approach to ART alone on HIV reservoirs in individuals with primary HIV infection (PHI); RIVER trial

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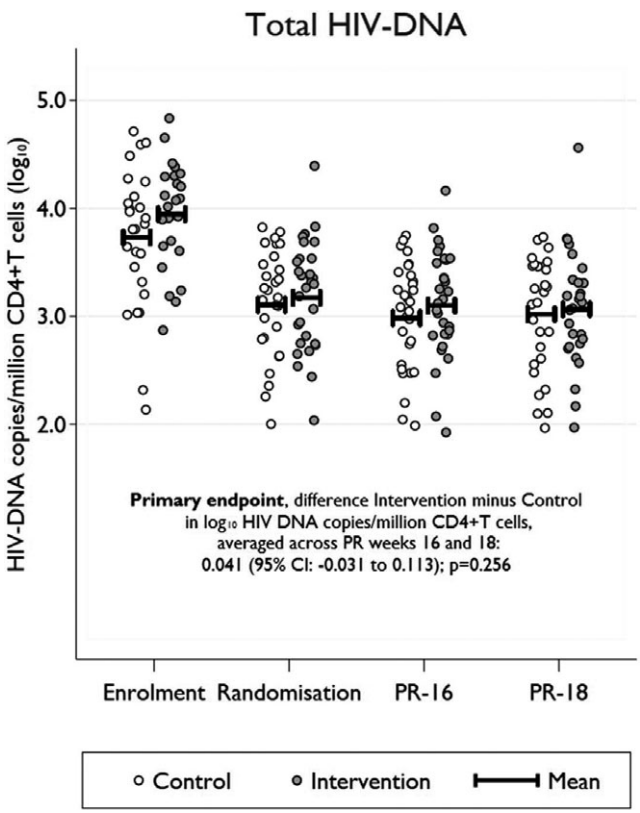
Background: ART alone is unable to cure HIV because of an inaccessible pool of latently infected cells, the HIV reservoir. In the first randomised controlled trial (RCT) of a "kick-and-kill" strategy, amongst participants with PHI on ART, we investigated the impact of HIV-specific T-cell vaccines and a latency reversing agent (vorinostat) on the HIV reservoir.

Methods: Individuals who started ART within four weeks of confirmed PHI diagnosis with suppressed plasma HIV-RNA were randomised to either ART plus vaccination with ChAdV63.HIVconsv prime <1 week post-randomisation (PR) and MVA.HIVconsv boost (eight weeks later) followed by 10 doses of 400 mg oral vorinostat taken every three days (intervention) or ART alone (control).

The two arms were compared for the primary outcome (log_{10} total HIV-DNA copies/million from CD4 + T-cells at weeks PR-16&18) using analysis of covariance adjusted for baseline level. Secondary endpoints included quantitative viral outgrowth measuring replication-competent HIV-1 reservoir at week PR-16, HIV-specific CD4 + and CD8 + T-cell responses by intracellular cytokine staining at weeks PR-9&12, histone acetylation pre&post vorinostat and adverse events.

Results: 60 male participants were randomised at 6 UK sites (30 intervention, 30 control), with median: age 32 years, 26 weeks since ART start and CD4 + count 708 cells/mm^3. All participants completed follow-up. There was no difference between the arms in the primary outcome (intervention vs. control: 0.041 (95% CI −0.031, 0.113) log10 HIV-DNA copies/million CD4 + T-cells $p = 0.256$), or in the proportion with undetectable viral outgrowth (0.42 (95% CI 0.13, 1.37) $p = 0.151$) Participants with undetectable viral outgrowth had significantly lower total HIV-DNA. Participants in the intervention arm showed significantly higher HIV-specific CD4 + (IFNg/IL2/TNFa/CD154) and CD8 + (IFNg/TNFa) T-cell responses post vaccination than control. Histone acetylation increased 3.2-fold two hours post-vorinostat ($p < 0.001$). There was no virological failure or intervention-related SAE. More clinical adverse events were reported in the intervention arm, all were mild/moderate.

Conclusions: In the first "kick-and-kill" RCT in PHI, despite evidence of robust vaccine-induced HIV-specific T-cell immunity and vorinostat activity, there was no impact on measures of HIV reservoir compared to ART alone. Vaccination and vorinostat did not raise any safety concerns. Further analyses are ongoing to explore mechanisms to explain these findings.



Abstract TUAA0202LB-Figure 1. of total HIV DNA by arm.

TUAA0206LB

Evaluation of an antibody to Alpha4Beta7 in the control of SIV infection

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Background: It was recently reported that treatment with an antibody to the a4b7 integrin in rhesus macaques infected with SIVmac 239 having a stop codon in nef (SIVmac239nefstop) was associated with prolonged post-treatment suppression of viremia. The present study was undertaken to try to confirm and extend those observations.

Methods: Twenty-two Mamu-A001, Mamu-B008 and Mamu-B017 negative juvenile to adult Indian rhesus macaques (>4 kg or three years; mixed sex) were infected intravenously with 200 $TCID_{50}$ SIVmac239nefstop (courtesy F. Villinger). At five weeks post-infection (wpi), combination anti-retroviral therapy (cART) was started with