Results: 5675 outpatients completed an exit survey. There were no differences by arm (Table 1). 52% of outpatients in the HIVST arm tested for HIV compared to 14% in Optimized PITC (AOR: 6.6 $p < 0.001$) and 12% in PITC (AOR: 7.6 $p < 0.001$). For HIVST, 60% of outpatients in need of testing (defined as tested >12 months ago and never tested HIV-positive) were tested compared to 18% in Optimized PITC and 16% in PITC. There was no significant difference in the proportion of clients tested who reported previously testing HIV-positive (≤1% for all arms). Positivity rates did not differ by arm, however, HIVST was associated with a higher absolute number of new positives identified compared to Optimized PITC (AOR: 2.9, $p = 0.01$) and PITC (AOR: 4.1, $p = 0.002$). Participants who were tested by HIVST were more likely to want to test again using the same method and more likely to recommend testing to others compared to those tested by Optimized PITC or PITC. No adverse events were reported in the HIVST arm.
Conclusions: Facility-based HIVST in outpatient waiting-spaces dramatically increased HIV testing and identification of HIV-infected persons among outpatients in Malawi, with minimal risk for loss of confidentiality or adverse events. Analyses for linkage to care are underway. Evaluations of routine program implementation are needed to determine best strategies to take facility-based HIVST to scale.

WEAA0101

Chidamide reactivates and diminishes latent HIV-1 DNA in patients on suppressive antiretroviral therapy

Y. Sun[1]; J. Li[1]; J. Ma[2]; C. Wang[1]; F. Bai[1,3]; K. Zhao[1,4]; Z. Yu[1,5]; W. Kang[6]; Y. Zhuang[1]; N. Yao[1]; Q. Liu[1]; B. Dang[1]; B. Wang[1]; Q. Wei[1]; Z. Liu[1]; L. Wang[1]; W. Kang[1]; L. Wang[1]; J. Xia[1]; T. Wang[7] and T. Zhu[8]
[1]Fourth Military Medical University, Xi'an, China, [2]Xi'an Jiaotong University, Xi'an, China, [3]323th Hospital of PLA, Xi'an, China, [4]Xi'an Communication Institute, Xi'an, China, [5]Political Work Department of People's Republic of China Central Military Commission, Beijing, China, [6]Fourth Military Medical University, Department of Infectious Diseases, Tangdu Hospital, Xi'an, China, [7]Jinan University, Institute of Life and Health Engineering, College of Life Science and Technology, Guangzhou, China, [8]University of Washington, Department of Laboratory Medicine, Seattle, United States

Background: A proposed strategy to purge HIV reservoir is to reactivate provirus transcription with latency-reversing agents (LRAs), inducing viral antigen expression and allowing immune-mediated clearance of reservoir cells in the presence of combination antiretroviral therapy (cART). Here we evaluated the safety and efficacy of chidamide, a benzamide histone deacetylase inhibitor, in patients on suppressive cART.
Methods: Seven aviremic HIV-1-infected patients received eight oral doses of 10 mg chidamide twice a week (Tuesday/Friday) for four weeks while maintaining baseline cART. Safety was evaluated at each visit and plasma concentrations of chidamide was measured by liquid chromatography-mass spectrometry. Histone acetylation levels in $CD4^+$ T cells were analyzed by flow cytometry. Plasma HIV RNA was determined using Cobas Taqman HIV-1 Test, v2.0. Cell-associated HIV RNA (CA-HIV RNA) and total HIV DNA (CA-tHIV DNA) were quantified by the SupBio PCR test in PBMCs. Thirteen plasma biomarkers of inflammation were evaluated by luminex multiplex assays and ELISA. Changes from baseline to specific time points were compared using Wilcoxon matched-pairs signed-rank tests, and a two-sided *p*-value of less than 0.05 was considered significant.
Results: All participants (6 male, 1 female) completed full chidamide dosing, and showed acceptable drug tolerance with only grade 1 adverse events presented. No drug accumulation effects were detected per chidamide dosing. In addition, the cyclic increase of histone acetylation in $CD4^+$ T cells was observed. All participants showed robust and cyclic viremia (peak viremia range 147 to 3850 copies/mL) as well as increased CA-HIV RNA (median peak increase 9.4-fold vs. baseline, range 2.0-fold to 34.9-fold) during chidamide treatment. At day 56, plasma HIV RNA of all participants recovered to undetectable level. Furthermore, we discerned the significant reduction of CA-tHIV DNA (day 27 vs. baseline, $p = 0.018$, and day 56 vs. baseline, $p = 0.028$). Equally important was that chidamide exhibited an anti-inflammatory property as evidenced by inhibition of pro-inflammatory cytokines: MCP-1, MMP-9, IP-10, LBP, P-selectin, and CD40 ligand.
Conclusions: Chidamide can safely disrupt the latency of HIV DNA resulting in the clearance of reactivated reservoirs, which makes it a promising candidate toward the eradication of HIV reservoir.

WEAA0102

The antiretroviral CCR5-inhibitor maraviroc effectively reverses HIV latency by phosphorylation of Nf-κB

J. Symons[1]; S.F.L. vanLelyveld[2];W. deSpiegelaere[3];A.M.J. Wensing[4]; J.M. Zerbato[1]; P.M. vanHam[4];J. Drylewicz[5]; A. Middel[2]; A.I.M. Hoepelman[2]; P.U. Cameron[1,6]; H.K. Lu[1]; A.I. Dantanarayana[1]; J.A.M. Borghans[5]; L. Vandekerckhove[3]; S.R. Lewin[1,6]; K. Tesselaar[5] and M. Nijhuis[4]
[1]The Peter Doherty Institute for Infection and Immunity, The University of Melbourne, Melbourne, Australia, [2]University Medical Centre Utrecht, Department of Internal Medicine and Infectious Diseases, Utrecht, Netherlands, [3]Ghent University, Department of Internal Medicine, Ghent, Belgium, [4]University Medical Centre Utrecht, Department of Medical Microbiology, Virology, Utrecht, Netherlands, [5]University Medical Centre Utrecht, Department of Immunology, Utrecht, Netherlands, [6]Alfred Hospital and Monash University, Department of Infectious Diseases, Melbourne, Australia

Background: One strategy to eliminate latently infected cells in HIV-infected individuals on antiretroviral therapy (ART) is to induce HIV transcription with latency reversing agents (LRAs). Potent non-toxic LRAs are urgently warranted. The clinically approved CCR5-inhibitor maraviroc (MVC) demonstrated an increase in HIV transcription *in vitro* and may therefore act as an LRA. We investigated the effect of MVC on HIV transcription and its mechanism of action *in vitro*, *ex vivo* and *in vivo* during a MVC-intensification trial.
Methods: Activated PBMCs were infected with HXB2 (MOI 0.01) and cultured with MVC. Seven days post-infection p24 was measured in supernatant by ELISA (n = 9). Changes in NF-κB phosphorylation were assessed by densitometry Western-Blot (n = 2). 5 million resting CD4 T-cells were isolated from HIV infected individuals on ART, treated with MVC or vorinostat and unspliced (US) and multiply spliced (MS) HIV-RNA were quantified by qPCR (n = 6). In a double-blind, placebo-controlled trial, MVC or placebo was added to suppressive ART in immune non-responders (MVC = 10, Placebo = 5). Changes in cell-associated (CA)-US HIV-RNA and NF-κB regulated gene mRNA were quantified by droplet-digital-PCR (ddPCR). Mann-Whitney-U-test and paired T-test were performed using GrapPad-Prism.
Results: *In vitro*, a significant increase in HIV production was observed when MVC (1 pmol/L to 1 μmol/L ($p < 0.02$) to infected PBMC. A 2.5-fold increase in phosphorylated NF-κB was observed in uninfected MVC treated CD4+ T-cells. Additionally, *in vivo*, a significant difference, between MVC and placebo, in NF-kB regulated gene expression, including IFN-g, IL6 and TNF-a, was observed ($p = 0.02$, 0.03, 0.05 respectively). Patients baseline characteristics did not differ between the MVC-intensification and placebo-group. A significant difference in CA-US HIV-RNA expression was detected between baseline and week eight (MVC 1.8-fold increase; placebo 2.5-fold decrease; $p = 0.0121$). *Ex vivo*, MVC induced a 3, 5 and 1.7-fold increase in US HIV-RNA compared to DMSO ($p = 0.0004$) and vorinostat ($p = 0.0496$) respectively. Additionally, MVC induced a 2-fold increase in transcription of MS HIV-RNA compared to DMSO ($p = 0.0245$).

Conclusions: MVC activates phosphorylation of NF-κB and increases HIV-RNA transcription in resting CD4 T-cells. Potency for latency reversal *ex vivo* was more effective than vorinostat. Given the excellent safety profile of MVC, further studies of MVC as an LRA are warranted *in vivo*.

WEAA0103

Activation of latent HIV and SIV RNA transcription *in vitro* and *in vivo* in ART suppressed SIV-infected rhesus macaques by the Ingenol-based protein kinase C agonist, GSK445A

A. Okoye[1,2]; R. Fromentin[3,4]; J. Brehm[5,6]; A. Maxwell[1,2]; M. Vaidya[1,2]; M. Pardons[3,4]; V. Tai[5]; J. Tang[5]; J. Smedly[2]; M. Axthelm[1,2]; J. Lifson[7]; L. Picker[1,2]; L. Trautmann[8,9]; D. Favre[5,6] and N. Chomont[3,4]

[1]Oregon Health and Science University, Vaccine & Gene Therapy Institute, Beaverton, United States, [2]Oregon National Primate Research Center, Beaverton, United States, [3]Centre de Recherche du CHUM, Montreal, Canada, [4]Université de Montréal, Microbiology, Infectiology and Immunology, Montreal, Canada, [5]GlaxoSmithKline, HIV Discovery Unit, Durham, United States, [6]University of North Carolina, HIV Cure Center, Chapel Hill, United States, [7]Frederick National Laboratory, Leidos Biomedical Research Inc., AIDS and Cancer Virus Program, Frederick, United States, [8]Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, United States, [9]Walter Reed Army Institute of Research, U.S. Military HIV Research Program, Silver Spring, United States

Background: Induction of HIV gene expression in latently-infected CD4+ T cells is an essential step for the clearance of proviral reservoirs in virally suppressed individuals. Activation of NF-kB signaling pathway by Protein kinase C agonists (PKCa) is a potent mechanism for HIV latency disruption *in vitro*. However, significant toxicity risks and the lack of evidence supporting their activity *in vivo* have prevented further evaluation of PKCa. Extending prior results, we sort to confirm that GSK445A, a stabilized Ingenol-B PKCa derivative, can induce HIV/SIV transcription *in vitro*, and demonstrate pharmacological activity *in vivo* in ART suppressed SIV-infected RM.
Methods: CD4+ T cells from 3 virally suppressed humans were exposed to increasing concentrations of GSK445A for 30 minutes to measure cell-associated multiply spliced (tat/rev) RNA after 18 hours. Next, CD4+ T cells from virally suppressed humans (n = 5) and RM (n = 3), were exposed for 30 minutes at an optimal dose of 25 nmol/L GSK445A to quantify cell-associated RNA and cell free RNA in the supernatant at 18 hours. Pharmacological activity and tolerability of GSK445A IV was assessed in 5 healthy RM at doses from 10 to 20mg/kg. Finally, 4 adult RM were IV inoculated with SIVmac239, and placed on ART (tenofovir/emtricitabine/dolutegravir) starting 56 days post-infection. After 34 weeks, RM received 3 biweekly doses of GSK445A, IV at 15mg/kg. SIV DNA and RNA in cells and plasma were quantified by qPCR/qRT-PCR.
Results: CD4+ T cells exposed to GSK445A produced unspliced HIV and SIV RNA (gag) and viral particles, indicating that GSK445A efficiently reverses HIV/SIV latency *in vitro*. In vivo, GSK445A tolerability was established around 10 to 15 mg/kg and pharmacological activity demonstrated by CD69 upregulation in CD4+ T cells in blood. In suppressed RM, 3 of 4 individuals showed blips in plasma viral loads approximately 0.5 to 1 log above threshold (15 RNA copies/mL). All but 1 RM showed increases in unspliced SIV RNA in PBMC and increases in SIV RNA/DNA ratio (average transcription per infected cell) following each dose of GSK445A.
Conclusions: These results indicate that GSK445A is a potent latency-reversing agent *in vitro* and is amenable to testing latency disruption strategies *in vivo* in RM models of HIV cure/remission.

WEAA0104

The RNA-binding proteins, SRP14 and HMGB3 play a crucial role in controlling HIV replication and latency

G. Khoury[1]; M.Y. Lee[1]; S. Ramarathinam[2]; S. Sonza[1]; A.W. Purcell[2] and D.F.J. Purcell[1]

[1]Peter Doherty Institute, Microbiology & Immunology, Melbourne, Australia, [2]Biomedicine Discovery Institute, Monash University, Biochemistry and Molecular Biology, Clayton, Australia

Background: HIV latency is known to be reinforced by many impediments to RNA transcription, however translational blocks to HIV replication are less well characterised. The transactivator of transcription Tat protein is essential for progeny virion production in natural infection of HIV. RNA-binding proteins that facilitate translation of Tat may be absent or downregulated in resting CD4+ T cells, the main reservoir of latent HIV. In this study, we examined the role of Tat RNA-binding factors in expression of Tat and control of latent and productive infection.
Methods: Affinity purification-mass spectrometry analysis (nanoLC-MS/MS) was used to detect binding partners of MS2-tagged *tat* mRNA in a T cell-line model of HIV latency (J-Lat6.3). 243 interactions were identified with high confidence using the MiST three parameter scoring system at a threshold cutoff of 0.7. 13 proteins were chosen for follow-up. The effect of knockdown and overexpression of the proteins of interest on Tat transactivation and translation was assessed by luciferase-based reporter assays, and infections with a dual colour HIV reporter virus allowed investigation of the dynamics of latent (BFP+/mCherry+) and productive (EGFP+BFP+/EGFP+mCherry+) infection. Changes over time in the levels of mRNA and protein in activated CD4+ and resting CD4+ T cells after NL4.3-eGFP infection were determined.
Results: After preliminary studies, two candidate proteins, SRp14 and HMGB3 were selected for detailed investigation. Knockdown of SRP14 negatively affected translation of Tat and Tat-mediated transactivation, which led to an increase in latent infection (BFP+ expression), while the knockdown of HMGB3 resulted in an increase in Tat transactivation and translation as well as an increase in productive infection (EGFP+BFP+/mCherry+ expression). Interestingly, these effects correlated with the levels of the proteins in rCD4+ T cells following HIV-1 infection as we observed a decrease in SRp14 levels while HMGB3 peaked very quickly after infection in rCD4+.
Conclusions: Our study revealed that SRp14 is a positive regulator of Tat expression and negative regulator of latent infection, whereas HMGB3 is a negative regulator of Tat expression and positive regulator of latent infection. The role of these proteins in controlling HIV-gene expression during latency will be further assessed as potential drug targets.

WEAA0105

Using the PPARg antagonism to block/lock HIV reactivation in Th17 cells

Y. Zhang[1]; D. Planas[1]; H. Chen[1]; A. Gosselin[1]; J.-P. Routy[2] and P. Ancuta[3]

[1]Universite de Montreal and CHUM Research Centre, Microbiology, Infectiology and Immunology, Montreal, Canada, [2]McGill University Health Centre, Montreal, Canada, [3]Universite de Montreal and CHUM Research Centre, Montreal, Canada

Background: The Th17-polarized cells represent a subset of CD4+ T-cells that orchestrate mucosal immunity against pathogens. The transcriptional profile of Th17 cells is compatible with optimal HIV replication. Th17 are strategically located at mucosal barrier surfaces and represent the first HIV infection targets during sexual transmission. Finally, Th17 cells are long lived and support HIV reservoir persistence during antiretroviral therapy (ART). Of note, the nuclear receptor PPARγ is a negative regulator of HIV replication and a