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Session: **CS3**: Saturday May 2 – 15:00:17:00 – Antiretroviral Therapy and Resistence

Track:	Clinical Sciences
Subject:	Clinical Trials and Observational Studies of Antiretrovirals and Other HIV Therapies
Presentation Type:	Oral
Title of Abstract:	**Effect of Metformin Treatment on Non-Diabetic HIV-Infected Individuals on ART**
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Abstract

HIV preferentially infects gut-homing CCR6^{+}Th17 cells *via* mechanisms dependent on the mechanistic target of rapamycin (mTOR), a positive regulator of HIV transcription. Here, we evaluated immunological/virological effects of Metformin (an indirect mTOR inhibitor) in a cohort of ART-treated people living with HIV (PLWH).

Metformin (850 mg bid) was administered for 12 weeks in 22 ART-treated PLWH. Participants were non-diabetic, on ART for >3 years, with <40 HIV-RNA copies/ml plasma for >3 months, and CD4/CD8 ratios ≤ 0.7. Blood was collected at baseline (Visit 1), after 12 weeks of Metformin (Visit 2), and 12 weeks after the end of Metformin (Visit 3). Sigmoid colon biopsies (≈32 biopsies/participant) were collected at Visits 1 and 2 (n=13). Matched blood/colon memory CD4^{+} T-cells were phenotypically characterized and sorted by flow cytometry. HIV-DNA/RNA were quantified by ultrasensitive real-time nested-PCR/RT-PCR. Plasma soluble factors were quantified using the R&D Systems Multiplex Assay and ELISA (sCD14, LBP, I-FABP).

Investigations on matched blood/colon samples revealed that Metformin ***i)*** decreased the frequency of colon CD4^{+} T-cells (7.34% vs. 4.71%; p=0.019; Visit 1 *vs.* 2), suggestive of reduced colon inflammation; ***ii)*** decreased mTOR phosphorylation in colon CCR6^{+}CD4^{+} T-cells (13% vs. 7.87%; p=0.0087; Visit 1 *vs.* 2); ***iii)*** tended to decrease the expression of CCR5 and integrin β7, and to increase expression of SAMHD1 in colon CCR6^{+}CD4^{+} T-cells; and ***iv)*** decreased sCD14 plasma levels (1,893 vs. 1,519 ng/ml; p=0.02; median, Visit 1 *vs.* 3). HIV-DNA levels were stable in blood/colon memory CD4^{+} T-cells at Visit 1 *vs.* 2. Noteworthy, residual HIV transcription was decreased in the colon at Visit 2 *vs.* 1.

Together, these results suggest benefits of Metformin in reducing immune activation and residual HIV transcription and support its further investigation in an HIV remission/cure strategy.