Improvement of liver metabolic activity in people with advanced HIV after antiretroviral therapy initiation

**Supplemental Data**

**SUPPLEMENTAL METHODS:**

1. **Participant enrollment details:**

**Healthy controls:** Control participants were recruited under protocol 13-H-0065 (Links Between Inflammation and Cardiometabolic Diseases, NCT01934660).

<https://www.clinicaltrials.gov/ct2/show/NCT01934660>

Eligibility Criteria

INCLUSION CRITERIA:

* Females and males 18 years of age or older without any clinical diagnosis of a chronic health condition that is known to accelerate vascular disease beyond traditional risk factors including lung disease or active infection

EXCLUSION CRITERIA:

* For imaging studies, pregnant women
* For imaging studies, lactating women
* For optional MRI, inability to participate due to in optional MRI metal within body, claustrophobia, or anything else that prohibits undergoing a MRI scan
* Any solid organ or liquid tumor within the past five years, with the exception of non melanomatous skin cancer,
* Active infectious diseases within 3 months requiring antibiotics, collagen vascular diseases such as RA, psoriasis and mixed connective tissue diseases and immune-mediated lung diseases (e.g. IPF, BOOP)
* Clinical diagnosis of diabetes or cardiovascular disease
* Fasting glucose >125,
* LDL>200,
* LFT s 3 times normal limit,
* eGFR<60,
* Subjects with severe renal excretory dysfunction will not receive the cardiac CT angiography, or gadolinium contrast agent during the PET/MRI.
* A BMI >40 kg/m(2) due to PET MRI restrictions.

**PWH participants:** PWH participants were recruited under protocol 14-I-0124 (PET Imaging and Lymph Node Assessment of IRIS in Persons With AIDS, PANDORA, NCT02147405):

<https://www.clinicaltrials.gov/ct2/show/NCT02147405>

Eligibility Criteria

ART NAIVE ARM INCLUSION CRITERIA:

* Documentation of HIV-1 infection. Results from outside facilities will be accepted for enrollment.
* No recent (within the past two years) treatment with combination anti-retroviral therapy (ART). Patients with limited (no more than 2-3 weeks) recent use of potent combination ART may be eligible for study participation if, the opinion of the investigator, the ART usage will not impact the scientific validity of the protocol
* Documented CD4+ cell count less than or equal to 100 cells/mm(3) within the past 8 weeks.
* Residence within the wider Washington D.C. area (within a 100-mile radius from the NIH Bethesda campus) and plans to stay in the area for 48 weeks
* Men or women age greater than or equal to 18 years.
* Ability and willingness of subject (or legal guardian/representative) to understand study requirements and give informed consent.
* Willingness to allow storage of blood or tissue samples for future research
* Willingness at time of screening to undergo study procedures (phlebotomy, apheresis, optional FDG-PET/CT and lymph node biopsy\*)
* Willingness to have genetic testing
* Participants should have a primary care physician or will need to agree to have one established by 24 weeks on study.
* In the event of an estimated reversible inability to consent, patients may enroll via a legally authorized representative (DPA) if they have the ability to assign a DPA. For these participants, baseline lymph node biopsy will not be performed however the week 4-8 lymph node biopsy may be performed if the participant regains the capacity to consent prior to that time. If a subject permanently loses the ability to consent during participation, they will be withdrawn from the study.

SUBJECT EXCLUSION CRITERIA:

* Active drug or alcohol use or dependence that, in the opinion of the investigator, would interfere with adherence to study requirements.
* Pregnancy will be an exclusion criterion for study entry given the intense nature of the protocol regarding blood draws, apheresis, biopsies and FDG-PET/CT imaging.
* Inadequate venous access for phlebotomy and apheresis procedures as assessed by the study team.
* Women who are breastfeeding.
* A life-threatening underlying illness that according to the study team requires immediate intervention such as PML requiring initiation of ARVs or lymphomas requiring chemotherapy initiation.
* An inability to consent that is estimated by the study team to be irreversible.
* History of significant medical non-adherence which would, in the opinion of the investigator, interfere with study participation

1. **Schematic description of PET study recruitment:**

N=71 participants enrolled in the PANDORA protocol (ART naïve arm) as of 2/21/2022

**PANDORA Protocol**

n=5 🡪 did not have PET scan performed (pre-ART, short-term, or both)

**n=23**

**Excluded from PET study**

n=1 🡪 had previous ART

n=1 🡪 did not have HIV

n=6 🡪 taken off PANDORA study

n=7 🡪 underlying liver disease

n=3 🡪 lymphoma diagnosis

n=48

Underwent baseline and short-term PET scans

n=27

Underwent one additional long-term PET scan

**n=48**

**Included in PET study**

1. **FDG-PET/CT imaging and image analysis**

Approximately 60 minutes following the injection of ~10 mCi of [18F]-FDG, each participant was positioned on the scanner table and a low-dose CT scan was performed from the base of the skull to the upper thighs for attenuation correction and anatomical localization. Emission scans were then obtained in 3-dimensional mode. Images were reconstructed with an iterative technique featuring an ordered subset expectation-maximization algorithm and attenuation and scatter corrected with a CT-based correction.

The liver and spleen were evaluated a priori to rule out structural abnormalities such as cysts or masses. Following co-registration of PET/CT scans, cylindrical volumes of interest (VOIs) (40 mm in diameter) were manually drawn in three distinct regions of the liver (upper, lower anterior, and lower posterior) and two regions of the spleen (anterior and posterior). Each VOI in the liver was drawn on ten consecutive slices while spleen VOIs were drawn on 5 consecutive slices each. Attention was given to avoid large intrahepatic vascular structures, the porta hepatis, and the gall bladder. SUVmean and HUmean values from the three liver VOIs and two spleen VOIs were averaged to estimate respective organ-level FDG uptake and density. VOI analysis and segmentation were performed by a single operator to avoid variability between measurements and were reviewed for appropriate placement and consistency by a physician with 20 years’ experience in radiology and nuclear medicine. All analyses were done using MIM Software (V. 6.9.4).

1. **Clinical and laboratory parameters**

Control blood samples were obtained once on the same day or within 1-3 days from the PET scans in 19 out of 20 controls. Only in one participant, blood tests were obtained five weeks before the PET scans. All PWH blood samples were collected within a few days from the baseline, short-term, and long-term follow-up PET/CT scans. Samples for both PWH and controls were analyzed for cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), and C-reactive protein (CRP). Additional laboratory measures acquired for the PWH group included viral load, CD4+ T lymphocyte count, hemoglobin (HgB), albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, total bilirubin (TB), direct bilirubin (DB), and prothrombin time (PT) with an international normalized ratio (INR). Only the lipid panel was not repeated in most short-term participants. For PWH participants, cryopreserved plasma was also obtained within one week of the FDG-PET/CT scans. D-dimer was measured by enzyme-linked fluorescent assay on a VIDAS instrument (bioMerieux, Durham, NC). Soluble CD14 was measured using enzyme-linked immunosorbent assay kit (R&D Systems, Minneapolis, MN). Additional immune and metabolic markers were measured using a custom multiplex kit and 3 single-plex kits by electrochemiluminescence (Meso Scale Discovery, Gaithersburg, MD) (Table.S1).

**SUPPLEMENTAL FIGURES:**

Figure S1: A. SUV mean values of the liver in controls (n=20) and PWH at baseline (n=48), short-term (n=48) and long-term (n=27) follow-up. B. Longitudinal changes in SUVmean values of the liver between baseline, short-term, and long-term follow-up (n=27). C. Longitudinal changes in SUVmean values of the liver between baseline and short-term follow-up (n=48). Non-parametric Mann-Whitney tests were performed to compare markers between control and PWH participants. Friedman tests (non-parametric repeated measures ANOVA) followed by Dunn’s multiple comparison tests were performed to compare changes between the three timepoints. Wilcoxon tests (nonparametric matched-pairs signed rank tests) were used to assess longitudinal changes in participants.

Figure S2: A. CT density (HUmean) values of the liver in controls (n=20) and PWH at baseline (n=48), short-term (n=48) and long-term (n=27) follow-up. B. Longitudinal changes in HUmean values of the liver between baseline, short-term, and long-term follow-up (n=27). C. Longitudinal changes in HUmean values of the liver between baseline and short-term follow-up (n=48). Non-parametric Mann-Whitney tests were performed to compare markers in control and PWH participants. Friedman tests (non-parametric repeated measures ANOVA) followed by Dunn’s multiple comparison tests were used to compare changes between the three timepoints.

Figure S3: A. Whole liver volume in controls (n=20) and PWH at baseline (n=27). B. Whole liver volume in controls (n=20) and PWH at long-term follow-up (n=27). C. Longitudinal changes in whole liver volume between baseline and long-term follow-up (n=27). Non-parametric Mann-Whitney tests were used to compare control and PWH groups. Wilcoxon tests (nonparametric matched-pairs signed rank tests) were used to compare changes from baseline to long-term in PWH participants.

Figure S4: SUV mean values of the spleen in controls (n=20) and PWH at baseline (n=48), short-term (n=48) and long-term (n=27) follow-up. B. Longitudinal changes in SUVmean values of the spleen between baseline, short-term, and long-term follow-up (n=27). C. Longitudinal changes in SUV mean values of the spleen between baseline and short-term follow-up (n=48). Non-parametric Mann-Whitney tests were used to compare markers in control and PWH participants. Friedman tests (non-parametric repeated measures ANOVA) followed by Dunn’s multiple comparison tests were conducted to compare changes between the three timepoints. Wilcoxon tests (nonparametric matched-pairs signed rank tests) were used to compare changes from

**SUPPLEMENTAL TABLES:**

Table S1: Immune and metabolic markers evaluated in PWH participants

|  |  |  |
| --- | --- | --- |
|  | lower limit of detection (LLD) | Unit |
| IFN-γ | 0.40 | pg/ml |
| TNF-α | 0.09 | pg/ml |
| MPO | 0.07 | ng/ml |
| MCP-1 | 0.11 | pg/ml |
| sPD1 | 0.00 | pg/ml |
| sCD14 | 2.5 E-7 | mg/L |
| IL-2 | 0.38 | pg/ml |
| IL-6 | 0.18 | pg/ml |
| IL-8 | 0.16 | pg/ml |
| IL-10 | 0.09 | pg/ml |
| IL-6R | 0.49 | pg/ml |
| G-CSF | 0.24 | pg/ml |
| C-peptide | 2.76 | pg/ml |
| GIP | 0.135 | pg/ml |
| GLP-1 | 0.0165 | pg/ml |
| Glucagon | 0.0189 | pM |
| Insulin | 0.00747 | uIU/ml |
| Leptin | 2.42 | pg/ml |
| PP | 0.108 | pg/ml |

Results from IL-1β and IL-12p70 were at or below LLD and thus excluded.

IFN-γ = Interferon-gamma. TNF-α = Tumor necrosis factor alpha. MPO = Myeloperoxidase. MCP-1 = Monocyte chemoattractant protein-1. sPD1 = Soluble programmed death 1 protein. sCD14 = Soluble CD14. G-CSF = Granulocyte colony stimulating factor. GIP = Glucose-dependent Insulinotropic polypeptide. GLP-1 = Active Glucagon-like peptide-1. PP = Pancreatic Polypeptide.

Table S2: Detailed characterization of PWH including treatment regimens, co-morbidities, IRIS status, and steroid use at the time of PET scanning pre and post ART.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient** | **Age** | **Sex (M/F)** | **PET Timepoint** | **CD4 T cells/μl (% of total lymphocytes)** | **VL (c/mL)** | **ART Backbone** | **Co-infections & Co-morbidities** | **IRIS** | **Steroids at or 30 days prior to PET** |
| #1 | 33 | M | Pre-ART | 9 (1%) | 154728 | None | Central nervous system (CNS) toxoplasmosis  Oral candidiasis | No | No |
|  |  |  | Short Term ART  (Week 4) | 48 (5%) | <40 | INSTI |
| #2 | 28 | M | Pre-ART | 82 (4%) | 17648 | None | Visceral Kaposi sarcoma (KS)  Kaposi sarcoma inflammatory cytokine syndrome | Yes, unmasking KS at week 12 | No |
|  |  |  | Short Term ART  (Week 4) | 230 (6%) | <40 | INSTI |
| #3 | 55 | M | Pre-ART | 38 (3%) | 1013672 | None | Oral candidiasis  Genital Herpes Simplex Virus (HSV)  Genital condyloma  Intrahepatic inferior vena cava thrombus  Hypothyroidism | No | No |
|  |  |  | Short Term ART  (Week 8) | 333 (13%) | <40 | INSTI |
| #4 | 43 | M | Pre-ART | 42 (4%) | 169124 | None | Oral candidiasis  Pneumocystis pneumonia (PCP)  Cutaneous KS  Latent Tuberculosis (TB)  Anal condyloma  Hypothyroidism | Yes,  unmasking anal condyloma at week 8 | No |
|  |  |  | Short Term ART  (Week 4) | 339 (13%) | 253 | INSTI |
| #5 | 37 | M | Pre-ART | 57 (5%) | 805519 | None | Presumed esophageal candidiasis Presumed disseminated Mycobacterium avium complex (MAC) | Yes, unmasking MAC at week 2 | No |
| Short Term ART  (Week 4) | 185 (12%) | 451 | INSTI |
| #6 | 39 | F | Pre-ART | 43 (4%) | 1241476 | None | Disseminated TB  Oral candidiasis | Yes,  paradoxical TB at day 11 | No |
| Short Term ART  (Week 7) | 170 (14%) | <40 | INSTI | Yes, prednisone taper of 6 weeks |
| #7 | 47 | M | Pre-ART | 5 (1%) | 310447 | None | Disseminated peritoneal TB  Oral candidiasis  Schistosomiasis | No | No |
| Short Term ART  (Week 4) | 37 (5%) | <40 | NNRTI |
| #8 | 37 | M | Pre-ART | 10 (1%) | 345011 | None | Pulmonary MAC  Oral candidiasis  HIV retinopathy | Yes, paradoxical MAC at week 4 | No |
| Short Term ART  (Week 4) | 163 (12%) | 45 | INSTI |
| #9 | 26 | M | Pre-ART | 15 (2%) | 863577 | None | Cryptococcal meningitis  PCP  Disseminated MAC | No | Yes, had completed prednisone taper 6 days before Pre-ART PET |
| Short Term ART  (Week 4) | 14 (2%) | 463619 | INSTI | No |
| #10 | 38 | F | Pre-ART | 71 (5%) | 3449744 | None | Disseminated MAC | No | No |
| Short Term ART  (Week 4) | 322 (20%) | 3013 | NNRTI |
| #11 | 23 | M | Pre-ART | 28 (3%) | 644695 | None | Cryptococcal meningitis  Genital HSV | No | No |
| Short Term ART  (Week 4) | 149 (10%) | 99 | INSTI |
| #12 | 23 | M | Pre-ART | 19 (3%) | 103897 | None | Oral candidiasis  Late latent syphilis  Perineal condyloma | No | No |
| Short Term ART  (Week 4) | 284 (13%) | <40 | INSTI |
| #13 | 33 | M | Pre-ART | 19 (2%) | 62345 | None | Cryptococcal meningitis  HSV encephalitis  CMV encephalitis (and recurrence with resistant strain) | Yes, paradoxical cryptococcal lymphadenitis IRIS at Week 36 | No |
| Short Term ART  (Week 4) | 41 (4%) | 148 | INSTI |
| #14 | 39 | M | Pre-ART | 26 (5%) | 7660088 | None | Oral candidiasis  Genital condyloma  Immune thrombocytopenic purpura | No | Yes, initiated prednisone taper 10 days before Pre-ART PET |
| Short Term ART  (Week 4) | 83 (7%) | 3014 | INSTI | Yes, prednisone taper of 5 weeks before Short Term PET |
| #15 | 45 | F | Pre-ART | 13 (2% | 93829 | None | Pulmonary/Gastrointestinal TB | No | No |
| Short Term ART  (Week 4) | 40 (5% | 92 | NNRTI |
| #16 | 51 | F | Pre-ART | 50 (4%) | 58715 | None | None | No | No |
| Short Term ART  (Week 4) | 70 (5%) | <40 | INSTI |
| #17 | 44 | F | Pre-ART | 36 (7%) | 286733 | None | Disseminated TB  CMV retinitis | Yes, paradoxical CMV at Week 3 | No |
| Short Term ART  (Week 4) | 84 (9%) | 320 | INSTI |
| #18 | 41 | M | Pre-ART | 18 (2%) | 226629 | None | PCP  Cutaneous and Visceral KS | Yes, paradoxical KS at Week 4 | Yes, had completed prednisone taper 2 days before Pre-ART PET |
| Short Term ART  (Week 4) | 77 (5%) | 128 | INSTI | No |
| #19 | 35 | F | Pre-ART | 99 (7%) | 67147 | None | Disseminated TB  Oral/esophageal candidiasis | No | No |
| Short Term ART  (Week 4) | 76 (9%) | <40 | NNRTI |
| #20 | 36 | M | Pre-ART (8/1/14) | 16 (2%) | 136677 | None | Presumed toxoplasmosis  Oral candidiasis | No | Yes, had completed prednisone taper 9 days before Pre-ART PET |
| Short Term ART  (Week 4) | 30 (3%) | <40 | INSTI | No |
| #21 | 34 | M | Pre-ART | 25 (2%) | 87685 | None | Oral candidiasis  Genital/rectal condyloma | No | No |
| Short Term ART  (Week 4) | 68 (2%) | 346 | PI |
| #22 | 53 | M | Pre-ART | 32 (6%) | 38645 | None | PCP  Oral candidiasis  Aphthous esophageal ulcer (negative workup on pathology) | No | No |
| Short Term ART  (Week 4) | 108 (14%) | 101 | INSTI |
| Long Term ART  (Week 96) | 214 (16%) | <40 | INSTI |
| #23 | 32 | F | Pre-ART | 41 (7%) | 19099 | None | Oral candidiasis  Anal condyloma  Low-grade squamous intraepithelial lesion  Asthma | No | No |
| Short Term ART  (Week 4) | 129 (14%) | <40 | INSTI |
| Long Term ART  (Week 96) | 236 (16%) | <40 | INSTI |
| #24 | 30 | M | Pre-ART | 7 (1%) | 385696 | None | Syphilis  Oral candidiasis  Anal HSV | No | No |
| Short Term ART  (Week 4) | 32 (3%) | <40 | INSTI |
| Long Term ART  (Week 96) | 651 (31%) | <40 | INSTI |
| #25 | 38 | M | Pre-ART | 27 (3%) | 507265 | None | Ocular Syphilis  Oral candidiasis | No | No |
| Short Term ART  (Week 4) | 133 (10%) | 1034 | PI |
| Long Term ART  (Week 96) | 173 (14%) | <40 | INSTI |
| #26 | 27 | M | Pre-ART | 18 (4%) | 977945 | None | MAC | Yes, unmasking MAC at week 3 | No |
| Short Term ART  (Week 4) | 182 (16%) | 2245 | INSTI |
| Long Term ART  (Week 96) | 466 (23%) | <40 | INSTI |
| #27 | 19 | M | Pre-ART | 43 (8%) | 465329 | None | PCP  HSV proctitis  Oral candidiasis  CMV esophagitis | No | Yes, had completed prednisone taper 6 days prior to Pre-ART PET |
| Short Term ART  (Week 8) | 188 (12%) | 823 | INSTI | No |
| Long Term ART  (Week 80) | 644 (28%) | <40 | INSTI | No |
| #28 | 46 | F | Pre-ART | 48 (8%) | 27890 | None | PCP  Anogenital HSV  Low-grade squamous intraepithelial lesion Vaginal condyloma Asthma  Slightly echogenic liver with nodular contour on imaging | No | Yes, had completed 7 days of prednisone taper at time of pre-ART PET |
| Short Term ART  (Week 12) | 82 (10%) | <40 | INSTI | No |
| Long Term ART  (Week 96) | 112 (18%) | <40 | INSTI | No |
| #29 | 28 | M | Pre-ART | 5 (1%) | 199128 | None | Oral candidiasis  PCP  Latent TB  Suspected pulmonary MAC | Yes,  Unmasking presumed MAC  at week 2 | Yes, had completed prednisone taper 4 days prior to pre-ART PET |
| Short Term ART  (Week 4) | 117 (7%) | 3146 | INSTI | No |
| Long Term ART  (Week 96) | 381 (19%) | <40 | PI | No |
| #30 | 28 | M | Pre-ART | 11 (4%) | 191817 | None | PCP  Oral candidiasis  Zoster | No | Yes, had completed 6 days of prednisone taper at time of pre-ART PET |
| Short Term ART  (Week 4) | 57 (3%) | <40 | INSTI | Yes, had completed prednisone course 4 weeks prior to short term PET |
| Long Term ART  (Week 96) | 214 (14%) | <40 | INSTI | No |
| #31 | 34 | F | Pre-ART | 24 (14%) | 712187 | None | Disseminated TB  Oral candidiasis | Yes, paradoxical TB  at week 2 | No |
| Short Term ART  (Week 4) | 112 (35%) | 294 | INSTI |
| Long Term ART  (Week 96) | 75 (17%) | <40 | INSTI |
| #32 | 38 | M | Pre-ART | 7 (1%) | 19520 | None | Esophageal candidiasis  PCP | No | Yes, had initiated prednisone taper 2 days before pre-ART PET |
| Short Term ART  (Week 4) | 47 (2%) | <40 | INSTI | Yes, had completed prednisone taper 3 weeks prior to short term ART PET |
| Long Term ART  (Week 96) | 277 (17%) | <40 | INSTI | No |
| #33 | 36 | M | Pre-ART | 6 (1%) | 133504 | None | PCP  Disseminated histoplasmosis  Latent TB  Esophageal candidiasis  Cutaneous warts | Yes, paradoxical Histoplasma at week 5 | Yes had completed prednisone taper 1 day prior to pre-ART PET |
| Short Term ART  (Week 8) | 89 (12%) | 104 | INSTI | No |
| Long Term ART  (Week 96) | 122 (14%) | <40 | INSTI | No |
| #34 | 39 | M | Pre-ART | 27 (3%) | 252823 | None | Oral candidiasis | No | No |
| Short Term ART  (Week 8) | 155 (7%) | 46 | INSTI |
| Long Term ART  (Week 96) | 335 (17%) | <40 | INSTI |
| #35 | 40 | M | Pre-ART | 0 (0%) | 3040390 | None | PCP  CMV retinitis  Recurrent pneumonias  Oral candidiasis | No | No |
| Short Term ART  (Week 4) | 21 (1%) | 674 | INSTI |
| Long Term ART  (Week 96) | 609 (18%) | <40 | INSTI |
| #36 | 46 | F | Pre-ART | 36 (6%) | 606285 | None | Esophageal candidiasis  Latent TB  Hypertension  Renal Insufficiency | No | No |
| Short Term ART  (Week 4) | 175 (25%) | 109 | INSTI |
| Long Term ART  (Week 96) | 221 (18%) | <40 | INSTI |
| #37 | 36 | M | Pre-ART | 11 (1%) | 143414 | None | Oral HSV  Mumps  Anal and genital condyloma | No | No |
| Short Term ART  (Week 4) | 86 (5%) | 163 | INSTI |
| Long Term ART  (Week 96) | 375 (14%) | <40 | INSTI |
| #38 | 59 | M | Pre-ART | 6 (1%) | 716531 | None | PCP  CMV colitis  Progressive multifocal leukoencephalopathy (PML) | Yes, unmasking PML at week 9 | Yes, completed prednisone taper same day as pre-ART PET |
| Short Term ART  (Week 4) | 164 (7%) | 864 | INSTI | No |
| Long Term ART  (Week 96) | 357 (14%) | 94 | INSTI | No |
| #39 | 34 | M | Pre-ART | 25 (3%) | 182106 | None | Esophageal candidiasis  Zoster  Syphilis | Yes, unmasking Zoster  at week 12 | No |
| Short Term ART  (Week 4) | 123 (10%) | 144 | INSTI |
| Long Term ART  (Week 96) | 177 (14%) | <40 | INSTI |
| #40 | 23 | M | Pre-ART | 28 (2%) | 502620 | None | Anal condyloma  Anal HSV  Neurosyphilis  Hookworm | Yes, unmasking anal condyloma at week 32 | No |
| Short Term ART  (Week 4) | 35 (3%) | 417336 | INSTI |
| Long Term ART  (Week 96) | 425 (22%) | <40 | PI |
| #41 | 42 | F | Pre-ART | 11 (2%) | 135450 | None | Disseminated TB | No | No |
| Short Term ART  (Week 4) | 8 (1%) | <40 | INSTI and PI |
| Long Term ART  (Week 96) | 642 (31%) | <40 | INSTI and PI |
| #42 | 39 | M | Pre-ART | 0 (0%) | 6641 | None | PCP  Oral candidiasis  Disseminated Cryptococcosis (not CNS)  HIV retinopathy | No | Yes, initiated prednisone taper about 3 weeks before pre-ART PET |
| Short Term ART  (Week 4) | 20 (2%) | <40 | INSTI | Yes, completed prednisone taper 3 weeks before Short Term ART PET |
| Long Term ART  (Week 96) | 241 (12%) | <40 | NNRTI | No |
| #43 | 61 | F | Pre-ART | 48 (12%) | 264033 | None | Crypto meningitis  Oral candidiasis | Yes, paradoxical Crypto at week 4 | No |
| Short Term ART  (Week 4) | 299 (19%) | 478 | INSTI |
| Long Term ART  (Week 96) | 470 (20%) | <40 | INSTI |
| #44 | 38 | F | Pre-ART | 48 (6%) | 716330 | None | Disseminated TB  Genital HSV  Oral and cutaneous candidiasis | Yes, paradoxical TB at week 8 | No |
| Short Term ART  (Week 4) | 73 (18%) | 254 | NNRTI |
| Long Term ART  (Week 96) | 407 (19%) | <40 | INSTI |
| #45 | 40 | F | Pre-ART | 16 (2%) | 265994 | None | CNS toxoplasmosis  Genital HSV  Oral candidiasis  HIV retinopathy | No | No |
| Short Term ART  (Week 4) | 185 (12%) | 2486 | INSTI |
| Long Term ART  (Week 96) | 458 (21%) | <40 | INSTI |
| #46 | 36 | M | Pre-ART | 5 (1%) | 40770 | None | Presumed PCP  Genital HSV  Oral candidiasis | No | Yes, had completed prednisone taper 7 days before Pre-ART PET |
| Short Term ART  (Week 4) | 82 (3%) | 97 | INSTI | No |
| Long Term ART  (Week 96) | 400 (20%) | <40 | INSTI | No |
| #47 | 34 | M | Pre-ART | 46 (4%) | 604659 | None | Zoster  Pulmonary M. Kansasii | No | No |
| Short Term ART  (Week 4) | 328 (26%) | 605 | NNRTI |
| Long Term ART  (Week 96) | 426 (20%) | <40 | INSTI |
| #48 | 36 | M | Pre-ART (4/15/15) | 29 (7%) | 1390286 | None | Disseminated TB  TB meningitis  Genital condyloma | Yes, CNS TB (week 2) | No |
| Short Term ART  (Week 7) | 44 (11%) | <40 | NNRTI | Yes, had completed 1 month of prednisone taper at time of Short-Term ART PET |
| Long Term ART  (Week 96) | 88 (10%) | <40 | INSTI | No |

**Table. S3A. List of response (dependent) and explanatory (independent) variables used in regression analysis with the control and PWH groups combined (baseline values only).**

Outcome Measures:

1. SUVmean
2. HUmean

Explanatory Variables:

1. BMI
2. HIV status
3. Liver volume
4. CRP
5. Glucose
6. Cholesterol
7. Triglycerides
8. HDL
9. LDL

**Table. S3B. List of response (dependent) and explanatory (independent) variables used in regression analysis within PWH group.**

Outcome Measures:

1. SUVmean
2. HUmean

Explanatory Variables:

1. BMI
2. CRP
3. Albumin
4. Alkaline phosphatase
5. ALT
6. AST
7. Cholesterol
8. Triglycerides
9. HDL
10. LDL
11. Total Bilirubin
12. PT
13. INR
14. CD4 count
15. Viral load
16. Hgb
17. D-dimer
18. IL-6r
19. MPO
20. PD-1
21. IFN-y
22. IL -10
23. IL -12p70
24. IL -1β
25. IL -2
26. IL -6
27. IL -8
28. TNF-α
29. G-CSF
30. MCP-1
31. sCD14
32. C-peptide
33. GIP
34. Active GLP-1
35. Glucagon
36. Insulin
37. Leptin
38. PP

CRP = C-reactive protein. HDL = High-density lipoprotein. LDL = Low-density lipoprotein. ALT = Alanine aminotransferase. AST = Aspartate aminotransferase. PT = Prothrombin time. INR = International normalized ratio. Hgb = Hemoglobin. MPO = Myeloperoxidase. sPD1 = Soluble programmed death 1 protein. IFN-γ = Interferon-gamma. TNF-α = Tumor necrosis factor alpha. G-CSF = Granulocyte colony stimulating factor. MCP-1 = Monocyte chemoattractant protein-1. sCD14 = Soluble CD14. GIP = Glucose-dependent Insulinotropic polypeptide. GLP-1 = Active Glucagon-like peptide-1. PP = Pancreatic polypeptide.