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ACTG TO PRESENT NEW HIV AND TB RESEARCH AT CROI 2020

Presentations Focus on Cure, Co-Morbidities, Contraception, Sex Differences, and Predictors of Clinical Outcomes

Los Angeles, Calif. – The [AIDS Clinical Trials Group \(ACTG\)](#), the world’s largest and longest-established HIV research network, will make 28 presentations at the Conference on Retroviruses and Opportunistic Infections ([CROI 2020](#)) held in Boston, March 8-11. ACTG investigators will present data in oral presentations and themed discussions on the impact of chronic antiretroviral therapy (ART) on a novel metric of the HIV reservoir, predictors of multidrug resistant tuberculosis (MDR-TB) in resource-limited settings, findings from the first HIV cure trial that exclusively enrolled women, and interactions between contraceptives and TB drugs and the vaginal microbiome.

“The ACTG has led research on HIV and its co-infections and comorbidities since the beginning of the epidemic, more than 30 years ago,” said ACTG Chair Judith Currier, M.D., MSc, of the University of California, Los Angeles. “The studies being presented at CROI this year reflect the diversity of ACTG’s research portfolio and demonstrate our commitment to addressing the full range of issues affecting people living with HIV. These studies provide insights into HIV cure, TB, the interaction between contraception and HIV treatment, sex differences, and co-morbidities in people living with HIV.”

The 28 ACTG presentations at CROI 2020, a premier global HIV research conference, demonstrate ACTG’s continued impact on the understanding of HIV pathogenesis, clinical interventions, clinical care, and the health of people living with HIV. Presentations are listed below:

ORAL PRESENTATIONS AND THEMED DISCUSSIONS

INTACT PROVIRAL DNA LEVELS DECLINE IN PEOPLE WITH HIV ON ANTIRETROVIRAL THERAPY (ART) (ACTG 5321; Oral Abstract Session 0-06: Targeting the Persistent HIV Reservoir, Tuesday, March 10 10:00 am – 12:00 pm) *Rajesh T. Gandhi, et al.*

(rgandhi@mgh.harvard.edu) Topic: HIV Cure, the Reservoir, and Persistence

The intact proviral DNA assay is a novel metric of the HIV reservoir. This study shows that intact proviral DNA levels decline for people on chronic ART and examines the relationship of that decline to other metrics of HIV persistence and immune activation.

PREDICTORS OF TUBERCULOSIS INFECTION IN MDR-TB HOUSEHOLD CONTACTS ≥15 YEARS OLD (ACTG 5300/IMPAACT2003; Oral Abstract Session 0-12: Tuberculosis, Opportunistic Infections, and HIV Testing, Wednesday, March 11 10:00 am – 12:00 pm) *Soyeon Kim, et al.* (skim@sdac.harvard.edu) Topic: Tuberculosis

This presentation provides insights into predictors of active TB infection among household contacts of individuals with MDR-TB.

EFFECT OF TAMOXIFEN ON VORINOSTAT-INDUCED HIV RNA EXPRESSION IN WOMEN ON ART (ACTG 5366; Themed Discussion Session TD-06: Curative Strategies: Trials and Tribulations, Tuesday, March 10 1:30 pm – 2:30 pm) *Eileen Scully, et al.* (escully1@jhmi.edu)
Topic: HIV Cure, the Reservoir, and Persistence

A5366 is the first study to examine a strategy to reduce the HIV reservoir exclusively in women using a hormone-modulating approach. Since estrogen in women blocks the expression of HIV when researchers try to ‘turn on’ the latent reservoir in women living with HIV, A5366 examines whether tamoxifen and vorinostat can reverse latency.

A COMBINED ESTROGEN/PROGESTIN VAGINAL RING IMPROVES VAGINAL MICROBIAL COMMUNITIES (ACTG 5316; Themed Discussion Session TD-15: Making Sense of it All: HIV Susceptibility in the Female Genital Tract, Wednesday, March 11, 1:30 pm – 2:30 pm) *Nicole H. Tobin, et al.* (ntobin@mednet.ucla.edu) Topic: Contraception

This presentation explores the relationship between the use of hormone-base intravaginal rings and vaginal flora.

ANTIRETROVIRAL AND RIFAMPICIN CO-TREATMENT AFFECTS DMPA EXPOSURE: DOSING IMPLICATIONS (ACTG 5338; Themed Discussion Session TD-13: The Long and Short of it: What’s Next for Long-Acting Drugs, Wednesday, March 11, 1:30 pm – 2:30 pm) *Jose Francis, et al.* (jose.francis@uct.ac.za) Topic: Contraception

Because TB coinfection among pregnant women living with HIV is associated with poor outcomes, effective contraception to prevent unintended pregnancy is important. This study examines the impact of HIV and rifampicin-based TB therapy on depot medroxyprogesterone acetate (DMPA) levels when used as an injectable contraceptive.

POSTER PRESENTATIONS

HIV Cure, the Reservoir, and Persistence

RISK AND PREVALENCE OF RESIDUAL VIREMIA AFTER cART IN RESOURCE-LIMITED COUNTRIES (NWCS 425; Poster Session P-E02: Measuring the HIV Reservoir, Monday, March 9, 2:30 pm – 4:00 pm) *Sivaporn Gatechompol, et al.* (sivaporn.k@hivnat.org)

This study compares factors associated with residual single copy viremia in people living with HIV who are virally suppressed on ART between the United States and resource-limited settings.

TELMISARTAN DECREASES MONOCYTE CX3CR1 EXPRESSION IN TREATED HIV INFECTION (ACTG 5317; Poster Session P-M02: Adipose Tissue and Obesity, Tuesday, March 10, 2:30 pm – 4:00 pm) *Jordan E. Lake, et al.* (jordan.e.lake@uth.tmc.edu)

Telmisartan is an angiotensin receptor blocker with anti-inflammatory properties, especially in adipose tissue. This presentation evaluates whether telmisartan improves inflammatory and obesity markers in patients on ART.

AMINOBISSPHOSPHONATES REVERSE LATENCY IN HIV-SEROPOSITIVE INDIVIDUALS (NWCS 464; Poster Session P-E07: HIV Curative Strategies: In Vitro Studies, Tuesday, March 10, 2:30 pm – 4:00 pm) *Natalia Soriano-Sarabia, et al.* (nataliasorsar@email.gwu.edu)

Aminobisphosphonates, which are used to treat osteoporosis, may reverse latency in chronic HIV infection due to disruptions in cell signaling. This study examines that association for the first time.

TH2 CYTOKINES ARE ASSOCIATED WITH HIGHER LEVELS OF INTACT PROVIRUSES ON ART (ACTG 5321; Poster Session P-E10: Immune Pressure on the HIV Reservoir, Wednesday, March 11, 2:30 pm – 4:00 pm) *Joshua C. Cyktor, et al.* (jcc114@pitt.edu)

This study examines the relationship between levels of various cytokines among people on ART and different metrics of the HIV-1 reservoir.

MODELING HIV RESERVOIR DECLINE AFTER ART INITIATION AS A FUNCTION OF NK CELL FEATURES (NWCS 441; Poster Session P-E10: Immune Pressure on the HIV Reservoir, Wednesday, March 11, 2:30 pm – 4:00 pm) *Elena Vandrane, et al.* (elenaven@stanford.edu) HIV DNA levels decline after ART initiation, and this study examines factors associated with that decline, including natural killer cells.

Viral Control with or without Structured Treatment Interruptions

FACTORS ASSOCIATED WITH VIRAL CONTROL AFTER STRUCTURED TREATMENT INTERRUPTION (NWCS 470; Poster Session P-E04: Insights from Analytical Treatment Interruptions, Monday, March 9, 2:30 pm – 4:00 pm) *Nikolaus Jilg, et al.* (njilg@partners.org) Structured treatment interruptions (STIs) will be a critical strategy to determine if HIV remission or cure efforts are successful. This study examines the factors immediately following STIs that predict longer periods of virologic control.

HIV POST-TREATMENT CONTROL DESPITE PLASMA VIRAL EVOLUTION AND DUAL INFECTION (NWCS 470; Poster Session P-E04: Insights from Analytical Treatment Interruptions, Monday, March 9, 2:30 pm – 4:00 pm) *Behzad Etemad, et al.* (betemad@bwh.harvard.edu) HIV post-treatment controllers (PTCs) serve as models for sustained HIV remission and may provide clues for HIV remission or cure studies. This study examines plasma virus composition and diversification within HIV PTCs.

FREQUENCY OF POST-TREATMENT CONTROL VARIES BY ART RESTART AND VIRAL LOAD CRITERIA (NWCS 380; Poster Session P-E04: Insights from Analytical Treatment Interruptions, Monday, March 9, 2:30 pm – 4:00 pm) *Jesse M. Fajnzylber, et al.* (jesse_fajnzylber@dfci.harvard.edu)

Analytic treatment interruptions (ATI) are critical strategies to examine the efficacy of HIV remission or cure strategies. This study examines an interactive tool for estimating viral rebound timing in the setting of an ATI.

Tuberculosis

GEOGRAPHIC AND INDIVIDUAL RISK FACTORS FOR TB OR DEATH IN THE BRIEF-TB TRIAL (ACTG 5279; Poster Session P-N02: Latent TB Infection: Risk Factors, Treatment, and Prevention, Monday, March 9, 2:30 pm – 4:00 pm) *Cynthia Riviere, et al.* (criviere@ghesiko.org) The original A5279 trial compared one month of isoniazid and rifapentine to nine months of isoniazid for TB prevention in resource-limited settings. This follow-up presentation explores clinical, demographic, and geographic factors associated with TB acquisition, TB-related death, and death in each group.

Comorbidities

ADVANCED GLYCATION END PRODUCTS ASSOCIATED WITH CARDIOMETABOLIC RISK ON ART (ACTG 5260; Poster Session P-L01: Inflammatory Biomarkers and Cardiovascular Outcomes, Monday, March 9, 2:30 pm – 4:00 pm) *Vanessa El Kamari, et al.* (Vanessa.ElKamari@UHhospitals.org)

This study evaluates changes in serum advanced glycation end products (AGEs), usually associated with aging, in the ACTG 5257 trial after ART initiation with one of three NNRTI-based regimens.

TRICARBOXYLIC ACID METABOLITES PREDICT METABOLIC COMORBIDITIES AND DEATH IN AGING PWH (NWCS 447; Poster Session P-M03: Metabolic Complications, Monday, March 9, 2:30 pm – 4:00 pm) *Corrilynn O. Hileman, et al.* (chileman@metrohealth.org) Monocyte activation may contribute to inflammatory and metabolic changes among people aging with HIV. This study analyzes associations between concentrations of monocyte activation markers and comorbidities in the HIV Infection, Aging, and Immune Function Long-Term Observational (HAILO) study.

PREDICTIVE VALUE OF THE CD8 COUNTS AND CD4/CD8 RATIO AT TWO YEARS OF SUCCESSFUL ART (DACS 322.1; Poster Session P-Q05: T Cell Patterns, Monday, March 9, 2:30 pm – 4:00 pm) *Sergio Serrano-Villar, et al.* (sergio.serrano@salud.madrid.org) Although CD4 cell counts predict clinical events, there is variability in the predictive power of CD8+ T cell counts and CD4/CD8 ratios on clinical outcomes in HIV. This study examines these factors in relation to clinical events on suppressive ART.

GUT INTEGRITY MARKERS AND ASSOCIATIONS WITH ADIPOSITY IN PEOPLE WITH AND WITHOUT HIV (ACTG 5260s; Poster Session P-M02: Adipose Tissue and Obesity, Tuesday, March 10, 2:30 pm – 4:00 pm) *Allison Ross Eckard, et al.* (eckarda@musc.edu) Fat accumulation after ART initiation remains a serious problem among people living with HIV, but little is known about the pathophysiology of this process, especially with Integrase Strand Transfer Inhibitors. This presentation assesses the relationship between gut integrity markers and body composition for the first time.

A CROSS-SECTIONAL ANALYSIS OF ANTIRETROVIRAL REGIMEN ACTIVITY IN CEREBROSPINAL FLUID (ACTG 5321; Poster Session P-G03: Pharmacokinetics and Pharmacodynamics in Special Populations and Body Sites, Tuesday, March 10, 2:30 pm – 4:00 pm) *Courtney V. Fletcher, et al.* (cfletcher@unmc.edu) This study analyzes the distribution of different antiretrovirals (ARVs) in cerebrospinal fluid and the relationship between that distribution and biomarkers of HIV persistence and inflammation in the cerebrospinal fluid.

T-CELL AND MONOCYTE ACTIVATION CORRELATE AND DECLINE DURING HCV THERAPY FOR HCV-HIV (ACTG 5329; Poster Session P-J06: HCV After the SVR: Gone but Not Forgotten, Tuesday, March 10, 2:30 pm – 4:00 pm) *Ann Auma, et al.* (awa28@case.edu) Successful hepatitis C (HCV) therapy has been associated with partial or complete normalization of immune activation during mono-HCV infection. This presentation shows that successful therapy for HCV among patients with HIV-HCV co-infection similarly leads to a decline in markers of immune activation, despite the ongoing HIV.

PLASMA CITRATE AND SUCCINATE PREDICT NEUROCOGNITIVE IMPAIRMENT IN OLDER PWH (NWCS 447; Poster Session P-F02: Neurocognition: Biomarkers, Therapies, and Outcomes, Tuesday, March 10, 2:30 pm – 4:00 pm) *Corrilynn O. Hileman, et al.* (chileman@metrohealth.org) This study evaluates the effect of specific neuroinflammatory markers on neurocognitive impairment among older people living with HIV.

PREVALENCE OF PHYSICAL FUNCTION IMPAIRMENT AND FRAILITY IN MIDDLE-AGED PWH (ACTG 5361; Poster Session P-M08: Functional Status and Frailty, Wednesday, March 11, 2:30 pm – 4:00 pm) *Triin Umbleja, et al.* (tumbleja@sdac.harvard.edu)

People living with HIV have an increased risk of falls, hospitalizations, and mortality due to frailty. This study evaluates the risk factors for physical function impairment among patients with HIV at low to moderate cardiovascular risk.

PRINCIPAL COMPONENTS ANALYSIS TO IDENTIFY BIOMARKERS PREDICTIVE OF NON-AIDS EVENTS (NWCS 411; Poster Session P-B08: Non-AIDS Consequences of HIV Infection, Wednesday, March 11, 2:30 pm – 4:00 pm) *Carlee Moser, et al.* (cmoser@sdac.harvard.edu)

In this presentation, biomarkers of monocyte and macrophage activation are examined in relationship to non-AIDS events among individuals living with HIV.

TOTAL HIV DNA LEVELS DO NOT PREDICT NON-AIDS-DEFINING EVENTS (NWCS 411; Poster Session P-B08: Non-AIDS Consequences of HIV Infection, Wednesday, March 11, 2:30 pm – 4:00 pm) *Colline Wong, et al.* (cwong22@bwh.harvard.edu)

While total HIV DNA levels predict the size of the HIV reservoir, this study shows that this biomarker is not associated with non-AIDS defining events among people living with HIV.

Sex Differences

SEX-SPECIFIC ANALYSES IN ORAL ABSTRACTS FROM CROI 2019 (A5001; Poster Session P-Q02: HIV in Key Populations, Monday, March 9, 2:30 pm – 4:00 pm) *William R. Short, et al.* (wshort@penntmedicine.upenn.edu)

Globally, women account for more than half of all people living with HIV yet remain underrepresented in research. CROI guidelines (starting in 2018) specifically recommend reporting sex distribution and sex-adjusted analyses, but adherence to these guidelines has been relatively poor. This updated analysis examines adherence to these guidelines among oral abstracts from CROI 2019.

DYNAMICS OF HIV-SPECIFIC T-CELLS ON DURABLE ART DIFFER BY ANTIGEN RECOGNIZED & BY SEX (ACTG 5321; Poster Session P-D08: Impact of Antiretrovirals on the Immune Response, Wednesday, March 11, 2:30 pm – 4:00 pm) *Eva M. Stevenson, et al.* (ems2200@med.cornell.edu)

In order to advance understanding toward HIV cure, sex differences must be examined to determine whether cure strategies will differ by sex. This study examines differences in HIV-specific T cell responses by sex among chronically treated patients on ART.

HIV Diagnosis/Predictors of Clinical Outcomes

INFLAMMATION AND MITOCHONDRIAL DYSFUNCTION NOT NRTIS DRIVE EVENTS IN ACTG A5241 (NWCS 423; Poster Session P-M10: Epigenetic and Mitochondrial Toxicities, Tuesday, March 10, 2:30 pm – 4:00 pm) *Carl J. Fichtenbaum, et al.* (fichtecj@ucmail.uc.edu)

A recent ACTG study found that among people living with HIV experiencing treatment failure, the treatment arm that added an NRTI to a regimen of two or more ARVs had more deaths and clinical events than the arm that did not. However, inflammation and mitochondrial dysfunction seem to drive these events (not the NRTIs) in this study.

NOVEL CRITERIA FOR DIAGNOSING ACUTE HIV IN A MULTI-NATIONAL ART INITIATION STUDY (ACTG 5354; Poster Session P-R06: Diagnosing Early HIV Infection, Wednesday, March 11, 2:30 pm – 4:00 pm) *Trevor A. Crowell, et al.* (tcrowell@hivresearch.org)
ART initiation during acute HIV infection (AHI) limits the size of the HIV reservoir, but identifying patients with AHI can be logistically challenging. This presentation evaluates a novel way to diagnose AHI incorporating modern diagnostic algorithms to facilitate early treatment.

About the AIDS Clinical Trials Group (ACTG)

Founded in 1987, the AIDS Clinical Trials Group (ACTG) is the world's largest and longest established HIV research network. The ACTG conducts groundbreaking studies to improve the treatment of HIV and its complications, reduce new infections and HIV-related illness, and advance new approaches to prevent, treat, and ultimately cure HIV in adults and children. ACTG investigators and research units in 12 countries serve as major resources for HIV/AIDS research, treatment, care, and training/education in their communities. ACTG studies have helped establish current paradigms for managing HIV disease, and have informed HIV treatment guidelines, resulting in dramatic decreases in HIV-related mortality worldwide.

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