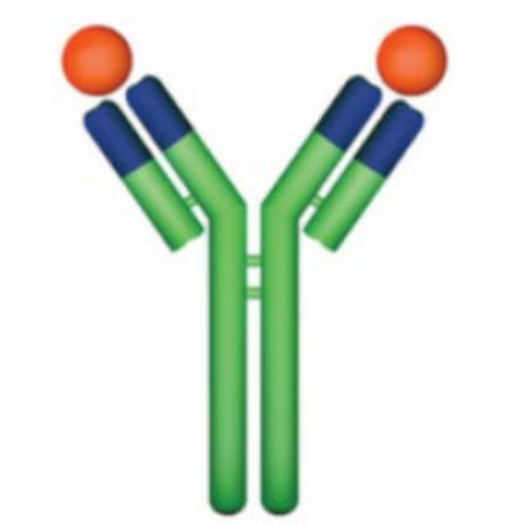
Welcome to the May 2019 ACTG Newsletter

Three New Study openings!



1) A new study called A5377 is the first in-human ascending dose study of SAR441236, a tri-specific broadly neutralizing antibody, in participants with HIV. The study will enroll two groups of participants: Arm A: Individuals currently on an antiretroviral regimen with an undetectable HIV viral load will receive either SAR441236 or placebo in one of four increasing dosing groups; Arm B: People with HIV who have never received anti-HIV medications will

receive SAR441236 in one of four increasing dosing groups. The study will look at safety, tolerability, and effects on viral load in both arms. Infusions will be given every 12 weeks, and Arm B participants will start taking antiretroviral therapy by day 28 of the study. Arm A participants will continue to take their anti-HIV medications throughout the study. Anti-HIV medications will not be provided by the study.

2) Also opening this month is **A5357** *(web link pending)*, a study of long-acting cabotegravir plus VRC01LS to maintain virologic suppression in adults living with HIV. This study is for individuals living with HIV who have been on stable treatment for at least 8 weeks and who have an undetectable viral load. The safety and effectiveness of long-acting cabotegravir and a novel monoclonal antibody (to be administered by injection) called VRC-HIVMAB080-00-AB (VRC01LS) will be evaluated. Participants will discontinue their current HIV regimen and be treated with oral cabotegravir for a lead-in period, followed by cabotegravir injection every 4 weeks plus VRC01LS infusion every 12 weeks.

3) The final ACTG study to open this month is **A5370**, which will test whether the anti-PD-1 antibody cemiplimab improves the ability of the immune system to target latently infected cells in individuals whose HIV infection is controlled by antiretroviral therapy. This important new cure strategy is being tested at 5 U.S. sites: UC Los Angeles, UC San Diego, UC San Francisco, University of Colorado, and Vanderbilit University. Participants with undetectable viral load on their current ART regimen will receive two doses of cemiplimab or placebo intravenously and will be followed for 48 weeks for safety and evaluation of the latent reservoir.

New ACTG Publications

The ACTG published a number of exciting manuscripts over the past few months, with just two highlighted below:

Nyaku AN, Zheng L, Gulick RM, Olefsky M, Berzins B, Wallis CL, Godfrey C, Sax PE, Acosta EP, Haas DW, Smith KY, Sha BE, Van Dam CN, Taiwo BO; ACTG A5353 Study Team. Dolutegravir plus lamivudine for initial treatment of

HIV-1-infected participants with HIV-1 RNA <500 000 copies/mL: week 48 outcomes from ACTG 5353. J Antimicrob Chemother. 2019 Jan 18. doi: 10.1093/jac/dky564. [Epub ahead of print]

This study is an important subset analysis of the AIDS Clinical Trials Group study A5353, which demonstrated the efficacy and safety of dolutegravir and lamivudine for the initial treatment of HIV-1 infection at week 24 in individuals with HIV-1 RNA levels 1000-500 000 copies/mL for the first time. This study shows the durability of these findings out to 48 weeks and also compares the efficacy of the regimen in participants with baseline HIV-1 RNA =100 000 copies/mL versus >100 000 copies/mL. Authors show that – in 120 enrolled eligible participants included in the analysis, 85% (95% CI 77%-91%) had virologic success at 48 weeks. At week 48, 102 of the 120 participants (85%; 95% CI 77%-91%) had virological success. Virological success was similar between those with starting HIV RNA levels below and above 100,000 copies/mL. No new drug resistance mutations were observed in any of the failures and the regimen was well-tolerated. This study, along with the GEMINI study, verifies the durability of DTG/3TC as initial therapy out to 48 weeks for those who are naïve to HIV therapy and have no baseline resistance mutations.

Bhagwat P, Kapadia SN, Ribaudo HJ, Gulick RM, Currier JS. Racial Disparities in Virologic Failure and Tolerability During Firstline HIV Antiretroviral Therapy. Open Forum Infect Dis. 2019 Feb 12;6(2):ofz022. doi: 10.1093/ofid/ofz022

Racial/ethnic disparities in HIV outcomes have persisted despite effective antiretroviral therapy. The landmark ACTG A5257 study, examining initial non-NNRTI based regimens for ART, used clinical and socioeconomic data to assess factors associated with virologic failure and adverse events within racial/ethnic groups. Study authors analyzed data from 1762 participants: 757 self-reported as non-Hispanic black (NHB), 615 as non-Hispanic white (NHW), and 390 as Hispanic. The proportion with virologic failure was higher for NHB (22%) and Hispanic (17%) participants compared with NHWs (9%). Factors associated with virologic failure were poor adherence and higher baseline HIV RNA level. Prior clinical AIDS diagnosis was associated with virologic failure among NHBs only, and unstable housing and illicit drug use for NHWs only. Factors associated with adverse events were female sex in all groups and concurrent use of medications for comorbidities in NHB and Hispanic

participants only. This important study shows that modifiable risk factors associated with virologic failure and tolerability of ART differ between racial groups, suggesting interventions to prolong the durability of first-line regimens.

"They Became My Family"

Tim Brehm, Baltimore, MD, USA

Belinda Ameterra, Worcester, South Africa

We're excited to introduce "They Became My Family," a new digital archive spotlighting the community members that are a vital component of the ACTG. Spearheaded by Community Scientific Subcommittee member Liz Barr, "They Became My Family" is named for a quote describing the ACTG community from the late Sharon Maxwell. As a long-time member of the ACTG Global Community Advisory Board and the Legacy Project's Women's HIV Research Collaborative, Maxwell worked to end HIV stigma, especially as it affected women and people living in rural communities.

"They Became My Family" offers members of the ACTG community the opportunity to share their experience and commitment, in their own words. Participants are asked to submit some type of self portrait (photograph or drawing) and to answer a few standard questions about their work with the ACTG, the community they represent, what they've been able to do, and their

hopes for the future. While each profile follows roughly the same format, the end results are as moving and diverse as our community itself. Click on the link below to see one of these powerful new profiles, which will be featured soon on the updated ACTG website.

For more information, or to submit your own “They Became My Family” profile, please contact Liz Barr at barrlizbarr@gmail.com.

Click here to read a profile from Sharon Maxwell of St. Louis, Missouri, USA

Angel Hernandez, Puerto Rico, USA

Danielle Campbell, Los Angeles, CA, USA

Investigator highlight:

Dr. Sunil Solomon, Johns Hopkins University School of Medicine

Dr. Sunil Suhas Solomon, MBBS PhD MPH is an Associate Professor of Medicine in the Division of Infectious Diseases at the Johns Hopkins University School of Medicine and the Co-Chair of A 5360, the ACTG MINMON study. Dr. Solomon completed his medical training at the Sri Ramachandra Medical University in Chennai, India and received a Masters in Public Health and a doctorate in Epidemiology (PhD) from the Johns Hopkins University. His research is primarily focused on epidemiology, clinical management, and access to care for HIV and viral hepatitis among vulnerable Indian populations such as people who inject drugs (PWID) and men who have sex with men (MSM). He has over 100 original peer-reviewed publications.

Dr. Solomon and his team recently completed one of the first cluster-randomized trials among MSM and PWID to evaluate an integrated care model to improve the HIV care cascade among key populations in India. In 2015, he was one of the first recipients of the Avenir award, a Director's award from the U.S. National Institutes of Health, aimed at identifying individuals who propose high impact research and who show promise for becoming tomorrow's leaders in the field of drug abuse and HIV. In April 2019, he was awarded a $20 million cooperative agreement from USAID to implement and evaluate novel models of HIV testing and treatment aimed at improving the HIV care continuum among key populations and their families in India.

Do you have news or information about an ACTG study or site you'd like to share for our next newsletter? Send it to ACTG Leadership & Operations

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