ACTG Network

ACTG HIV Reservoirs Cohort (AHRC) Updates

Volume 1, Issue 1

JUNE 2016

INSIDE THIS ISSUE:

AHRC Activities at the June 2016 ACTG Meeting

Monday 6/27 11am: GCAB Session III

Tuesday 6/28 7am: A5321/A5341s Sites/Team Meeting

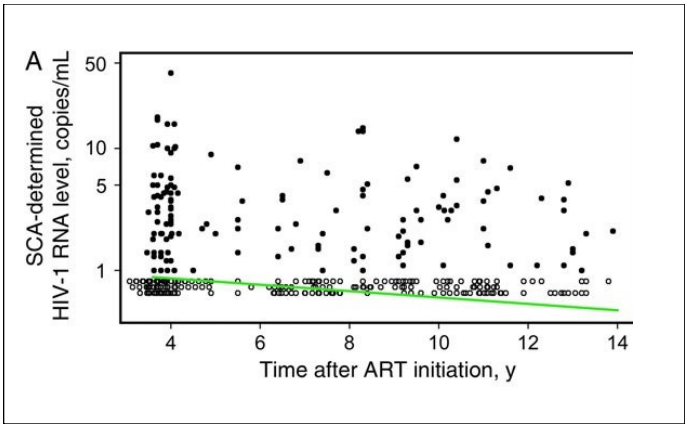
Tuesday 6/28 8-10am A5321 in Plenary Session II

Continued Decrease in Low-Level Viremia: Results of A5276s

Scientists planning the ACTG HIV Reservoir Cohort (ARHC) study got a head start with results from a sub-study of a previous ACTG study commonly referred to as the ALLRT study. In fact, because of information learned from this sub-study (A5276s), all of its participants were offered the chance to enter the ARHC study.

The ALLRT study followed participants who started HIV treatment in one of many ACTG treatment studies. Participants were followed in ALLRT even after their original study ended. A sub-study involves the collection of more information from some but not all the study participants.

The sub-study that led to the creation of the ARHC study was named A5276s. It looked at trends in plasma (the liquid part of blood) viral load over time in people taking HIV treatment using a sensitive measure of plasma viral load. The sensitive test was called a "single copy" assay (SCA). This test accurately measures much smaller levels of HIV in the plasma than routine viral load tests. The participants in the A5276s sub-study had their plasma viral loads measured by a SCA for an average of 11 years after starting HIV treatment, and some for almost 14 years (see Figure). The results were surprising in that plasma viral load levels gradually decreased throughout the study (see green line). These results suggest that cells with HIV may not persist indefinitely.



Plasma HIV RNA (viral load) SCA levels over time in A5276s

The sub-study also looked at immune system (body's defenses) tests to see if they had an impact on

See page 2

AHRC By the Numbers

- 344 participants
- 61 women & 283 men
- 73 Hispanics/Latinos
- 31 different ACTG sites
- 66 spinal taps to date

- Main Study
  Group 1: 321 (93%)
  Group 2: 15(4%)
  Group 3: 8 (2%)
- A5341s:
  Screened 11
  Enrolled 9

- Reported Race
  White: 250
  Black: 73
  Amer. Indian 6
  Asian 4
  More than 1 4
  Unknown 7

Continued Decrease in low-level Viremia (from page 1)

levels of plasma viral load. By looking at both virus and host immune system results, the researchers hoped to figure out what characteristics predicted higher (or lower) plasma viral load levels while taking HIV treatment.

A total of 334 participants from ALLRT joined this sub-study.

So, what did the investigators of this sub-study find? Did they see characteristics that might help predict who was more likely to have higher (or lower) plasma SCA viral load levels?

Participants with a high viral load in their blood plasma *before starting treatment* were more likely to have detectable viral loads by SCA *at later time-points*. Participants with high CD8 T cell count and low CD4:CD8 T cell ratios four years into anti-HIV treatment were also more likely to have detectable viral loads by SCA. Neither age, race, ethnicity, use of injection drugs, nor the type of anti-HIV drugs being taken predicted who might still have detectable viral load by SCA after four years of HIV treatment.

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Previous research has suggested that HIV viral load in the blood decreases a lot in the first several months after a person starts treatment for HIV, but that the rate of decrease slows and eventually stops after a few years. This pattern has been reported even in people who continue to take HIV treatment and have an "undetectable" viral load on routine viral load tests.

Interestingly, *the A5276s sub-study showed a different pattern.*

As expected, plasma viral load generally decreased a lot over the first year of HIV treatment. But In many participants, plasma viral load continued to decrease over a much longer time. The decrease was estimated to be about 6% per year after the fourth year on treatment. The researchers found that participants who had SCA values above 1 copy per milliliter of plasma after 4 years on treatment were more likely to continue to have decreases over time.

While the decreases in plasma viral load in this study were small, they suggest that being on HIV treatment for a long time may impact the levels of HIV hidden in the body, often referred to as HIV reservoirs. These results also suggest that the SCA may be useful in future studies of HIV reservoir size.

None of this information would be known if it were not for the contributions of the participants in the A5276s sub-study. We deeply appreciate the willingness of the participants in this and other ACTG studies to help answer questions important to the health and well being of people everywhere living with HIV. There would be no results to share without their contributions!

Demystifying A5341s

When people think about sampling human tissue, even blood, some of us get queasy or anxious or both.
One strategy to help deal with these feelings is information. It may not be enough, but it is a start.

A5341s is seeking participants *willing* to have procedures to collect tissues in addition to blood.

- Participants in this sub-study will *choose* the procedures they have.
- Results will be *more valuable* if more participants agree to have multiple tissues sampled than if they each have one tissue sampled.
- Leukaphersis is only done once.
- Did you know that gut tissue doesn't have pain receptors?
- Reservoirs studied:
  - Central Nervous System (via spinal taps)
  - Blood (via leukapheresis)
  - Gut lymphoid tissue (via rectal biopsies)
  - Genital tract (via genital secretions)

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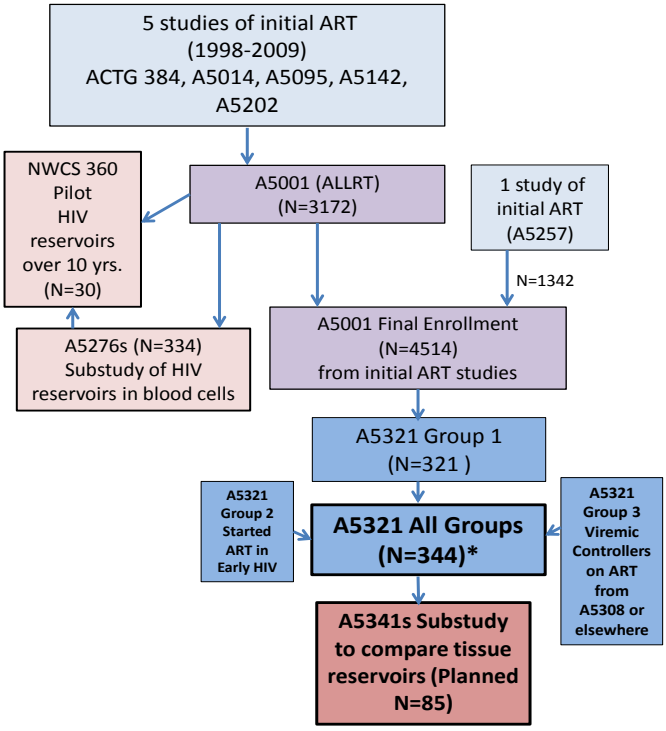
AHRC's Family Tree

Like many modern families, the ACTG's HIV Reservoir Cohort)(AHRC) Study has complex family tree (See Figure).

Most AHRC Study (A5321) participants entered the AHRC after participating in other ACTG studies.

All 5321 participants in the *AHRC's Group 1* were previously enrolled in the ALLRT (A5001) study. The ALLRT study looked at long-term outcomes of persons who participated in ACTG treatment studies. Many also participated in the A5276s sub-study of ALLRT (see article on page 1).

Group 2 enrollees in the AHRC started ART in acute or early HIV. Most of these participants were enrolled in studies not done by the ACTG. We are very grateful to Group 2 participants and the investigators that did these other studies for providing the AHRC with the valuable stored specimens that will allow AHRC to compare participants in Group 2 to those in Groups 1 and 3.



***Still open for Groups 2 and 3. Enrollment as of 6/1/16**

Group 3 participants are rare folks who controlled HIV without ART. They volunteered to take ART in A5308 or from their primary provider and have stayed on ART.

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Q and A

Q1: Can a spinal tap for the main study be done before week 72?

A1: Yes, a spinal tap can be done at any visit once a participant has consented.

Q2: How much blood is safe to draw at one time?

A2: The amount of blood that is safe to draw depends upon a person's health status and size. For healthy persons of average size, the volume limit is 450 mL ("a pint") in 56 days. The A5321 blood draws are well below the safe and acceptable amount (see picture at right).

Volume of A5321 blood draw (left), a can of soda pop (center), & a "pint" of blood (right)

The blood draws for A5321 are well below the safe and acceptable amount.

Your site Info

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The mission of the ACTG Network is to reduce the burden of disease due to HIV, tuberculosis, and viral hepatitis.

ACTG AIDS CLINICAL TRIALS GROUP

actgnetwork.org

***ACTG HIV Reservoirs Cohort** study (or **AHRC**) is a long-term study, designed to assess patterns of reservoir decay, including what factors determine both the size of HIV reservoir and its decay in people living with HIV on long-term ART*

AHRC PATHWAY TO THE CURE

- *Substantially larger than previous studies*
- *Samples stored over time available from participants who have received ART for much longer than in previous studies*
- *Greater ability to assess whether participants on long-term ART have different reservoir decay patterns (e.g. a subset with continuous decay) and to identify factors associated with reservoir decay*

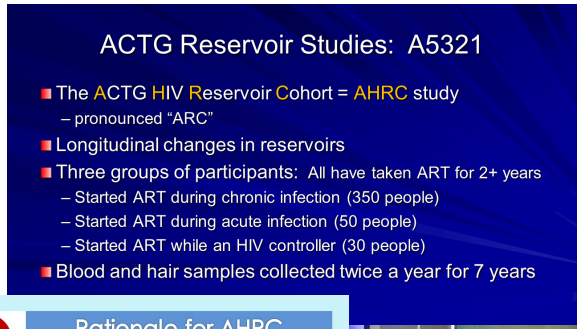
SITE HIGHLIGHTS: UNIVERSITY OF WASHINGTON CAB

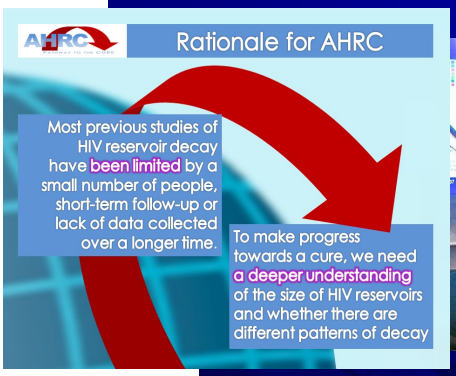
Each site has a community group to advise the site about issues related to the ACTG.

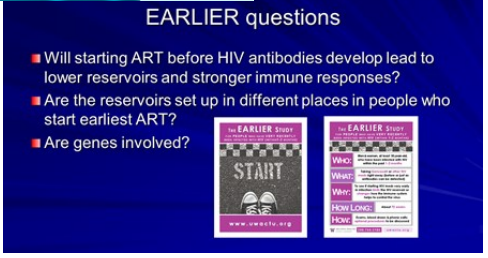
A recent meeting of the University of Washington AIDS Clinical Trials Unit Community Advisory Board (CAB) offered an opportunity to highlight a few ACTG studies including the AHRC (A5321), its tissue sub-study (A5341s), and A5354, a upcoming ACTG study looking at whether treatment of acute HIV can impact HIV reservoirs.

Dr. Janine Maenza provided an overview about :

- What is a 'reservoir'?
- Why are reservoirs important?
- How reservoirs are studied (sampled)?
- Studies looking at reservoirs being done at the UW ACTU and the UW Primary Infection Clinic







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