Laboratory Technologists Committee Lends Its Expertise

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Laboratory Technologists Committee Offers Its Expertise to the Network

What do a blood volume tool, a leukapheresis standard operating procedure and a laboratory processing chart all have in common? These are three examples of how the AIDS Clinical Trials Group (ACTG) Network’s Laboratory Technologists Committee (LTC) is ensuring study uniformity and quality results. The LTC works with other committees and members within the Network as well as experts in different scientific disciplines to develop standardized operating procedures and tools that will help to ensure uniform specimen collection, processing and testing with the ultimate goal of generating quality data.

“The only differences in a study should be the treatment arms, not any variables due to sample collection, processing or testing,” says Christopher Lane, Associate Laboratory Director at the ACTG’s University of Rochester site. “This not only guarantees the integrity of one study’s results, but it allows investigators to compare more than one study because all samples are collected, processed and tested the same way every time.”

The LTC wants to get the word out to more members of the ACTG Network that they are a dedicated group of laboratorians who are committed to serving as a resource for developing new tools and strategies to help standardize procedures and processes contained within the clinical trial protocols. As clinical trials become more complicated and utilize more esoteric assays to answer very complex scientific questions, it becomes more apparent how important it is to work together to ensure everyone is educated and trained to perform the requirements of the protocol to the best of his or her ability. It’s important to the Network and the study subjects who volunteer to help find the answers to these crucial questions.

“How do we make a protocol’s sample collection more efficient? How do we ensure the objectives of a protocol can be achieved?” asks Cheryl Jennings, Lab Manager of the Virology Quality Assurance (VQA) Program and LTC Co-Vice Chair. “We, as a committee, will work and strive to get these answers.”

More Than 150 Years of Experience

LTC members represent many of the ACTG’s sites around the world and come from a variety of backgrounds. Before running the Network’s laboratory at Ohio State University, Lori Kryspin came from a microbiology background with experience working with samples containing the bacterium known to cause tuberculosis.

“I knew very little about immunology at first, but the LTC has been the single biggest career growth experience of my life. You are pushed to gain expertise in a lot of areas and stretch in different ways,” says Kryspin, former LTC Co-Chair. “I think we added up all of our experience.
Laboratory Technologists Committee Offers Its Expertise to the Network

once and it came to something like more than 150 years of lab experience accumulated on the LTC, which is pretty impressive.”

A term on the LTC lasts for three years. Many members opt to serve more than one term, which shows the level of commitment the members feel to this committee. However, the committee is eager to have new members, particularly from international sites, in order to help spread the committee’s expertise throughout the Network. The committee has voting and non-voting members.

Most of the voting members manage the laboratories at their particular ACTG-affiliated Clinical Research Site or Clinical Trials Unit. The Network’s laboratories typically receive specimens from one or more local clinics, often from varying distances, and process the samples into the derivatives outlined in the study or protocol. More intensive studies may require that a laboratory extend their operating hours, introduce multiple shifts or learn specialized procedures in order to accommodate protocol collection and processing requirements. Since the infrastructure for each site varies, processes must be robust enough to accommodate different settings.

Laboratory and site capability need to be defined up front to determine if a site is eligible for participation in a study. The only way to understand the requirements for a given protocol is to ensure that the protocol and supporting documents are well-defined and fully developed before the first subject is even enrolled. LTC voting members contribute to protocol development; prepare instructional Laboratory Processing Charts (LPCs); and contribute to protocol Manual of Operations (MOPs), various study team communications and site laboratory trainings.

“Specimens have to be collected, processed and then either tested or stored depending on the needs of the individual protocols, labs and sites,” says Kryspin. “Supporting these processes must be flexible, creative and dependable in order to meet all these needs and maintain the quality of the samples to ensure that the analyses are of good quality and produce good data.”

Non-voting members hail from a variety of backgrounds within the ACTG such as pharmacology, data management and biostatistics. All together, the committee offers a diverse starting point for tackling any questions about collecting, processing or testing study samples.

The Cure TSG Challenge
The ACTG’s Cure Transformative Science Group (TSG) approached the LTC to request assistance writing and maintaining standardized operating procedures (SOPs) for sample collection and processing for their upcoming studies. The requests included an SOP for leukapheresis, a clinical procedure where white blood cells are separated from a sample of blood while the blood is being col-
lected from the subject, as well as SOPs for the collection of gut-associated lymphoid tissue (GALT), bone marrow, cerebral spinal fluid and genital secretions. These SOPs not only define the collection process for these complicated specimen types, but they also outline the standardized handling and processing that must be done to ensure the integrity of the sample.

“ACTG Lab Leadership wanted them to be standardized, put into a format the new investigators could easily use and then maintain over time,” Kryspin says. “They felt the LTC was a good group to do this because of our track record of maintaining the ACTG Lab Manual over many years.”

Before developing the SOPs, the LTC members did their research, says Carmen Irizarry, Laboratory Supervisor at the ACTG’s University of Puerto Rico site and former LTC Co-Vice Chair.

“We reached out to immunologists for guidance about the gut biopsies and we reviewed the HIV Vaccine Trials Network’s process for leukapheresis,” she says. “The LTC might not have all of the answers initially, but we will go and find out whom to ask to get what we need. This group works hard and we will not pass off any questions.”

When creating SOPs, the LTC also looks at the guide they are developing from the eyes of all the product’s end-users, including other laboratory staff, investigators and clinicians. That is another reason it is helpful the committee is made up of people with different backgrounds.

“We try to see from diverse perspectives and we will get the answers to make the SOPs relevant to every person who will be using them,” says Joan Dragavon, Laboratory Manager of the ACTG’s University of Washington site and LTC Co-Chair.

Once the SOPs are created, the LTC ensures the processes can be followed at the ACTG’s domestic and international sites. The LTC identifies areas where specialized training will be required and collaborates with others to provide training options and tools.

“All of our sites worldwide need to be able to use the SOP because if procedures are handled differently at each site, we will have a problem with quality assurance of study results,” Jennings says. “We can develop innovative research questions, set up great clinics and recruit patients, but if what comes out of the laboratory isn’t good, all else is wasted.”

Not Working 9-5
In addition to working at their site’s lab, laboratory technologists are also members of multiple ACTG protocol teams. For example, Lane currently serves as the laboratory technologist on two of
the ACTG’s tuberculosis studies and two of the Network’s hepatitis trials. Becoming a member of the LTC and the commitments this role brings are above and beyond the daily routine.

“I’ve been in the car with my children before, but I still managed to be on that conference call,” jokes Irizarry. “Despite phone connections, speaking different languages and time zone differences, we all make it on those calls even if it is not during normal working hours.”

Lane, who joined the LTC in 2011, agrees saying committee members do not mind the role cutting into personal time because they feel “honored to be on the LTC and contributing to HIV research.” He recommends likeminded Network members consider joining.

“Being a new LTC member was daunting at first, but the level of support you get from other members makes it a wonderful learning experience,” Lane says. “You can ask them anything. In fact, the only silly question is the unasked question. You can express your frustrations. It really is a level of camaraderie I haven’t seen since the military. The LTC is a little family motivated to contribute to the ACTG and furthering HIV research.”

Christopher Lane says the LTC is like a family with the shared goal of contributing to the ACTG and furthering HIV research.

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Communications Corner: 
Listen to Our “Why Women” Campaign

One in four people living with HIV in the United States is a woman. Yet enrolling women into clinical trials and engaging with them in our Community Advisory Boards continues to be more challenging than recruiting men.

Network investigators, site staff and CAB members share why women’s participation in research can benefit them and help in the fight to end AIDS. Below is a screenshot of the Why Women campaign on our website. Listen to your colleagues give their top 10 reasons women are needed to further HIV research. From the unique way antiretroviral therapy affects women to creating a diverse support network, women are our ally in this fight and we hope our staff’s encouraging words inspire them into action!

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A5317: TRAFIC Study Seeks to Reduce Inflammation

Any time the body has an infection irritation and inflammation can occur. For people living with HIV, this inflammation can persist despite taking antiretroviral therapy (ART) to control the virus. Chronic inflammation can damage tissues and prevent organs from working properly. AIDS Clinical Trials Group (ACTG) Network researchers hope to reduce inflammation and the formation of excess scar tissue, or fibrosis, in the organs of people living with HIV through the TRAFIC study.

“When your fat is unhappy, your whole body is unhappy,” says Jordan Lake, MD, MSc, Investigator at the ACTG’s University of California, Los Angeles CARE Center site and Co-Chair of the TRAFIC study. “Fat produces many hormones and chemicals. When fat isn’t functioning normally, inflammation can occur and the hormones fat makes can become unbalanced. Dysfunctional fat has been associated with health problems like diabetes, memory loss and heart disease. Inflammation can also lead to scarring of the lymph nodes or glands. When lymph nodes become scarred, the body cannot make as many T cells. We want to see how inflammation is affecting the lymph nodes and fat tissue of people living with HIV, and see if we can find a treatment to prevent fibrosis and allow the lymph nodes and fat tissue to function normally.”

The TRAFIC study (or A5317) stands for Telmisartan to Reduce AIDS-Related Fibrotic and Inflammatory Contributors. Study participants will take either telmisartan, a medication with anti-inflammatory properties, or no study drug in addition to their anti-HIV medications for 48 weeks. They will also undergo lymph node and fat tissue biopsies at the beginning and end of the study.

“A biopsy is a small section of tissue taken through an incision,” says Netanya Sandler, MD, Investigator at the University of Texas Medical Branch at Galveston and Co-Chair of the TRAFIC study. “We can only get so much information from a person’s blood. If we want to know how a specific tissue is impacted by HIV, we must go get a sample of the tissue itself.”

Sandler and Lake hope telmisartan will reduce inflammation in people living with HIV and improve lymph node and fat tissue function. Healthy lymph nodes and fat tissue could lead to increased T cell production and improved metabolism, which could decrease the risk for diseases including heart disease and diabetes.

The study is enrolling at ACTG-affiliated clinical research sites in the United States. Study volunteers should be 18 years or older and have an undetectable viral load for at least one year on anti-HIV medications. Click here to learn more about the TRAFIC study.
Researchers from the AIDS Clinical Trials Group (ACTG) Network have identified a combination of HIV medications that is well tolerated and suppresses viral load.

The Network’s A5257 study sought an option for treatment naïve patients that did not include efavirenz, a drug from the Non-Nucleoside Reverse Transcriptase Inhibitor or NNRTI class of HIV medications that is not always well tolerated. Instead, A5257 compared three alternative treatment options - two once daily combinations from the Protease Inhibitor (PI) class of HIV medications and one twice daily combination from the Integrase Inhibitor (II) class. Although all three treatment arms successfully suppressed study participants’ viral loads, the twice daily Integrase Inhibitor combination was better tolerated.

“Tolerability was the key factor here, not once daily dosing,” says Jeffrey Lennox, MD, A5257 Co-Chair and a Principal Investigator at the ACTG’s Emory CDC Clinical Trials Unit in Atlanta. “Patients will take a medication twice a day if there are not a lot of side effects.”

Some participants who took either of the two Protease Inhibitor arms - either a combination with atazanavir or darunavir - experienced nausea and diarrhea. Those on atazanavir also sometimes reported a yellowing of the skin and eyes. Study volunteers who had been randomized to the Integrase Inhibitor arm took raltegravir twice daily and were less likely to develop these side effects.

“From a purely virologic standpoint, all three treatment arms were successful,” says Lennox. “If as a physician you want to prescribe a medication combination for your patient that he or she can remain on long term, raltegravir would not necessitate a change due to side effects down the road.”

The study included 1,809 treatment naïve participants from ACTG and International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network sites around the United States. Lennox says the participants’ demographics closely mirrored the populations in the US where most new HIV infections occur. Twenty-four percent of participants were women, 42 percent were African American and 22 percent were Hispanic. Study Co-Chair Judith Currier, MD, says addressing tolerability of anti-HIV medications is critical as people with HIV live longer.

“When we consider that people living with HIV are going to be taking these medications for decades, it is critical that we assess the tolerability of the drugs regimens and their impact on longer term complications,” says Currier, the ACTG’s Vice Chair and Principal Investigator of the University of California, Los Angeles CARE Center Clinical Research Site. “For this reason a detailed metabolic substudy was included as a part of A5257 and the results from that trial are expected soon.”

Findings from A5257 were presented at the 21st annual Conference on Retroviruses and Opportunistic Infections (CROI) in Boston in early March.
Small Site Helps Christie Lyn Costanza Realize Passion for Community Outreach

Christie Lyn Costanza is truly a jack-of-all-trades within the AIDS Clinical Trials Group (ACTG) Network. Currently serving as the Data Manager and Study Coordinator for the New Jersey Medical School’s (NJMS) Adult Clinical Research Site, Costanza is constantly finding new ways to get involved and stay busy.

In 2008 Costanza started working part time with the ACTG as the Data Manager. At the time she was also working for Planned Parenthood. With Planned Parenthood, Costanza was able to go out and become a part of the community. This sparked her interest in HIV-related issues and community outreach.

In January of 2009 Costanza accepted a full time job as the NJMS site’s Data Manager. While Costanza still does data entry, she really enjoys working directly with the patients. Since starting with the ACTG she has received her HIV testing certificate, research coordinating certificate and Master’s in Public Health.

“My real passion is with the people and patient education,” she says.

Costanza attributes her success in multiple areas of interest with her site and the community. NJMS, located in Newark, New Jersey, is a smaller site with only four employees. With a smaller group they are able to get involved on every level and work closely as a team. The most unique thing about NJMS Adult CRS is that their office is located right next to a nurse’s station.

“In such an urban and diverse area that is historically skeptical about research, it’s nice to be so close to answer all the patients’ questions,” says Costanza.

Nancy Reilly works with Constanza at the NJMS site as its Research Program Manager.

“It was obvious early on that she was so talented. She has such a big picture view of the whole thing,” says Reilly. “She is all in when it comes to her work. And her enthusiasm rubs off.”

Aside from her work at her site, Costanza is also involved in the ACTG’s Outreach, Recruitment and Retention (OR&R) subcommittee. This was a role that she applied to because of her background with Planned Parenthood and community outreach.

“OR&R is a real natural fit for Christie Lyn,” says Reilly. “She has such innovative ideas. She is a problem solver and has clever and creative solutions.”

Costanza has since been named Co-Vice Chair of OR&R. OR&R is a resource available to all ACTG sites that tackles issues with recruitment and retention.
One of OR&R’s major projects is to develop recruitment materials for protocols. “For example A5322 is small and selective so instead of a flyer we created more of an info sheet,” described Costanza. “We cater the material we make to fit the protocol.”

Savita Kanade works closely with Costanza as OR&R’s other Co-Vice Chair.

“Christie Lyn’s skill of making things simple to understand and execute makes her an asset to the community,” says Kanade, who works at the ACTG’s B.J. Medical College site in Pune, India.

OR&R also developed a participant appreciation project in 2013 that it hopes will become an annual tradition at the Network’s many sites. Costanza was instrumental with getting the project off the ground photographing Network members and their messages of gratitude during the ACTG’s November meeting in Washington, DC.

“The most important thing to OR&R is the patients, so we created Participant Appreciation Day as a constant reminder,” explains Costanza. “On Dec. 2, 1986, the first patient was enrolled in an ACTG study. Now, on December 2, the ACTG remembers to take a second and thank all participants.”

OR&R recently finished elections which will be finalized soon. “We welcome people to come and visit and join our calls to find out what we are doing,” notes Costanza.

Costanza is currently pursuing her nursing degree. When she isn’t busy studying she enjoys spending time with her family and dancing.

“I like to stay busy!” she says. “I am a huge nerd and I think I will forever be in school.”

Questions, Comments and Story Ideas

This is the seventh edition of the ACTG Update. If you would like your enrolling study featured or results from your completed trial highlighted, please contact Morag MacLachlan at mamaclachlan@partners.org. Any questions, comments and story ideas are also welcomed!