New Trial Aims to Curb HPV-Related Cancers in HIV+ Women and Children

International ‘dream team’ to use new technologies and prevention approaches to help those at highest risk.

November 25, 2019 By Diane Mapes

A “dream team” of researchers from Fred Hutchinson Cancer Research Center just received funding from the National Institutes of Health for an ambitious five-year collaboration designed to help a population at high risk for cervical and other HPV-related cancers: women and children living with HIV.

Through the project, which comes with around $1.8 million each year, researchers will conduct three separate trials in three major Latin American cities: Lima, Peru; Rio de Janeiro, Brazil; and Santa Domingo in the Dominican Republic. Principal investigators include Hutch global health expert Ann Duerr, MPH, MD, PhD, Hutch epidemiologist Margaret Madeleine, MPH, PhD and Robinson Cabello, MD, executive director of Asociación Civil Vía Libre, Peru’s oldest community-based AIDS service organization.

“It really is a dream team of Fred Hutch HPV and HIV researchers who came together for this project,” said Duerr, who’s worked in HIV and global health for decades. “We’re also working with [Seattle-based health nonprofit] PATH and with great partners in our Latin American trial sites.”

Many cancers have been linked to the human papillomavirus, or HPV, including cervical, anal, penile, vulvar and some head and neck cancers. While cervical cancer rates in the U.S. have stayed low for years thanks to screening and an effective HPV vaccine, it remains the fourth-leading cause of cancer and cancer death worldwide.

Women and children infected with HIV are at a much-increased risk for HPV-related disease — especially cervical cancer, which is more prevalent in low and middle-income countries. In the U.S., seven out of every 100,000 women are diagnosed with an HPV-related disease; in Latin America, it’s three times that.

The large collaboration aims put a dent in the rate of diagnosis and death of HIV-positive women and boost cancer prevention for children born with HIV.

Optimizing HPV vaccination in girls with HIV

The first of the trials will focus on HIV-positive children in Lima, Peru, and Rio de Janeiro, Brazil, with participant recruitment scheduled for spring of 2020. This study will give HPV vaccines to preteens and adolescents (9- to 13-year-olds) with the aim of providing the most protection possible for this high-risk group.

“This study stems from work [Hutch scientist] Denise Galloway, PhD, did on the schedule of vaccinations,” said Duerr (she and Galloway are protocol co-chairs for the preteen/teen trial). “Adults and HIV-infected kids get three vaccinations — one to start, one at two months and another at six months. [Children] who are HIV-negative get two vaccinations, one to start and another at six months. They have more robust immune systems.”

Galloway, scientific director of the Hutch’s Pathogen-Associated Malignancies Integrated Research Center and holder of the Paul Stephanus Memorial Endowed Chair, played a pivotal role in identifying how HPV causes cancer and showed that the virus was associated with nearly all genital-tract cancers and some head and neck cancers.

Galloway’s research showed that the third HPV dose might actually not boost memory B cell response in kids infected with HIV. Memory B cells are a type of immune cell that arise after an infection — or a vaccination — launching a strong, fast response by targeted immune proteins called antibodies. Antibodies respond to pathogens like HPV.

Vaccination promotes strong antibodies to HPV. The trial will drill down into different vaccination schedules, measuring the body’s response after each dose, in an effort to zero in on the sweet spot — the fewest doses and the highest amount of protection — or peak response.

“We’re studying different timing of doses to try and elicit the strongest, longest-lasting B cell memory response we can get,” she said. Researchers will use a nine-valent vaccine, which protects against more strains of HPV.

Improving cervical cancer prevention and treatment in HIV-positive women

The new NIH grant will also fund two clinical trials aimed at improving both cervical cancer prevention and treatment in HIV-positive women.

A screening trial, led by Madeleine and Silvia de Sanjose, MD, PhD, of PATH, will take place in the Dominican Republic, where cervical screening via Pap smear can be onerous and unreliable. It will field test two new techniques designed to find cervical cancers or precancers more effectively.

“All women need to be screened, even after they’ve had the HPV vaccine, but for HIV-positive women, it’s even more important because they’re at a much increased risk for HPV-related disease,” Madeleine said. “Our hope is that by streamlining screening using new technologies, we can improve access and accuracy.”

Participants will use a new device to gather cervical cells — a tampon-type device for self-collection — then the gathered cells will be tested for HPV. Those who are HPV-positive will go on

to receive a colposcopy, a test where a doctor looks for potential cancers using a light, magnification and a special solution.

Madeline said the new technique may actually prove superior to other current screening tests.

“The thing about the self-collection test we’re using is that it tells you the HPV oncogenic type that’s present,” she said. Oncogenic or high-risk strains of HPV are linked to cancer. “It will help us determine not only that HPV is there, but that it’s expressing high levels of HPV viral proteins that are more likely to lead to a cancer.”

The clinical trial will also test the effectiveness of a tool called a “field colposcope.”

“It’s basically a cell phone that’s been adapted to be a colposcope, a microscope,” Madeleine said. “It’s packaged as a medical instrument and has a magnifier that doctors can use to look at the cervix.”

The third trial will also take place in Rio de Janeiro and will test the efficacy of a therapeutic vaccine for HIV-positive women who’ve developed HPV-driven precancers. That is, they’ll use the vaccine as a treatment for existing precancers, not as a preventive.

“We’ll be looking at HIV-infected women who have high-grade precancerous lesions [high grade lesions are more likely to become cancerous and spread] and using an HPV vaccine on them with therapeutic intent,” Madeleine said. “The vaccine will be only effective in people who have precancerous lesions.”

The large collaboration will also include international expert on HIV-related cancers Thomas Uldrick, MD, Ying Chen, PhD, head of the project’s data management and statistics core, and Rachel Bender Ignacio, MPH, MD, all of Fred Hutch; Silvia de Sanjose, MD, PhD director of PATH’s Scale-Up project for cervical cancer protection; Yeycy Donastorg, MPH, MD, in the Dominican Republic; Lenka Kolevic, MD, in Peru and Beatriz Grinsztejn, MD, PhD, in Brazil.

This U54 award is part of the NCI Division of Cancer Prevention’s U.S.-Latin American-Caribbean Clinical Trials Network (ULACNet) for Prevention of HPV-related Cancers in People Living with HIV.

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