Phase III Study of the Efficacy and Safety of the Microbicide Carraguard in Preventing HIV Seroconversion in Women (Population Council Protocol 322)

Summary

In response to the urgent need for widely available, easy-to-use protection against the sexual transmission of HIV, Population Council scientists developed a candidate topical microbicide called Carraguard®. Prior Population Council research demonstrated that Carraguard successfully blocked the HIV virus in laboratory studies and results from Phase I and II clinical trials showed that Carraguard was safe for and acceptable to women in those trials.

This was a Phase III prospective, randomized, parallel group, two arm, placebo controlled, double-blind trial of Carraguard conducted at three sites in South Africa (Soshanguve, Gugulethu/Nyanga districts, and Durban) between March 2004-March 2007. The primary objectives were to determine the efficacy of Carraguard gel in preventing HIV transmission when applied vaginally prior to sexual intercourse and its safety for long-term use.

Eligible participants were HIV-negative, sexually active, non-pregnant women, aged 16 or older, without signs of cervical cancer, and willing to give informed consent. Women participated for a minimum of nine months up to 24 months. Participants were recruited from a range of sites around the study clinics, such as family planning and primary health clinics, community and church groups, shopping and transport areas, and other public locations.

Each study site developed an outreach process for consultation with the local community before, during, and after the trial to help ensure that the research teams were aware of and responsive to local cultural and political concerns. This included, in some cases, Community Advisory Groups (comprised of local researchers, activists, NGO representatives, health authorities), community meetings and information sessions, and posters, fliers, and advertisements about the trial.

During screening visits at the study clinics, women had a physical exam, including a pelvic exam, received tests for pregnancy, HIV, and STIs, and were engaged in a comprehensive informed consent process. Written informed consent was obtained from all study participants. Trial objectives and procedural details were explained to participants, along with potential risks and benefits, via a mandatory study booklet, study video, and informed consent form. Each participant was assured that she was free to withdraw at any time.

At enrollment study participants were randomized into one of two study arms: Carraguard and condoms, or placebo and condoms. Participants in both arms were instructed to empty one full, single-use applicator of gel into the vagina within one hour prior to each vaginal intercourse, to use the gel only vaginally, not to use other vaginal products or cleanse the vagina for at least one hour after intercourse, to use condoms, and to return to the site between visits if they needed more gel.

Women attended follow-up visits at one month, then quarterly for up to two years, for clinical evaluation, pelvic exam, HIV counselling and testing, diagnosis and treatment of curable STIs, condom and gel re-supply, applicator return, and other compliance measures. Samples were collected at selected visits and when clinically indicated for STI testing.

Women in the study were advised of the potential risks of participation, including: minimal vaginal bleeding or discomfort during the pelvic exam; discomfort at the site of blood drawing; embarrassment during the pelvic exam; anxiety about a positive HIV test result; stress on relationships after being diagnosed with HIV or an STI; genital lesions or vaginal flora disturbances due to the potential toxicity of the gels; potential loss of confidentiality and stigma from involvement in the study and association with being at risk for HIV infection; and, unlikely, but possible risk of contracting HIV.

Participants were provided with the following benefits free of charge: diagnosis of sexually transmitted and vaginal infections, and treatment for curable infections; HIV testing and risk reduction counseling; male condoms; diagnosis of cervical dysplasia and referral for treatment; and, for their male partners, referrals for STI diagnosis and treatment, and HIV counseling and testing. Any participants who tested positive for HIV at screening or seroconverted during the trial were withdrawn from the study and provided with referrals to counselling and medical services in the community. Information on study participants was considered confidential and transmitted only in a form that did not permit identification of the individual, and all records were kept in a secure storage area with limited access.

Adherence to study gel use was assessed through behavioral interviews and the use of a dye test to determine vaginal use of applicators. Safety was assessed through documenting adverse events and the change from baseline in clinical laboratory tests, STI infections, and physical examination findings. Serious adverse events, regardless of causality, were immediately reported to the Population Council, and also directly reported to local health/regulatory authorities and the local IRB or Ethics Committee. An independent Data Safety Monitoring Board (DSMB) convened three times to review interim analyses for safety, including adverse events; the last review also included efficacy.