Investigational Gel, Condom Reduce HIV Spread

BY ROBERT FINN

SAN FRANCISCO — When used intravaginally in combination with a condom, the investigational microbicide PRO 2000/5 gel appeared to reduce HIV transmission by 30% in a large, international, randomized clinical trial.

The finding, which fell short of statistical significance, was seen in a study called HPTN 035 (Phase II/IIb Safety and Effectiveness Study of the Vaginal Microbicides BufferGel and 0.5% PRO 2000/5 Gel [P] for the Prevention of HIV Infection in Women). A reduction of 33% would have reached statistical significance, according to Dr. Willard Cates, Jr., president of research at Family Health International, which designed and launched the trial. FHI is a nonprofit foundation in Research Triangle Park, N.C.

The study followed 3,099 women at one U.S. site and at sites in five African countries. All women were given free condoms, HIV risk reduction counseling, and diagnosis and treatment of sexually transmitted diseases. The study participants were then randomized to one of four groups. One-quarter were given PRO 2000/5 gel, one-quarter were given another microbicide called BufferGel, one-quarter were given a placebo gel, and the remaining women did not receive any gel. The gels were provided as single-use, prefilled applicators and the study participants were instructed to apply one dose of the contents intravaginally up to 60 minutes before each vaginal intercourse. The women were followed for an average of 20 months and were evaluated monthly; 94% of the women completed study visits through the follow-up period.

Participants in the three gel groups reported using the gel during 81% of all sex acts, and nearly all women (99%) said they would use the products if approved for HIV prevention. Women in the three gel groups reported using condoms 72% of the time, and women in the no-gel group reported using condoms 81% of the time.

In all, 194 of the women acquired HIV; 36 women in the PRO 2000/5 group, 54 in the BufferGel group, 51 in the placebo gel group, and 53 among participants who used no gel. This corresponds to an effectiveness rate of 30% for PRO 2000/5; a rate of 33% would have been statistically significant. In a subanalysis based on reliability of condom use, there was little difference in the infection rate among women who used condoms more than 85% of the time. However, the infection rate was 4.6 per 100 person-years among the low-condom-use women given the placebo gel compared to 1.0 per 100 person-years among the low-condom-use women given PRO 2000/5 gel. The variation corresponded to an effectiveness rate of 78% for the microbicide.

Dr. Cates acknowledged at a meeting on contraceptive technology sponsored by Contemporary Forums that this post hoc subanalysis did not carry the statistical weight of a primary outcome. "It's not conclusive, not etiologic reasoning in its purest, but at least it's a hint and a ray of hope in a field that was looking for any good news," he said.

Dr. Cates said that a separate trial of PRO 2000/5 gel, involving about 9,000 women, is expected to be completed by the end of 2009, with data available early in 2010.

The investigational microbicide PRO 2000/5 gel (0.5% dose) was developed by Indevus Pharmaceuticals Inc. of Lexington, Mass., and is an entry/fusion inhibitor designed to make it difficult for HIV to attach to and infect healthy cells. The investigational microbicide BufferGel was developed by ReProtect Inc. of Baltimore and is thought to work by boosting the natural acidity of the vagina in the presence of seminal fluid.

The study was funded by the National Institute of Allergy and Infectious Diseases (NCT00074425). Invedus and ReProtect provided the microbicide gels, and the U.S. Agency for International Development provided funding to manufacture BufferGel for the study. Dr. Cates disclosed that he had no conflicts of interest.

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