



in the news



There was exciting news from two major conferences this year. Dr. Harold Dion reports from the 17th annual Conference on Retroviruses and Opportunistic Infections (CROI), held on February 16 to 19 in San Francisco, California, and the XVIII International AIDS Conference held in July 2010 in Vienna, Austria.

More on the preventive vaccine

In the last issue of *Relay*, I mentioned that the US Military HIV Research Program and Thailand's Department of Public Health had found that the RV 144 vaccine (a combination of two vaccines, ALVAC-HIV and AIDSVAX/B/E) demonstrated some effectiveness in preventing HIV. The study has been ongoing in Thailand since 2003 and includes more than 16,000 HIV-negative men and women aged 16 to 30. It showed that the transmission of HIV was reduced by 31.2% in those receiving the vaccines compared to those taking the placebo.

At CROI, researchers described the protective effect as "early and transitory" — not the best news. However, the vaccine study will continue as it remains the only one to show a capacity to reduce HIV transmission. Further results are expected in 2013 and 2019.



Early treatment improves longevity and quality of life

Data from the HOPS (HIV Outpatient study) presented at CROI supported the theory that starting HAART when CD4 cell counts are higher than 350 cells/mm³ can protect against later complications. More than 1,300 people living with HIV in the US were followed from 1996 to 2007. People who started treatment early (that is, with CD4 counts above 350 cells/mm³) achieved higher CD4 cell counts and were less likely to die from causes other than HIV.

Two other studies provided possible explanations for this protective effect of early HAART. In the first, Dr. Priscilla Hsue from the University of California at San Francisco analyzed the impact of the nadir (lowest-ever) CD4 level on artery stiffness, a marker of risk for heart disease. She found that a nadir CD4 count under 350 cells/mm³ was independently associated with significant arterial stiffness that persisted despite HAART.

A second study presented at the CROI conference called CHARTER (CNS HIV Antiretroviral Therapy Effects Research), which included more than 1,500 people, looked at neurocognitive disorders associated with HIV, such as difficulties with memory, concentration, learning and information processing. Researchers demonstrated that people who started HAART when their CD4 cell count was higher had less risk of developing neurocognitive problems and this was true regardless of age, viral load, gender or duration of treatment.

New treatments

Results at 24 weeks from two Phase II clinical trials on the effectiveness of a new “quadruple pill” were presented at CROI. (This combination was mentioned in the Annual Progress Report in the last issue of *Relay*, under “More one-pill-a-day regimens”). Called the “Quad” pill, it combines four different ARVs: the integrase inhibitor elvitegravir, emtricitabine (FTC), tenofovir (Viread®) and GS-9350 (also called cobicistat, a new PI booster medication similar to ritonavir but with no activity against HIV).

The first study compared the “Quad” pill to Atripla® in 71 treatment naive people with CD4 counts higher than 50 cells/mm³, a viral load greater than 5,000 copies/mL and no resistance to NRTIs, NNRTIs or PIs. The second compared the new medication to Truvada® (a combination of tenofovir and emtricitabine) combined with atazanavir (Reyataz®), boosted with ritonavir, in 79 people with the same characteristics as in the first study. The “Quad” pill appeared to work as well as the two other ARV combinations and produced fewer side effects. Phase III studies will therefore proceed

in 2010. The “Quad” is not currently available in Canada, nor has it been approved for use by Health Canada.

Finally, a new CCR5 receptor antagonist (TBR-652), was prescribed once a day in pill form as monotherapy over a period of 10 days to 54 men older than 40 with CD4 counts over 250 cells/mm³, a viral load higher than 5,000 copies/mL and an R5 viral tropism (meaning that viruses have mostly R5 co-receptors on their surface and no CXCR4 virus). The 75 mg per day dose decreased the viral load from a baseline of 100,000 copies/mL to 10,000 copies/mL in 10 days and was well tolerated. The drug doesn’t act on cytochrome P450 enzymes in the liver, so interactions with other medications are less likely.

No change was seen in the co-receptor tropism (e.g. the virus didn’t switch to the other co-receptor type), and no resistance appeared. (See the article “Why CCR5 inhibitors won’t work for everyone,” *Relay* magazine Vol 3 No. 2 for more on CCR5s and viral tropism). These optimistic findings mean that further research will go ahead.

At last, a gel that reduces transmission!

The news that generated the most enthusiasm at the 18th International AIDS Conference held in July in Vienna, Austria, was evidence that a vaginal microbicide gel tested in South Africa reduced the risk of transmission of HIV and genital herpes in women by 39% and 51%, respectively.

The study, known as CAPRISA (Centre for the AIDS Program of Research in South Africa) 004 is being conducted in urban and rural parts of South Africa. A total of 889 HIV negative women aged 18 to 40 at high risk of infection (e.g. having more than two sexual relations involving penetration in the last 30 days) received a gel containing either tenofovir or placebo. Women were instructed to use an applicator to apply the product in the vagina no more than 12 hours before and after sexual relations (to a maximum of two doses in a 24-hour period). Each month for over two and a half years, the researchers asked the women about their use of the gel and condoms.

Among women who used the gel, the incidence of HIV fell by 39% compared to women using the placebo gel. Incidence fell by 54% among women who used the gel more often (more than 80% of the time). As well, a sub-study showed a 51% reduction in the incidence of herpes (HSV-2).



No side effects or resistant virus were reported during the study period. The women appreciated using the product and hoped to continue using it after the study ended. A Phase III study has already begun with a group of 4,000 women, and the first results should be available in 2013. The gel will also be adapted for use during anal penetration by men who have sex

with men. The gel is not currently available in Canada, nor has it been approved for use by Health Canada.

These results may not seem like the news story of the year. But the consequences are huge given the size of the epidemic in many African countries and the fact that women are disproportionately affected in many parts of the world. Over a dozen gels tried in the past two decades have proven ineffective and even sometimes dangerous in clinical trials.

Women will finally have a way to protect themselves even when their partner refuses to wear a condom. For the first time, we see encouraging results with a microbicide that has the potential to revolutionize prevention, help slow the AIDS epidemic, and save millions of lives.

A complete list of abstracts from the International AIDS Conference can be found at www.aids2010.org. 