Most of South Africa and the world’s top HIV/AIDS scientists are ‘excited and hopeful’ about the first-ever trial of a vaginal microbicide gel containing the highly effective ARV agent tenofovir, launched in Durban last month.

The test product, even if partially successful, has profound self-protection implications for millions of HIV-vulnerable sub-Saharan women, with the potential to directly impact the dynamics of HIV transmission.

With highly enhanced adherence potential (it needs application within 12 hours before and after coitus) and a sophisticated ‘chain terminator’ cell mechanism, tenofovir gel has already proved an effective barrier to HIV infection in monkeys.

Until now microbicide gels had to be applied within, at most, an hour of coitus.

Tenofovir is one of the most effective new-generation antiretrovirals (until now in oral form) because of its minimal side-effects, high genetic barrier for resistance and long half-life.

**Different to controversial predecessors**

Unlike the controversial two failed microbicides (Ushercell cellulose sulphate-based vaginal gel and nonoxynol-9), where trial participants sero-converted, the tenofovir gel does not act in the vaginal lumen to kill the virus. Instead, the drug is rapidly absorbed into the tissue and blood cells where it prevents the virus from growing.

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(Ushercell cellulose sulphate-based vaginal gel and nonoxynol-9), where trial participants sero-converted, the tenofovir gel does not act in the vaginal lumen to kill the virus.

With a formulation of just 1% tenofovir in the gel, the researchers are aiming at further reducing the chances of resistance developing. One of the most exciting ‘bonus’ prospects is that even if a participant becomes infected, the drug may have a major impact in slowing the progression of the disease.

Says Henry Gabelnick, director of CONRAD, the international reproductive health foundation backing the project, ‘we’ve been trying to get a microbicide going since 1998 and we’re very enthusiastic about tenofovir’.

Adds Doug Taylor, Associate Director of BioStatistics for Family Health International, the other major international co-sponsor, ‘this product has a very good chance of success and the investigators are best suited to make that happen’.

While the final data on what went wrong with the Ushercell trial remained outstanding at the time of writing, researchers believe nonoxynol-9 harmed participants by causing lesions in the vagina.

Results on the recently completed Carraguard microbicide study (done at Medunsa, Durban and Cape Town) are expected in the next 4 months (Carraguard prevents the virus from attaching to cells in the vagina).

**Momentum ‘vital’ argues Karim**

Lead investigator and Director of the Centre for the AIDS Programme of Research in South Africa (Caprisa), Professor Salim Abdool Karim, said 3 microbicide trials had so far been stopped for futility and 2 for harm.

‘In reality we’ve had a series of disappointments, but to retain perspective you must remember that there’ve been even fewer trials for an HIV vaccine – and you don’t see them giving up! We have to keep a clear focus on our goal to find a woman-controlled HIV prevention method – I think that’s the challenge,’ he added.

The tenofovir trial is being conducted among 1 000 HIV-negative women attending the Ethekwini Clinical Research Site in Durban and the rural Malakathini clinic at Vulindlela, 90 km

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July 2007, Vol. 97, No. 7  SAMJ
Quarraisha Abdool Karim explained that, by necessity, they had to embrace large cohorts to identify women who had not used condoms or face turning it into an exercise in futility. The study would however take into account any additional benefit of the gel when used by participants in coital acts that involved condoms.

She said the gel had no contraceptive function and did not act against other STDs.

‘We need to prove that we have a product that can prevent HIV infection – further down the line there will be more stratification to determine if it has any benefit on STDs and pregnancy,’ she added.

Asked what happened if a participant fell pregnant, she said they would be advised to stop using the gel, referred to an antenatal clinic and then, depending on the outcome of the pregnancy, allowed to rejoin the trial.

The wellbeing of all participants was ‘paramount’, with condoms and frequent prevention counselling provided to all participants. Those who had unprotected sex with an infected partner during the study, or anyone who sero-converted during the follow-up period, had several choices. These included taking part in one of Caprisa’s long-term acute infection cohort studies that had excellent care, ARV and support systems or being referred to their preferred AIDS care provider.

‘People must always come first,’ she emphasised, adding that the study had rigorous scientific and ethical oversight and approval.

Cate Hankins, chief scientific advisor to UNAIDS, told Izindaba that, if successful, an ARV microbicide gel would dramatically increase the prevention/treatment options available to clinicians. Any efficacy would be highly significant, ‘especially in a situation where most women cannot negotiate the use of a condom and female condoms are too expensive’.

Chris Bateman