Still a long wait for approved HIV-protective gel

Gelling together for an AIDS breakthrough: Dr Quarraisha Abdool Karim and her husband, Professor Salim Abdool Karim, flank Dr Catherine Hankins, the Chief Scientific Officer at UNAIDS.

Picture: Chris Bateman

June 2013 – that's the 'realistic' date by which vulnerable South African women can expect to begin using an officially approved vaginal microbicide gel that would provide them with an unprecedented tool to protect themselves from HIV infection.

This is the belief of biochemist and epidemiologist, Dr Quarraisha Abdool Karim, who, together with her clinician and fellow epidemiologist husband, Professor Salim Abdool Karim, led the now world-renowned 'proof of concept' trial of tenofovir vaginal gel to prevent HIV infection in women.

In a 3-year study of 889 women in both rural and urban KwaZulu-Natal, they demonstrated a 39% reduction in HIV infection and a 51% reduction in genital herpes infection among women who used the gel (containing 1% of the antiretroviral (ARV), tenofovir).

'Given the dire need for prevention methods for women, we need to set some time lines … if we give ourselves 3 years from today [she was speaking in June this year] … we can have this product available to women in June 2013,' she asserted.

The trial results dominated the XVIIIth International AIDS Conference in Vienna, Austria, in July and led to a clamour for confirmatory studies and fast-tracking of the gel, of which the efficacy increases with use. (Women who used the gel in more than 80% of their sex acts had a 54% reduction in HIV infections.) Unlike other HIV prophylactic trials that use available tablets, the tenofovir gel was manufactured only for the trial, run by the Durban-based Centre for AIDS Programme Research in South Africa (CAPRISA), of which the research couple are directors.

Spotlight turns to government agency

Dr Abdool Karim said the South African 'road map' for registration would be laid out by the Medicines Control Council (MCC) after application by the Department of Science and Technology's Technology Innovation Agency (TIA), which holds the royalty-free licence. The TIA was set up as a public entity to enhance South Africa's capacity to translate a greater proportion of local research and development into commercial technology, products and services. As the licence holder of the gel, it is now responsible for all the steps that lead to registration as a drug product. Dr Karim's 'optimistic scenario' has the TIA making submissions to the MCC this month (September) and studying any subsequent recommendations on what additional data are needed for licensing of tenofovir gel by the MCC. 'Given the dire need for prevention methods for women, we need to set some time lines … if we give ourselves 3 years from today [she was speaking in June this year] … we can have this product available to women in June 2013,' she asserted.

This was 'a very generous timeline', given that it took her team 3 years to reach their findings. She added that it would no longer be as difficult (as it was for them) to find donors (for the required confirmatory studies). There was already a study in the field (the Microbicide Trials Network, VOICE, study comparing the efficacy of the tenofovir vaginal gel formulation with an oral equivalent, and adding the ARV Truvada (tenofovir and emtricitabine) to the mix).

The Karim pair is excited and almost overwhelmed by the wall-to-wall international media attention since their findings were released. The World Health Organization's reproductive health chief, Dr Tim Farley, is due in South Africa within days to hold urgent meetings with South African stakeholders to fast-track the research needed for licensure of the gel. 'The momentum is quite unique; everybody's rallying together and sharing things to make it happen; UN agencies are calling this the biggest development in the AIDS field they've ever seen,' she said.

Health Minister wants to 'fast-track' gel

Health Minister Dr Aaron Motsoaledi told the Vienna AIDS Conference that the government would consider fast tracking regulatory processes to get the gel into clinics 'as fast as possible', raising fears that short-cuts were imminent. However, Dr Karim said that in her discussions with Motsoaledi it became 'quite clear that he has no intention of circumventing any regulatory processes – he's articulated the autonomy of the MCC very well,' she added. The MCC's recent history is rife with political interference, especially at the height of the government's AIDS denialism, but a succession of health

ministers since the infamous late Dr Manto Tshabalala-Msimang has slowly rebuilt confidence in it.

The trial team observed no substantive safety concerns from use of the gel and no increase in risky behaviour by the women.

Karim said her team's next step was to understand why 38 women in the tenofovir arm of their double-blind study contracted HIV infections. The study participants had 'almost uniformly' asked her when this study of the gel would take place and expressed their availability to participate. They were very keen to know when the product would be available for general use.

The CAPRISA 004 trial saw 98 of the 889 participants become HIV positive – 38 out of 445 in the tenofovir gel group and 60 out of 444 in the placebo gel group. Out of the 434 women who tested negative for genital herpes at the start of the trial, 29 became infected in the tenofovir group and 58 in the placebo group. The women were advised to use the gel up to 12 hours before sex and soon after having sex for a maximum of 2 doses in 24 hours – a dosing strategy referred to as BAT24. Participants used the gel for a minimum of 1 year and a maximum of 2.5 years. The trial team observed no substantive safety concerns from use of the gel and no increase in risky behaviour by the women.

Researchers 'stunned' by study outcome

Professor Salim Abdool Karim, Pro Vice-Chancellor at the University of KwaZulu-Natal and CAPRISA Director, said he was 'stunned when the statistician came in and gave us the results. We just looked at each other in disbelief and couldn't speak for a while.' The couple and their team's work has been solidly grounded in population-based studies, with the alarming age and gender graph showing a sharp rise in infections for women from 15 years old versus men, for whom this trend occurs 8 years later. A full 60% of all new infections occur among women and girls.

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'As the epidemic matured we stayed focused on things that would have the biggest public health impact and rooted our work in what the epidemiological data told us,' Dr Abdool Karim said. Her husband added, 'This has the potential to alter the course of the HIV epidemic, especially in southern Africa where young women bear the brunt of this devastating disease.' A spokesperson for the TIA said her agency's role in product development was to ensure the MCC received all the information required to make a decision 'as soon as possible'. Once approved for use in South Africa, the TIA was responsible for ensuring that the tenofovir gel was manufactured and distributed affordably in Africa. 'We're committed to ensure women in Africa get access to the product a soon as it is approved by the regulatory authorities,' she added.

Chris Bateman

Bullish new medical measures to give more pilots wings

The Civil Aviation Authority (CAA) plane used for crashed investigations.

Pilots, cabin crew members and air traffic controllers, frustrated by outdated protocols for medical certification which lead to lengthy delays and unnecessary and expensive appeals, will by this September begin benefiting from a major systemic upgrade.

An over-reliance by South Africa's Civil Aviation Authority (CAA) on the under-resourced military for the verification of medical certificates plus the lack of a clear definition of 'acceptable medical risk' are now being addressed as top priorities.

A vital additional quality assurance instrument will be the newly formed 15-member Aeromedical Committee, established by the CAA late this April to