



CAPRISA

CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA



CAPRISA IS A UNAIDS COLLABORATING CENTRE FOR HIV PREVENTION RESEARCH

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Bobby Ramakant's informative overview of microbicide research published during the AIDS Vaccine 2012 conference is reproduced on page 2.

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TWAS Prize accolade for Quarraisha Abdool Karim

Professor Quarraisha Abdool Karim has been named by the Academy of Sciences for the Developing World (TWAS), as a recipient of the Academy's 2012 Prize for Medical Sciences "for her exceptional and distinguished contributions to HIV prevention and women's health".

The Academy made its announcement of the winners this week following its deliberations at the 23rd TWAS General Meeting held in Tianjin, China. The TWAS prizes are among the most prestigious scientific prizes recognizing scientific excellence in the developing world in the fields of agricultural sciences, biology, chemistry, earth sciences, engineering sciences, mathematics, physics and medical sciences. Prof Abdool Karim is one of two recipients of the 2012 TWAS Prize in Medical Sciences - the other recipient being Professor George Gao from the Beijing Institute of Microbiology for his work on influenza.

Following the news, Professor Abdool Karim said: "I am deeply humbled to be awarded the TWAS Prize in Medical Sciences. It has been an arduous but fascinating journey of scientific discovery."



Professor Quarraisha Abdool Karim

"Every bit of the effort was worth it, as the need for HIV prevention methods for women, especially in Africa, was critical and urgent. I hope my findings contribute to the dream of an AIDS-free generation and inspires today's aspiring young scientists in Africa to pursue their dreams."



Vaginal microbicide offers hope for partial anti-HIV protection

Bobby Ramakant discusses the status of gel trials and presents evidence why microbicides are a promising HIV-prevention option.

There are clear reasons why the vaginal microbicide research and development offers more hope in 2012. Vaginal microbicide research is going ahead and scientists are waiting for study results to tell them whether the CAPRISA-004 study results that reported 39% overall efficacy for women in July 2010 can be replicated in FACTS-001 study, and if so, is the evidence strong enough for licensure.

Microbicides are new products being developed vaginal or rectal use to protect against HIV and possibly other sexually transmitted infections. It could be produced in gel, cream, suppository, film, sponge or ring form.

Dr Salim S Abdool Karim, Director of Centre for the AIDS Program of Research in South Africa (CAPRISA) said to Citizen News Service (CNS) at AIDS Vaccine 2012 in Boston, that CAPRISA-004 study assessing the effectiveness and safety of a 1% vaginal gel formulation of tenofovir found reduced HIV acquisition by an estimated 39% overall, and by 54% in women with high gel adherence. The results of CAPRISA-004 study were announced at the XVIII International AIDS Conference in July 2010 amidst historic euphoria and excitement.

Licensure of this anti-HIV gel will first need replication of the CAPRISA-004 study results. The MTN-003 study, also known as VOICE (Vaginal and Oral Interventions to Control the Epidemic), evaluated the safety and effectiveness of ARV gel or tablet based approaches for preventing sexual transmission of HIV in women as well as determining which of these women are more likely to follow. The VOICE study had three arms: one, with women study participants applying daily 1% tenofovir gel; second, with study participants taking oral tenofovir and third, with study participants taking oral Truvada. The oral tenofovir and tenofovir gel arms of VOICE study were dropped following interim reviews of data that determined neither product was effective. This was a disappointment. Truvada arm continues to be evaluated and final results to be reported early 2013.

Dr Kenneth H Mayer, Medical Research Director and co-chair, The Fenway Institute; Director of HIV Prevention, Beth Israel Deaconess Hospital; and Visiting Professor, Harvard Medical School, explained to CNS: *"The difference between VOICE and CAPRISA-004 studies was that in CAPRISA study women used the gel right before and after sex, whereas in the VOICE study women were asked to use the gel everyday - so we don't know yet as one of its arms - oral Truvada (Tenofovir + FTC) medication arm - is still ongoing and it is not considered appropriate to share partial data, so all we know is that*



Left to right: Dr Morgane Rolland (US Military HIV Research Program), Prof Salim Abdool Karim (CAPRISA), and Dr Jared Baeten (University of Washington) at the AIDS Vaccine 2012 press conference in September 2012. (Photograph ©Rick Friedman)

in VOICE study the gel didn't work. There could be two competing hypotheses - it could be that gel taken every day causes more problems and taking less gel would be better or it could be that women were actually non-adherent and if they were not adherent they will not be able to show benefit even if the gel does work. So we have to learn more about what the VOICE study said to learn more about vaginal microbicides."

However future is not that bleak for 1% tenofovir gel which showed reasonable protection against HIV in CAPRISA-004. The FACTS-001 study is also testing the same 1% tenofovir gel in about 2200 women study participants who will use it before and after sex (coital use). The FACTS-001 was launched in October 2011 at nine clinical trial sites across South Africa. This study is jointly funded (50:50) by US and South African governments. So all fingers are crossed for the FACTS-001 study results and also to know more from the VOICE study data analysis.

"Concept of microbicide has now been proven. It took 20 years after the microbicide concept was first proposed and 18 years after the first human trials began, that the proof of concept finally came through in July 2010," said Dr Abdool Karim. A noted icon in the field of HIV prevention research and advocacy, Zena Stein, had first published a seminal article in 1989: *"HIV Prevention: The need for methods women can use"* that had set the ball rolling.

The good news is that researchers such as Dr Abdool Karim had met US FDA to discuss licensure of this 1% tenofovir gel after the 2010 study announcement. The US FDA had said that a positive result of VOICE and CAPRISA-004 studies together could be sufficient for licensure. So, when the VOICE

study disappointingly didn't show efficacy of this gel, the US FDA was asked what would now be required for licensure. The US FDA said that a confirmatory result from FACTS-001 study together with CAPRISA004 could be used for licensure. Results of FACTS-001 may come in 2014.

Fingers are crossed on the other microbicide research taking place and whether they enter large scale efficacy trials, and eventual introduction. MTN-020 study is testing a dapivirine vaginal ring in 3476 women study participants in Malawi, South Africa, Uganda, Zambia, and Zimbabwe; IPM-027 study is also testing dapivirine vaginal ring in 1650 women study participants in Malawi, Rwanda and South Africa; CAPRISA-008 study is testing the tenofovir gel in 700 women in South Africa (coital use); and the ongoing oral Truvada arm of VOICE continues in 5000 women study participants in Malawi, South Africa, Uganda and Zimbabwe.

Dr Abdool Karim, who has a long and distinguished history with HIV prevention research, shared five key challenges confronting microbicide research and development.

- *No validated surrogate marker or correlate of protection: can only assess efficacy through HIV endpoints*
- *No validated measure of products' biological activity (like vaccine immunogenicity) - Particular challenges in measuring drug concentrations*
- *Intensity of follow up and study procedures (monthly) - at times women study participants were required to come to the study clinics 22 times over 18 months*
- *Studies assess effectiveness and not efficacy (constraints of sub-optimal adherence in real world situation)*
- *Ethical challenges on what standard of prevention and care to provide since providing prevention reduces endpoints in trials.*

Vaginal microbicides are critically important for women who aren't able to negotiate the use of existing HIV prevention options with their male partners. Women and young girls share a disproportionate burden of HIV in many low and lower middle income countries. HIV prevention options such as microbicides will help expand the range of choices for women and men.

- Bobby Ramakant, Citizen News Service

Article first appeared online on 11 September 2012 and is reproduced by kind permission of the journalist.



Guest lecture by University of Sydney's Prof Adrian Mindel

CAPRISA recently hosted Adrian Mindel, Professor of Sexual Health Medicine, University of Sydney, who presented a guest lecture entitled "Herpes—hope or hype" at UKZN.

Comparing available data, Prof Mindel showed that the HSV-2 high risk groups in Australia include HIV +ve men who have sex with men, whereas in South Africa, sexually active women, commercial sex workers and HIV positive men were most likely to have been exposed to HSV-2. HSV-2 is also associated with a doubling in the risk of HIV acquisition. Inconsistent use of condoms, which only provided 30% protection even if used in 100% of sexual encounters, were amongst several other risk factors mentioned.

Most herpes transmission occurs from subclinical viral shedding from lesions and from intact skin and mucous membranes. Shedding can occur in short bursts or over longer periods, with or without symptoms.



Prof Adrian Mindel (right) is pictured with CAPRISA's Dr Nigel Garrett

HSV is treated with antiviral drugs (acyclovir, valaciclovir, famciclovir, or helicase-primase inhibitors). Control and management of herpes is supported by education, counselling, abstinence, or no sexual intercourse during HSV recurrences. Condoms and male circumcision also provide partial protection.

Whilst there is still hope for an HSV vaccine, clinical trials to date have not yielded significant results.

Award-winning US reporter visits CAPRISA

Award-winning San Diego-based science and medical correspondent, Jon Cohen, visited CAPRISA and other Durban-facilities in September 2012, for a special report on TB. The feature is expected to be published in the prestigious journal, Science, in early 2013.



Science's Jon Cohen (left) with Prof Salim Abdool Karim at CAPRISA's offices in Durban

Young scientists at Summer Davos

This year, The World Economic Forum invited CAPRISA's ethics specialist, Prof Jerome Singh to attend Summer DAVOS, in Tianjin, China, in September 2012. Jerome was part of a group of 40 young scientists from around the world, who participated in this high-profile meeting of leading businesspeople and politicians.

Jerome reported that discussions concerning the need for new recruitment models to attract a new generation of young scientists in order to ensure continuous innovation were amongst the many highlights of the meeting.

Focused on women's health

Maynolia Naidoo is a 5th-year medical student and has been a CAPRISA research trainee since her second year at UKZN. The recent Students' Clinical Conference held at UKZN Medical School provided Maynolia with the opportunity to share her research conducted at CAPRISA on the prevalence and incidence of genital tract abnormalities in HIV/TB co-infected women initiating highly active anti-retroviral therapy (HAART). With a passion for women's health, Maynolia intends to specialise in obstetrics and gynaecology after graduation.

"My future plans are to present this research study at an international conference and to pursue research involving human papilloma virus and other sexually transmitted infections associated with cervical lesions and cervical carcinoma," says Maynolia.



Maynolia Naidoo at the Student's Clinical Conference held in Durban in August 2012



Jerome Singh, pictured in front third from left, with other young scientists at Summer Davos.



Research papers published in 2012

- 35* Sokal D, **Abdool Karim Q**, Sibeko S, Yende-Zuma N, Mansoor LE, Baxter C, Grobler A, Frohlich J, Kharsany A, Mlisana K, Maarshalk S, **Abdool Karim SS**. Safety of Tenofovir Gel, a Vaginal Microbicide, in South African Women: Results of the CAPRISA 004 Trial. *Antiviral Therapy* 2012; DOI: 10.3851/IMP2311. [Epub ahead of print]
- 36 **Naranbhai V**, Altfeld M, **Abdool Karim Q**, Ndung'u T, **Abdool Karim SS**, Carr WH; on behalf of the CAPRISA 004 TRAPS Team. Natural Killer cell function in women at high risk for HIV acquisition: Insights from the CAPRISA 004 microbicide trial. *AIDS* 2012; 26(14):1745-1753
- 37 Chirenje ZM, Masse BR, Maslankowski LA, Ramjee G, Coletti AS, Tembo TN, Magure TM, Soto-Torres L, Kelly C, Hillier S, **Abdool Karim S**. Utility of colposcopy in a phase 2 portion of a microbicide clinical trial of BufferGel and 0.5% PRO 2000 Gel. *Journal of the International AIDS Society* 2012, 15:17376. Doi:10.7448/IAS.15.2.17376
- 38 **Ntale R**, **Chopera D**, Ngandu N, Assis de Rosa D, Mlotshwa M, **Werner L**, Woodman Z, **Mlisana K**, **Abdool Karim S**, **Gray C**, **Williamson C**, and the CAPRISA 002 Study Team. Temporal association of HLA-B*81:01 and B*39:10 mediated HIV-1 p24 sequence evolution with disease progression. *Journal of Virology* 2012; Aug 29. [Epub ahead of print]
- 39 **Naidoo K**, **Yende-Zuma N**, **Padayatchi N**, **Naidoo K**, **Jitho N**, **Nair G**, **Bamber S**, **Gengiah S**, El-Sadr W, Friedland G, **Abdool Karim SS** The Immune Reconstitution Inflammatory Syndrome After Antiretroviral Therapy Initiation in Patients With Tuberculosis: Findings From the SAPiT Trial. *Annals of Internal Medicine*. 2012;157:313-324
- 40 Dezzutti CS, Richardson BA, Marrazzo JM, Tugetman J, Ramjee G, Taha T, Chirenje ZM, **Abdool Karim SS**, Hillier SL, Herold BC, on behalf of the MTN Biomedical Sciences Working Group and the HPTN 035 Protocol Team. Mucosal E. coli bactericidal activity and immune mediators are associated with HIV-1 seroconversion in women participating in the HPTN 035 trial. *Journal of Infectious Disease* 2012; Sep 10. [Epub ahead of print]

* continued from previous issue



Scientific Reviews

Abstracts submitted for review		Manuscripts submitted for review		Ancillary studies submitted for review	
Total#	Cumulative [^]	Total#	Cumulative [^]	Total#	Cumulative [^]
0	279	1	220	1	37

for month, [^] since committee initiation

Conference & Workshop Reminders

Conference	Dates	Deadlines		Website
		Abstracts	Registration	
6th Annual Workshop on Advanced Clinical Care (AWACC) – AIDS Durban, South Africa	4-5 Oct 2012	N/A	23 Sept 2012	http://www.mccord.org.za/cause_data/images/1285/AWACC_2011_Registration_Form.pdf
International Union against Sexually Transmitted Infections World Congress 2012 Melbourne, Australia	15-17 Oct 2012	8 June 2012	4 Oct 2012	www.iusti2012.com
7th Southern African HIV/TB Drug Resistance & Treatment Monitoring Workshop Cape Town, South Africa	28-29 Nov 2012	N/A	1 Oct 2012	www.bioafrica.net/workshops/7th-saturnresistanceworkshop.html
8th Federation of African Immunological Societies Conference Durban, South Africa	2-5 Dec 2012	19 Sep 2012	From 2 Sep 2012	www.faisconference2012.com

CAPRISA is an official research institute of the University of KwaZulu-Natal and Columbia University.

CAPRISA was established in 2002 through a CIPRA grant from the NIH, as a multi-institutional collaboration, incorporated as an independent non-profit AIDS Research Organization

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